Rat Small Intestinal Transit Is Independent of Glucose Consumption in the Strenuous Exercise

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Abstract

The present study was to determine the effect of strenuous exercise on glucose utilization, lactate accumulation and small intestinal transit (SIT). In strenuous exercises, rats would be put on the runway of a moving treadmill for a one-hour compulsive running. Rats first performed running treadmill for 45 min. After orogastric feeding of radiochromium marker, they resumed running for additional 15 min until sacrifice to measure SIT. Saline and various doses of glucose and lactate were infused through previously placed jugular vein during the whole procedure. Blood was finally obtained to measure plasma glucose and lactate levels. Saline infusion had no effect on running rat SIT during strenuous exercise, but plasma glucose level was significantly lowered ($P < 0.01$). Infusion of various doses of glucose did not alter SIT during strenuous exercise; however, the initially lowered plasma glucose was restored even to a hyperglycemic state. Meanwhile, strenuous running markedly increased plasma lactate level, irrespectively of saline or glucose infusion ($P < 0.01$). Lactate infusion did not change rat SIT obtained on the quiet runways. In conclusion, rat SIT remained unchanged in the strenuous exercise although obvious hypoglycemia and higher plasma lactate level did exist. Glucose utilization and lactate accumulation after the strenuous exercise may not directly mediate small intestinal motility.

Key Words: gastrointestinal motility, glucose, lactate, running, small intestinal transit

Introduction

Recreational sports are usually encouraged for health issue since this kind of physical activities diminishes lean body tissues, elevates mood and also provides protection against breast, prostate and colon cancers (20, 28). On the other hand, moderately to severely sustained exercise sometimes results in adverse gastrointestinal symptoms in terms of anorexia, abdominal cramping, urgent defecation, nausea, retching, and bloody stool (11, 23, 26). Exercise effects including pounding on visceral organs, increased parasympathetic and sympathetic tones, gut ischemia, increased releasing gut / adrenergic peptides and cortisones, and energy exhaustion have been suggested responsible for these exercise-related gastrointestinal symptoms (11-13, 16, 27, 30). With regard to small intestinal transit (SIT), reports of exercise effect on SIT are discordant, either slow (15~17) or unchanged (14, 24, 30). Since rapid energy exhaustion occurs during the moderate to severe exercise, perhaps glucose supplement is unable to meet the rapid energy expenditure leading to lactate accumulation *via* epinephrine stimulation (2, 29). It is why measured blood lactate level may represent the exercise performance, whereas restrictive actions are recommended to undertake if its blood level exceeds expectation (1). To the best of our knowledge, no study has ever addressed the effect of exercise on SIT

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and its link to glucose consumption and lactate accumulation. The purpose of present study was to determine the relationships between glucose utilization, lactate accumulation, and SIT during a strenuous exercise.

Materials and Methods

Animal Preparation and Running Design

Adult Sprague-Dawley male rats, 3-4 months old and 300-400 g in body weight, were obtained from the Animal Room of National Yang-Ming University. All studied animals were housed under the controlled conditions of light (06:00-20:00), humidity and temperature (22 ± 1°C). Standard laboratory chow and water were available *ad libitum*. Rat running was conducted on a four-runway exercise treadmill (EXER-4R, Columbus Inst., Columbus, OH, USA). The runways are kept in a horizontal plane with a forward running speed of 20 m/min. Since an electrode is placed at the rear of runways, the rats must run forward at least following the runway moving speed; otherwise, a light electrical shock would be elicited when the rats are too lazy to touch the electrode (6). Studied rats did not receive previous run training. After an overnight fast, the rats were respectively put on one of the moving runways for 45-min continuous running. Then the running rats were removed outside and an orogastric catheter was temporarily placed to feed radiochromium motility marker. The rats were put back on the moving runways for additional 15 min until sacrifice to measure their SIT. Sham running rats were those on the quiet runways throughout the whole study period, while their feeding of motility marker remained the same.

Effect of Glucose Infusion on Rat Small Intestinal Transit after Running

Studied rats were placed a right jugular vein catheter using a silastic tubing connection (PE-50, OD: 0.965 mm, ID: 0.58 mm, Clay Adams, Parsippany, NJ, USA) *via* pentobarbital anesthesia (30 mg/kg, i.p., TCI, Tokyo, Japan). On the following day, sham-running rats (n = 8) received saline infusion in the speed of 2 ml/h via a peristaltic pump (Gilson, minipuls-2, France). After 45-min infusion, the motility marker was fed while the saline infusion was not interrupted. Then they kept quiet on the runways for additional 15 min until sacrifice. Another group of rats (n = 8) received similar saline infusion but ran on the moving runways, feeding motility markers and resumed running until sacrifice. The third group of running rats, however, received glucose infusion treatment (2 mg/kg/min, n = 8; 8 mg/kg/min, n = 8; and 16 mg/kg/min, n = 8) as those infused with saline and also run on the moving runways until sacrifice.

Effects of Lactate Infusion on Small Intestinal Transit of Rats without Running

One day before the motility study, a new group of 24 rats received similar right jugular vein catheterization. On the following day, they were divided into 3 subgroups to receive various infusions *via* a peristaltic pump with a speed of 2 ml/h including saline (n = 8), lactate of 7 mg/kg/min (n = 8), and lactate of 14 mg/kg/min (n = 8), respectively. Initially, the infusing rats were put on the quiet runways. At the 45th min of the infusion, the motility marker was fed while the infusion was not interrupted, and then they were put back on the quiet runways again for additional 15 min until sacrifice.

Measured Small Intestinal Transit, Plasma Glucose and Lactate Levels

SIT was measured based on the propulsion of fed non-absorbable marker within gut. Briefly, the feeding procedure was achieved with a temporarily placed orogastric catheter (ID: 1.67 mm, OD: 2.42 mm, PE-205, Clay-Adams, Parsippany, NJ, USA). The nutrient-free motility marker was $Na^{51}CrO_4$ (Dupont, NEN Research Products, Boston, MA, USA) with radioactivity of 0.5 μCi/ml, while the feeding amount of each animal was adjusted to 3 ml/kg. After the successful feeding, studied rats were immediately killed with a guillotine 15 min later, and the entire small intestine was carefully removed outside. Ten equally divided small intestinal segments were separated with a bipolar coagulator while both ends of each intestinal segment were sealed to avoid the leakage of test marker. A gammacounter (10/880 Plus, ICN Biomedicals, Costa Mesa, CA, USA) measured the radioactivities of all SI segments for one min. The geometric center (GC) of radiochromium traveled within small intestine is computed from the formula (5, 18, 21):

Geometric center = Σ Radioactivity of segment / Total intestinal radioactivity X Segment number

The fresh plasma glucose level was measured using a glucose analyzer (23-A, Yellow Springs Inst. Co., Yellow Springs, OH, USA), and the plasma lactate level was measured based on YSI STAT analyzer (YSI 2300 STAT Plus, Yellow Springs).

Statistics

All values were expressed as mean ± SE. The numerical data were analyzed using either Student's *t*-test or one-way analysis of variance (ANOVA) with Dunnett's post test. A *P* value less than 0.05 was considered significant.

Table 1. Measured geometric center (GC) represented small intestinal transits and plasma glucose levels of rats having received fluid infusion

Type of exercise and fluid Infusion (study no.)	GC, segment	Plasma glucose level, mg/dl
Rest plus saline (n = 8)	2.91 ±0.18	101.9 ±5.83
Running plus saline (n = 8)	3.27 ±0.46	52.4 ±9.3*
Running plus glucose 2 mg/kg/min (n = 8)	2.79 ±0.27	92.3 ±18.4
Running plus glucose 8 mg/kg/min (n = 8)	2.56 ±0.39	105.8 ±16.3
Running plus glucose 16 mg/kg/min (n = 8)	2.73 ±0.45	136.3 ±33.8@

Results are mean ± SE; *: *vs.* rest plus saline, $P < 0.01$; @ *vs.* rest plus saline, $P < 0.05$

Table 2. Measured geometric center (GC) represented small intestinal transits and plasma lactate levels of sham running rats having received one-hour lactate infusion

Type of infusion	GC, segment	Plasma lactate level, mM	
		Basal	Final
Saline (n = 8)	2.81 ± 0.33	3.28 ± 0.29	4.53 ± 0.49
Lactate, 7 mg/kg/min (n = 8)	2.51 ± 0.31	3.17 ± 0.57	4.94 ± 0.30@
Lactate, 14 mg/kg/min (n = 8)	2.76 ± 0.29	3.43 ± 0.44	5.96 ± 0.48#

Results are mean ± SE; Comparison with category, basal *vs.* final: @, $P < 0.05$; #, $P < 0.01$

Results

The measured GC to represent SIT of rats on the quiet runway of treadmill was 2.91 ± 0.18. This value served as the sham exercise to assess running effect on SIT of studied rats. Table 1 illustrates the effects of various infusions on both GC and plasma glucose level when the rats were conducted on the strenuous one-hour running. Saline infusion had no effect to change GC at the end of running but this kind of strenuous running diminished rat plasma glucose level ($P < 0.01$). Using various doses of glucose infusion, the measured GCs of running rats remained unchanged, whereas their suppressed plasma glucose level gradually restored in a dose dependent manner even corrected to hyperglycemia ($P < 0.05$). Figure 1 depicts the simultaneously measured plasma lactate levels of sham running and fluid infused rats. Strenuous running markedly increased plasma lactate level after the saline and glucose infusion ($P < 0.01$). Besides, glucose infusion had no additional effect to change plasma lactate level, compared with their counterparts having received saline infusion after the running course. Table 2 denotes the effect of lactate infusion on GC and plasma lactate level when the rats only received one-hour sham running. Various doses of lactate infusion did not change GC-represented SIT, whereas their plasma lactate levels showed increase in a dose dependent manner.

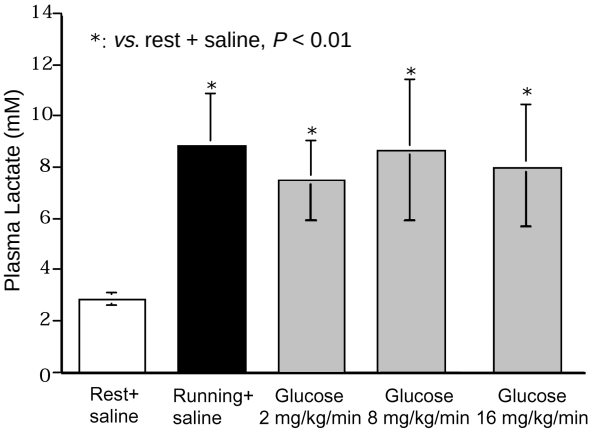

Fig. 1 Measured plasma lactate levels of rats at the end of one-hour rest or running plus various fluid infusions (□: rest plus saline infusion, ■: running plus saline infusion, ▨: running plus glucose infusion). No matter of saline or glucose infusion, one-hour running effectively elevated plasma lactate level ($P < 0.01$). The bars above columns are SE.

Discussion

The present study mainly demonstrated that rat SIT did not change with one-hour strenuous treadmill running, while plasma lactate level was elevated immediately after exercise. It means that such kind of treadmill running is at least moderate to severe exereise for the experimental animals although we did not measure their oxygen consumption (1). Among the human motility studies, measured orocecal transit time (OCTT) is usually employed as a noninvasive method to assess exercise effect on SIT. Some studies conclude no change in OCTT with exercise in patients (10), untrained subjects (4), and trained athletes (14, 24, 25, 30). Also, reports disclose increased OCTT to represent delayed SIT in women with mild exercise (16), non-athlete young men with mild exercise (15) and young adults with one-hour walking (17). It is likely that the differences in the studied subjects, exercise modes or methodologies in measuring SIT account for these discrepancies. Based on the observation of our study conducted on untrained rats, we suggest that the strenuous exercise may not directly mediate SIT.

Exercise or running is reported to have an apparent pounding effect on internal organs (22). It can be predicted that visceral pounding results in gut dysmotility. Surprisingly, our study found unchanged SIT in moderately to severely exercised rats as well as others obtained in humans. Perhaps exercise-related pounding has no definite impact on SIT although small intestine is the free organ within abdominal cavity. During the sub-maximal exercise, blood flow to gut is usually reduced particularly for the untrained subjects, while the reduced blood flow has a chance to delay SIT (7, 8). Our study found similar SIT in running rats despite of moderate to severe exercise. It is likely that other physiological events such as released peptides/vasodilators, and activated autonomic and cardiovascular activities attenuate the gut ischemia in strenuous exercise (19, 27), thus the expected small intestinal motor disturbance does not exist.

Glucose oxidation to produce adenosine triphosphate is required for the muscle contraction (13). During the emergent and sustained energy supplement such as moderate to severe exercise, the orders of supplemental fuel sources have been plasma glucose, muscle glycogen, liver glycogen, and fat (31). However, stored glucose is quickly consumed in the sustained exercise and other energy sources are additionally needed to meet this kind of physiological expenditure. It is estimated that almost half of energy expenditure during running is contributed by the anaerobic glycolysis (3). Oxygen delivery and removal of carbon dioxide are essential in the sustained exercise, thus lack of adequate oxygen supply leads to intramuscular lactate production (13). It means that lactate derived from muscle or liver becomes the predominant fuel supplement to meet additional physiological requirement. Lactate has been an important intermediate between carbohydrate storage and metabolic products of water and carbon dioxide serving as a gluconeogenic precursor during the sustained exercise (2). Our observations of elevated plasma lactate level and suppressed plasma glucose level illustrate the rapid energy exhaustion in these rats having received strenuous running. To the best of our knowledge, no studies have ever addressed whether lactate has a direct influence on SIT. This was why we conducted lactate infusion for the resting rats in examining its effect on SIT. Our study of lactate infusion was successful because markedly elevated plasma lactate was found. In contrast, SIT remained unchanged after lactate infusion. Accordingly, we suggest that the elevated plasma lactate level after a strenuous exercise does not affect SIT.

Blood glucose has been the first energy source to supply an urgent expenditure (13), our observation of diminished plasma glucose level in untrained rats following one hour running confirmed this rapid energy exhaustion, whereas glucose infusion during their running effectively corrected the exercise-related hypoglycemia. Interestingly, cyclists also have lower blood glucose level immediately after one-hour exercise, and their glucose level is restored after glucose infusion (3). It has been suggested that diminished splanchnic blood flow is accounted for this kind of decreased glucose uptake among the cycling exercise (30). Blood glucose level is closely linked to the vagal-cholinergic system. For example, induced hyperglycemia *via* glucose clamp may partially blunt the gut vagal tone leading to impaired gut motor functions including SIT (9). Our previous animal study indicated that hyperglycemia in early streptozotocin-induced diabetic rats delayed SIT. This delay was corrected *via* insulin controlling blood glucose level. Besides, even an over-correction to hypoglycemia led to enhanced SIT (5). This interactive adjustment of blood glucose level and gut motility may be important in the regulation of nutrient assimilation. Since the present study did not find glucose infusion disturbed SIT after rat running, it means that neither hypoglycemia nor higher plasma lactate can change SIT after strenuous running.

In conclusion, SIT of untrained rats is not affected by the strenuous exercise resulting in hypoglycemia and higher plasma lactate level. Glucose utilization and lactate accumulation during the strenuous running may not directly mediate SI motility.

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