Sodium bicarbonate treatment prevents gastric emptying delay caused by acute exercise in awake rats

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THE WORLD HEALTH ORGANIZATION identified physical inactivity as the fourth leading risk factor for global mortality. Such sedentary behavior is increasing worldwide, thus increasing the prevalence of noncommunicable diseases and compromising the general health of the population (5, 15). Physical activity is frequently prescribed for patients with gut dysmotility to improve the patients’ complaints and symptoms related to bloating and constipation (10). However, isotonic (dynamic), and resistance (static and dynamic) exercise may trigger potential hazards for the gastrointestinal tract, such as bloody stool, diarrhea, vomiting, and gastroesophageal reflux, especially after very prolonged, strenuous exercise that may involve heat stress (3, 32).

Physical fitness is achieved via aerobic and anaerobic exercise. Aerobic exercise is characterized by activities with a low intensity but long duration, with sustained elevation of heart rate. In contrast, anaerobic exercise is characterized by intense muscular recruitment over a short period of time with lactic acid accumulation in the blood, a metabolite that may establish acidemia and muscle fatigue (29, 34). The effects of physical exercise on human gut motor behavior are diverse. Studies have reported increases, decreases, or no changes in gastric emptying (GE) rate (3). Exercise with a mild to moderate intensity either enhances or does not affect GE, while an intensity that is 65–80% of the maximal aerobic capacity may delay the GE rate (17). The discrepancy of these findings may be explained by different experimental conditions, such as physical conditioning, exercise protocols, nature of the test meal, and duration of the postprandial interval for GE analysis. In sedentary awake rats, gavage with a 0.5 M NH4Cl solution causes metabolic acidosis and delays the GE of a liquid test meal (1). Nonetheless, the interaction between high-intensity short-term exercise, acidemia, and GE rate remains unclear. In this work, we studied the relationship among these factors, testing the hypothesis that acute exercise alters the acid-base equilibrium, causing gastric dysmotility in rats.

METHODS

Animals. Male Wistar rats (230–280 g) were obtained from the animal house center of the Federal University of Ceará and kept under conditions of stable temperature (22 ± 1°C) so that

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followed by a drying procedure that used an absorbent towel and blow dryer. The rats were then returned to their cages. One day after the last swimming session, all of the rats were anesthetized with tribromoethanol (250 mg/kg ip) for cannulation of the right femoral artery and right jugular vein, as described by Harms and Ojeda (20). They were then kept individually in Bollman’s cages and fasted for 18 h with free access to an oral rehydration solution composed of 75 mM Na\(^+\), 65 mM Cl\(^-\), 20 mM K\(^+\), 75 mM glucose, and 10 mM citrate (41).

After 24 h, the rats were subjected (acute exercise group) or not subjected (sedentary group) for 15 min to another swim session, but this time supporting a load equivalent to 5% of their body weight. The loading was achieved by tying fishing sinker weights with elastic string around the rats’ chest. The sedentary rats remained in the swimming pool for 15 min without the additional load, and the cylindrical tank was nearly empty, containing water at a depth of only 5 cm.

All of the rats were consecutively subjected to a drying procedure, hemodynamic monitoring, and gastrointestinal motility assessment. Exercised rats were allocated to groups defined by different resting intervals (i.e., 0, 10, or 20 min). Immediately after each resting time, the rats were gavage fed a liquid test meal that consisted of 1.5 ml of 0.5 mg/ml phenol red in a 5% glucose solution. Sedentary animals were allowed to rest for 10 min and then gavage fed. All of the rats were killed 10 min postprandially by an overdose of thiopental (50 mg/kg iv). Mean arterial pressure (MAP; in mmHg) and heart rate (HR; in beats/min) were continuously monitored by connecting the femoral catheter to a pressure transducer coupled to a digital acquisition system (PowerLab/8SP, AD Instruments, Bella Vista, NSW, Australia; see Figs. 1 and 2).

Fractional gastric dye recovery was assayed according to Reynell and Spray (36), which was previously adapted by our laboratory (41). By means of laparotomy, the pylorus, cardia, and terminal ileum were quickly clamped. The gut was carefully removed, stretched along a meter stick on a plain tabletop, and divided into consecutive segments: stomach and proximal (40%), middle (30%), and distal (30%) small intestine. The volume of each segment was evaluated by adding it to a graduated cylinder that contained 100 ml of 0.1 N NaOH solution. The segments were then cut and homogenized with a mixer for 30 s. The suspension was allowed to settle for 20 min, and 10 ml of the supernatant were centrifuged for 10 min at 2,800 rotations/min. Proteins in 5 ml of the homogenate were precipitated with 0.5 ml of 20% trichloroacetic acid (wt/vol), and the solution was centrifuged again for 20 min. Finally, 3 ml of the supernatant were added to 4 ml of 0.5 N NaOH. All of the samples were spectrophotometrically read at 560 nm and are expressed as the optical density (OD). In each experiment, a standard dilution curve was obtained by plotting the dye range of the concentrations against the OD of 0.1 N NaOH solution (i.e., the blank). The linear coefficient (α) of the dilution curve defined the solution concentration (C = OD) and the amount of phenol red (m) recovered from each segment (m = C × volume). Fractional dye gastric recovery (in %) was calculated according to the following equation:

\[
\text{Gastric dye retention (\%)} = \frac{\text{amount of phenol red recovered in stomach}}{\text{total amount of phenol red recovered from all segments}} \times 100
\]

All of the subgroups listed below had a resting interval of 10 min and postprandial period of 10 min. To exclude the possible influence of gastric acid secretion on the effects of acute exercise on gastric dye recovery assessment, a separate group of rats received a single injection (0.1 mg/kg) of omeprazole (20 mg/kg ip) or its respective vehicle (saline) 30 min before the acute exercise testing. To verify the influence of acidemia on acute exercise-induced GE delay, we studied two additional groups of rats, one exercised and another sedentary, previously treated by gavage with NaHCO\(_3\) (500 mg/kg) solution (1 ml/100 g) 40 min before the acute exercise testing (4). Other rats were randomly subjected or not subjected (sham subgroup) to pretreatment with 4% NH\(_4\)Cl in drinking water (tap water) for 72 h. Afterward, they all underwent gastrointestinal motility assessment, as described above.

Fig. 1. Timeline of the experimental protocol used to compare the gastric retention in sedentary and exercised rats.
**Small-intestine transit assessment.** To assess the effect of acute exercise on small-intestine transit, another group of rats underwent a different protocol. One day after the last free-swimming session, they were anesthetized with triethylmalonate for the insertion (via a fistula at the stomach wall) of a silicone cannula (0.3 mm outer diameter) that was advanced into the gut lumen 1 cm distally to the pylorus. It was fixed to the stomach fundus by a purse-string suture, with its free end fixed at the dorsal region. After 24 h, they were randomly subjected or not subjected (sedentary subgroup) to another swimming session for 15 min, but this time against a load equivalent to 5% of their body weight (acute exercise subgroup). They were then gavage fed a test meal (1.0 ml) via the duodenal cannula and killed 10 min later. After gut exeresis, the stomach and first 1 cm of the duodenum that contained the tip of the cannula comprised segment 1. Obstructive ligatures were performed to obtain five consecutive segments of the small intestine (~20 cm long). Each segment was homogenized, and its dye content was determined spectrophotometrically, as described above. Fractional marker retention was calculated for each gut segment as the ratio between the amount obtained in it and the sum of the amounts of all of the segments, including the gastroduodenal segment. The value obtained for each segment was then multiplied by its respective number and summed to calculate the geometric center of the marker distribution throughout the gut, as previously reported (38).

**Gastric tonus assessment.** To verify the effect of acute exercise on gastric tonus, another group of rats was studied using a barostatic system. After the sedentary or acute exercise protocol, they were euthanized by cervical dislocation. After laparotomy, the gastroduodenal segment was carefully removed and immersed in a Petri dish that contained modified Tyrode solution with the following composition: 136 mM NaCl, 5 mM KCl, 0.98 mM MgCl₂, 2 mM CaCl₂, 0.36 mM NaH₂PO₄, 11.9 mM NaHCO₃, and 5.5 mM glucose. After dissection, the stomach was cut via the lesser curvature and folded to obtain 1-cm-long strips taken from the fundus or pylorus. The strips were connected by a silk thread to a force transducer (MLT0201, AD Instruments, Bella Vista, NSW, Australia) with an initial resting muscle tension of 1 g and suspended longitudinally in a 5-ml organ bath that contained the Tyrode solution, which was maintained at 37°C, pH 7.4, and continuously bubbled with a mixture of 5% CO₂ in O₂. Isometric muscle tension was continuously recorded using a data acquisition system (LabChart). A 1-h interval was allowed for equilibration. Segments without spontaneous activity were discarded. The strips were then subjected to increasing concentrations of carbachol (0.001–30 μM) to construct a concentration-effect curve, which was obtained from the asymptotic value recorded at each concentration. At the end of the study, each tissue was maintained for 2 h at 80°C to express the force data relative to the dry mass of the tissue.

**Blood analysis.** At the end of sham and exercise testing, we obtained a drop of blood from the rats’ tails for lactic acid concentration measurements using an automatic analyzer (Accutrend Plus, Roche Diagnostics, Mannheim, Germany). At the end of the study, we also collected a sample of blood from the retro-orbital plexus to spectrophotometrically determine plasma creatine kinase (CK; Labtest kits, Ribeirão Preto, Brazil). Other 3-ml sample of arterial blood was used to measure pH, Pco₂, Po₂, base excess, O₂ saturation, and bicarbonate concentration ([HCO₃⁻]) using a gasometric analyzer (Cobas b 121, Roche Diagnostics, Mannheim, Germany).

**Statistical analysis.** All of the data are expressed as means ± SD. Each subgroup consisted of 8–10 rats. Differences in gastric retention values were assessed by one-way ANOVA, followed by Tukey’s
multiple-comparison test. Intragroup differences in hemodynamic indexes between the basal period and subsequent intervals were compared using repeated-measures ANOVA, followed by Tukey’s test. Values of $P < 0.05$ were considered statistically significant. Statistical analysis between two groups was made using Student’s $t$-test for unpaired data.

**RESULTS**

As shown in Table 1, top, the load imposed by acute exercise testing increased blood lactate and CK levels ($P < 0.05$) compared with the control values observed in sedentary rats. However, these changes were transient, and lactate and CK levels returned to baseline values at 30 min postexercise. Acute exercise testing decreased ($P < 0.05$) blood pH compared with the sedentary group. Other biochemical indexes confirmed a scenario compatible with plain acidemia of the milieu intérieur. For example, the exercise group had lower values ($P < 0.05$) of base excess and $\left[ \text{HCO}_3^- \right]$ compared with the sedentary group. No significant difference in $\text{PCO}_2$, $\text{PO}_2$, or $\text{O}_2$ saturation values was found between the exercise and sedentary rats ($P > 0.05$).

Table 1, bottom, shows the impact of acute exercise testing on the hemodynamic indexes. Compared with the respective values of sedentary rats, acute exercise testing increased MAP and HR levels in the acute exercise group ($P < 0.05$). However, such a response was transient, and the MAP and HR values returned to baseline levels 30 min postexercise.

Figure 3 shows the effect of acute exercise testing on the GE rate of a liquid test meal in awake rats. Compared with the respective values of the sedentary control group, fractional gastric retention increased ($P < 0.05$) in animals subjected to acute exercise at time 0 and 10 min postexercise time points (41.4 ± 5.7 vs. 72.8 ± 5.9 and 66.8 ± 8.5%, respectively). This phenomenon faded as the resting interval increased, and no significant difference in fractional gastric retention values was found between the control rats and exercised rats with the 20-min resting time (41.4 ± 5.7 vs. 38.2 ± 3.7% in the control and exercise groups).

The GE delay caused by acute exercise testing appeared to be unrelated to a putative effect on gastric acid secretion.

![Fig. 3. Comparison of fractional (%) gastric dye retention in awake rats in the sedentary (open bar) and acute exercise (solid bars) groups. Rats previously trained to freely swim in a thermoneutral tank for 5 days were subjected or not subjected (sedentary) 2 days later to another swimming session for 15 min, but this time against a load equivalent to 5% of body weight (acute exercise). They were then gavage fed (1.5 ml) with a test meal (phenol red in glucose solution) and euthanized 10 min later to spectrophotometrically determine gastric dye recovery. Each subgroup consisted of 6–9 rats. Values are means ± SD. *$P < 0.05$ (ANOVA followed by Tukey’s test). T0, T10, T20: time 0, 10, and 20 min, respectively.](http://jap.physiology.org/)

![Fig. 4](http://jap.physiology.org/)

Omeprazole pretreatment did not alter the increase in gastric dye recovery in response to high-intensity exercise (47.9 ± 10.2 vs. 70.0 ± 10.9% in the control and exercise groups; $P < 0.05$; data not shown).

Figure 4A shows a significant ($P < 0.001$) positive correlation ($r = 0.963$) between the individual values of plasma lactate and the respective fractional gastric retention in rats subjected to acute exercise testing. Such a relationship was absent in rats in the sedentary group (data not shown). Moreover, the GE delay caused by high-intensity exercise was clearly prevented when NaHCO$_3$ was administered 40 min before acute exercise testing. Figure 4B shows no significant difference in the fractional gastric retention values in NaHCO$_3$-pretreated rats subjected to either the sedentary (control) or exercise protocols (39.5 ± 15.3 vs. 40.3 ± 10.2% in the control and exercise groups). Table 2 shows that NaHCO$_3$ treatment also prevented the acid-base imbalance after exercise, although the lactate levels in the exercise group were higher ($P < 0.05$) than the respective values in sedentary rats. Figure 5 shows the effects of metabolic acidosis on the present phenomenon. The addition of NH$_4$Cl to the tap water decreased ($P < 0.05$) blood pH (Fig. 5A), shifting the status of sedentary and vehicle-treated rats to an acidic condition (7.32 ± 0.02 vs. 7.14 ± 0.17 and 7.29 ± 0.04 vs. 7.17 ± 0.07, respectively). Furthermore, NH$_4$Cl also decreased ($P < 0.05$) $\left[ \text{HCO}_3^- \right]$ values (Fig. 5B) in sedentary and vehicle-treated rats (22.6 ± 1.03 vs. 17.7 ± 5.53 and 23.5 ± 1.4 vs. 16.2 ± 2.4 mmol/l, respectively). With regard to the GE rate, Fig. 5C shows that NH$_4$Cl administration increased ($P < 0.05$) fractional gastric retention compared with the respective values in vehicle-treated rats, similar to what occurred in the acute exercise group compared with the sedentary group (41.4 ± 5.7 vs. 66.8 ± 8.5 and 37.8 ± 9.7 vs. 65.1 ± 6.5%, respectively).

As shown in Fig. 6A, high-intensity exercise inhibited gastric tonus in anesthetized rats. Compared with the respective

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Table 1. **Arterial gasometrical parameters in sedentary or acutely exercised rats**

<table>
<thead>
<tr>
<th></th>
<th>Sedentary</th>
<th>10 min</th>
<th>20 min</th>
<th>Postexercise</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Blood lactate and creatine kinase levels</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lactate, mmol/l</td>
<td>3.17 ± 0.57</td>
<td>6.10 ± 0.88*</td>
<td>4.28 ± 1.16</td>
<td>7.92 ± 0.17*</td>
</tr>
<tr>
<td>pH</td>
<td>7.32 ± 0.02</td>
<td>7.14 ± 0.17*</td>
<td>7.35 ± 0.01</td>
<td></td>
</tr>
<tr>
<td>Base excess, mmol/l</td>
<td>-1.38 ± 0.73</td>
<td>-5.43 ± 2.91*</td>
<td>-1.18 ± 0.72</td>
<td></td>
</tr>
<tr>
<td>$\left[ \text{HCO}_3^- \right]$, mmol/l</td>
<td>22.60 ± 1.03</td>
<td>17.73 ± 5.53*</td>
<td>23.20 ± 1.20</td>
<td></td>
</tr>
<tr>
<td>$\text{PCO}_2$, Torr</td>
<td>51.79 ± 7.56</td>
<td>53.54 ± 9.05</td>
<td>45.80 ± 5.44</td>
<td></td>
</tr>
<tr>
<td>$\text{PO}_2$, Torr</td>
<td>64.97 ± 12.55</td>
<td>74.68 ± 15.20</td>
<td>77.66 ± 9.30</td>
<td></td>
</tr>
<tr>
<td>$\text{SO}_2$, %</td>
<td>71.70 ± 10.81</td>
<td>71.01 ± 14.13</td>
<td>83.72 ± 3.93*</td>
<td></td>
</tr>
</tbody>
</table>

**Hemodynamic indexes**

<table>
<thead>
<tr>
<th></th>
<th>Sedentary</th>
<th>10 min</th>
<th>20 min</th>
<th>Postexercise</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAP, mmHg</td>
<td>110.4 ± 4.3</td>
<td>121.8 ± 3.6*</td>
<td>117.9 ± 2.7</td>
<td></td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>351.3 ± 25.0</td>
<td>421.7 ± 26.8*</td>
<td>353.1 ± 36.5</td>
<td></td>
</tr>
</tbody>
</table>

Values are means ± SD; $n = 5–8$ rats per group. $[\text{HCO}_3^-]$ bicarbonate concentration; $\text{SO}_2$, oxygen saturation; MAP, mean arterial pressure; HR, heart rate. *$P < 0.05$ vs. sedentary group (unpaired Student’s $t$-test).
values in sedentary control rats, stepwise distension of the stomach with intraluminal pressure of 4, 8, and 12 cmH₂O led to higher \((P < 0.01)\) gastric volumes in animals in the exercised group (1.3 ± 0.1 vs. 2.2 ± 0.6 ml, 1.5 ± 0.1 vs. 2.3 ± 0.6 ml, and 1.7 ± 0.2 vs. 2.4 ± 0.7 ml, respectively). Acute exercise testing enhanced small-intestine transit in awake rats (Fig. 6B). Compared with the median values of marker progression in the gut of sedentary control rats, the meal’s geometric center in the acute exercise group progressed significantly farther along the small intestine [3.30 (2.82–3.57) vs. 3.51 (3.07–3.99)].

Figure 7 presents the cholinergic responsiveness of isolated strips obtained from the stomach fundus and pylorus of rats previously subjected to sedentary (control) or acute exercise testing. In such preparations, carbachol concentration-dependently induced \((P < 0.001, \text{ANOVA})\) contractions. In fundic strips (Fig. 7, A and C), but not pyloric tissues (Fig. 7, B and D), the magnitude of the tension was significantly lower \((P < 0.05)\) in the exercise group (0.31 ± 0.09 vs. 0.90 ± 0.11 g/mg of dry tissue in the sedentary group). No differences were

Table 2. Arterial gasometrical parameters in sedentary and acutely exercised rats previously treated with \(\text{NaHCO}_3\) (500 mg/kg po)

<table>
<thead>
<tr>
<th></th>
<th>Sedentary + (\text{HCO}_3^-)</th>
<th>Acute exercise + (\text{HCO}_3^-)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatine kinase, U/l</td>
<td>199.53 ± 20.50</td>
<td>210.00 ± 16.32</td>
</tr>
<tr>
<td>Lactate, mmol/l</td>
<td>3.83 ± 0.15</td>
<td>4.81 ± 0.29*</td>
</tr>
<tr>
<td>pH</td>
<td>7.43 ± 0.01</td>
<td>7.38 ± 0.01</td>
</tr>
<tr>
<td>Base excess, mmol/l</td>
<td>7.85 ± 0.51</td>
<td>5.68 ± 1.33</td>
</tr>
<tr>
<td>[(\text{HCO}_3^-)] mmol/l</td>
<td>30.71 ± 0.46</td>
<td>28.76 ± 1.14</td>
</tr>
<tr>
<td>(\text{PCO}_2), Torr</td>
<td>52.91 ± 3.42</td>
<td>55.31 ± 1.93</td>
</tr>
<tr>
<td>(\text{PO}_2), Torr</td>
<td>61.78 ± 4.77</td>
<td>63.29 ± 4.82</td>
</tr>
<tr>
<td>(\text{SO}_2), %</td>
<td>76.17 ± 3.12</td>
<td>72.18 ± 5.91</td>
</tr>
</tbody>
</table>

Values are means ± SD. \(*P < 0.05\).
Although we did not measure O₂ consumption in rats subjected to constant-load swimming, the adopted exercise protocol implied a high-intensity demand that forced the rats to work near or above their maximal aerobic capacity, reflected by the clear acid-base imbalance and lactic acidemia. According to Voltarelli et al. 2002 (46), rats subjected to such an experimental protocol achieved their anaerobic threshold during acute exercise. The increase in blood lactate levels observed herein was similar to the levels reported by others (2, 9, 16, 18, 33). We also assessed the intensity of effort by measuring blood CK levels, a well-known marker of exercise-induced muscle cell injury (5). Compared with the respective values in the sedentary control group, CK levels increased after exercise, which is consistent with a previous study that used a different exercise protocol (34). Thus the present decrease in blood pH may have resulted from the anaerobic conditions imposed on skeletal muscle cells. The fact that blood PCO₂ remained unchanged in the exercised rats in the present study suggests that the respiratory system fully compensated for metabolic acidosis elicited by acute exercise.

In the present study, the high-intensity exercise increased MAP and HR. Such hemodynamic changes are mediated by an increased discharge of the sympathetic nervous system, as well as an inhibited parasympathetic drive via three distinct mechanisms: central command, the exercise pressor reflex, and modulation of the arterial baroreflex (30). Hemodynamic changes could be involved in the present gastrointestinal effects caused by exercise. Notable hemodynamic changes could be elicited by acute physical exercise that contributes to blood-flow redistribution between the viscera and skeletal musculature (13, 25). In the gastrointestinal tract, such redistribution may reduce blood perfusion by one-half, thus generating splanchnic ischemia (37) that may ultimately result in tissue hypoxia, the depletion of adenosine triphosphate and acidosis, injury beyond the mucosa, increased gut permeability, and bacterial translocation from the luminal environment (45). Full occlusion of the vascular supply toward the gut delays the GE of a liquid test meal in awake rats (42). However, such an ischemia-reperfusion technique does not reproduce the actual hemodynamics in splanchnic vessels after physical activity because the ischemia-reperfusion procedure does not allow the natural compensatory fluctuation of tissue perfusion because of the production of cellular metabolites (i.e., the myogenic reflex). In the present study, stomach tissue oximetry was not monitored, but the exercise-induced GE delay was unlikely related to eventual gut ischemia caused by high-intensity exercise, because exercised rats showed an increased progression of the dye through the small intestine. We are aware that acute exercise testing determines hyperthermia and dehydration, which could per se alter both antral and duodenal smooth muscle activity, thus modulating the GE rate (19, 31).

Data from clinical studies that used noninvasive methods to assess orocecal transit time (OCTT) in humans are controversial. Some have concluded that exercised patients or even athletes under moderate aerobic exercise may suffer no changes in OCTT (6, 11, 22, 40), whereas others have reported an increase in OCTT (23, 24, 25). According to Leiper et al. (26, 27), even soccer and running exercises inhibit the GE of a liquid test meal in healthy, physically active men. Such divergent results may be related to the adoption of different exercise types or different methodologies to measure intestinal transit.

**DISCUSSION**

The present study showed that high-intensity exercise, such as acute swimming with a constant load of 5% body weight, induced lactic acidosis in awake rats and inhibited the GE of a liquid test meal, a phenomenon prevented by NaHCO₃ treatment.

We assessed the GE rate using the dye dilution method, a simple but reliable technique (36). Nonetheless, the phenol red dye used as the gastrointestinal motility marker is a pH-dependent reagent, which may have biased the present analysis, whether one considers that acute exercise testing eventually increases gastric acid secretion, thus inhibiting GE by chemically stimulating duodenal structures. However, such a possibility may be excluded, because both vehicle and omeprazole-pretreated rats that were subjected to acute exercise had similar gastric retention values.

**Fig. 6.** Effects of acute anaerobic exercise (swimming session for 15 min against a load equivalent to 5% of body weight) on gastric compliance in anesthetized rats (A) and small-intestine transit in awake rats (B). Rats previously trained to freely swim in a thermonutral tank for 5 days were subjected or not subjected (sedentary) 2 days later to another swimming session for 15 min, but this time against a load equivalent to 5% of body weight (acute exercise). The gastric volume was determined by means of a balloon catheter previously inserted via the fistula at the fundus of the stomach coupled to a plethysmometer. The dye marker progression in the small intestine was monitored, but the exercise-induced GE delay was unlikely related to natural or compensatory fluctuation of tissue perfusion because of the ischemia-reperfusion procedure does not allow the production of cellular metabolites (i.e., the myogenic reflex). In the present study, stomach tissue oximetry was not monitored, but the exercise-induced GE delay was unlikely related to eventual gut ischemia caused by high-intensity exercise, because exercised rats showed an increased progression of the dye through the small intestine. We are aware that acute exercise testing determines hyperthermia and dehydration, which could per se alter both antral and duodenal smooth muscle activity, thus modulating the GE rate (19, 31).

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Data from preclinical studies with rats are also controversial. According to Van Liere et al. (44), exercised rats (either male or female) had greater propulsion of a charcoal marker throughout the small intestine compared with sedentary rats. Chang et al. (7) found no alterations in the gastrointestinal transit of a radioactive marker in rats (300–400 g of body weight) subjected to exhaustive exercise on a treadmill.

Under the present experimental conditions, the acute exercise test elicited a significant GE delay, which appeared to be attributable to blood acidemia because of the following facts: 1) the occurrence of a positive correlation between blood lactate and gastric dye recovery in exercised rats; 2) the effects caused by the administration of an NH₄Cl-containing meal that lowered blood pH and induced metabolic acidosis in control rats and increased gastric retention to a similar degree in the exercised group; and 3) the restorative effects of NaHCO₃ pretreatment that corrected lactacidemia, restored acid-base balance, and prevented the increase in gastric retention caused by acute exercise. Moreover, lactate infusion inhibits per se the GE of sedentary and exercised awake rats (8).

NaHCO₃ pretreatment has recently been proposed as a therapy to avoid the deleterious effects of strenuous exercise and minimize the increase in lactate and blood CK levels in athletes subjected to endurance physical training under anaerobic conditions (38, 42). According to Edge et al. (14), the buffering property of NaHCO₃ shifts the lactate threshold curve to the right, delaying the onset of acidosis-induced muscular fatigue. In the present work, NaHCO₃ treatment prevented the GE delay caused by high-intensity swimming. In this sense, Belangero and Collares (1) reported that NaHCO₃ treatment prevented the increase in gastric retention in awake rats subjected to acute metabolic acidosis induced by NH₄Cl ingestion.

The gastroduodenal flow of liquid meals in awake mammals is modulated by complex processes (35). The present exercise-induced GE delay may have resulted from an increase in gastric relaxation, decrease in antral contractility, or increase in pyloric or duodenal resistance (12). This last hypothesis is unlikely because we used an isotonic liquid test meal, making it improbable that such an effect was mediated by an enhancement of the small-intestine-mediated inhibition of GE (i.e., the “duodenal brake”). Moreover, rats subjected to acute exercise testing exhibited an increase in dye marker progression throughout the small intestine compared with the respective controls. In contrast, an inhibited muscle tonus of the proximal stomach seems to contribute to the phenomenon of GE delay.

Fig. 7. Effect of the cumulative addition of carbachol (CCh) on responsiveness in isolated strips of the gastric fundus (A and C) and pylorus (B and D). ○, Sedentary rats; ●, exercise rats. Values are means ± SD. *P < 0.05, sedentary vs. exercise rats.
We observed significantly higher gastric volumes in the exercise group compared with the sedentary group when they were subjected to increasing gastric distension. Additionally, Fig. 7A shows that the cholinergic responsiveness of isolated strips of the gastric fundus obtained from rats previously subjected to acute exercise testing was significantly lower than in control rats.

Although stimulating, the present findings cannot necessarily be extrapolated to athletic conditioning and performance training. Physical exercise is often accompanied by the ingestion of beverages, the composition, volume, and energy density of which can alter the GE rate, which then may influence several factors, such as exercise intensity and training conditions.

In summary, the present study showed that high-intensity exercise delayed the GE of a liquid test meal in awake rats, a phenomenon likely elicited by acid-base imbalance caused by the blood accumulation of H^+ mainly derived from lactic acid produced by skeletal muscle cells during force development under anaerobic conditions. The magnitude of gastric retention depended on the increase in blood lactate levels, which was preventable by ingesting NaHCO_3 before acute exercise testing.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS


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