Glucoregulatory responses to intense exercise performed in the postprandial state

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Kreisman, Stuart H., Anthony Manzon, Sharon J. Nessim, Jóse A. Morais, Réjeanne Gougeon, Simon J. Fisher, Mladen Vranic, and Errol B. Marliess. Glucoregulatory responses to intense exercise performed in the postprandial state. Am J Physiol Endocrinol Metab 278: E786–E793, 2000.—A seven- to eightfold increment in hepatic glucose production (endogenous Ra) occurs in postabsorptive (PA) intense exercise (IE). A similar response is likely present in the postprandial (PP) state, when most such exercise is performed, because 1) little evidence for increased intestinal absorption of glucose during exercise exists, and 2) intravenous glucose does not prevent it. We investigated IE in 10 PA and 8 PP fit, lean, young males who had exercised for 15 min at >84% maximum O2 uptake, starting 3 h after a 412-kcal mixed meal. The meal induced a small rise in glycemia with sustained insulin and glucagon increases. Preexercise glucose total Rg and utilization (Rg) were equal and ~130% of the PA level. Exercise hyperglycemia in PP was delayed and diminished and, in early recovery, was of shorter duration and lesser magnitude (P = 0.042). Peak catecholamine (12- to 16-fold increase) and Ra (PP: 11.5 ± 1.4, PA: 13.8 ± 1.4 mg·kg⁻¹·min⁻¹) responses did not differ, and their responses during exercise were significantly correlated. Exercise glucagon, insulin, and glucagon-to-insulin responses were small or not significant. Ra reached the same peak (PP: 8.0 ± 0.6, PA: 9.3 ± 0.8 mg·kg⁻¹·min⁻¹) but was greater at 20–120 min of recovery in PP (P = 0.001). Therefore, the total Ra response to IE is preserved despite the possibility of prior PP suppression of endogenous Ra and is consistent with catecholamine mediation. Post-IE hyperglycemia is reduced in the postprandial state.

glucose turnover; postprandial exercise; catecholamines; insulin; glucagon

The glucoregulatory responses to intense exercise (IE, >80% of maximum O2 uptake [VO2max]) differ from those to exercise of lesser intensities. IE is characterized by a rapid and massive increase (up to 8-fold) in hepatic glucose output (endogenous Ra) and a rise in glycemia. Plasma insulin either remains constant or decreases slightly, whereas glucagon increases <2-fold, and catecholamines increase up to 15-fold (25, 26, 37, 38). This Ra response was unaffected in islet cell clamp studies that used somatostatin and exogenous hormone infusions, in which peripheral glucagon-to-insulin ratios (glucagon/insulin) were unchanged or decreased, and catecholamine responses were intact (37). Consequently, we (25, 26, 37, 38) and others (6, 20) have proposed that the catecholamines could be the major regulators of the IE Ra response. In contrast, it is generally accepted that the glucagon/insulin responses mediate the Ra response at lesser exercise intensities.

Although such studies have all been performed in the postabsorptive (PA) state, most such exercise is done in the postprandial (PP) state, in which endogenous Ra is suppressed during glucose absorption from meals that contain protein and fat as well as carbohydrate. A variety of responses occur during moderate-intensity PP exercise. Although these depend on the timing of the exercise, they are elegantly regulated, and the corresponding glucagon/insulin responses appear to continue to be the primary regulators (8, 19, 28, 29, 43). Mimicking the PP state by glucose infusion has tended to attenuate the endogenous Ra response to moderate exercise, again probably mediated by the induced glucagon/insulin changes (3, 17, 18, 41, 44). We are unaware of prior published studies of PP IE. Because it is both improbable that a large Ra increase could come from increased intestinal absorption and difficult to quantify such absorption in this setting, we first tested responses during intravenous glucose infusion to mimic the fed state, as had been done in moderate exercise. We showed that the huge endogenous Ra response in IE still occurred when starting from a state of complete endogenous Ra suppression (23).

Therefore, we hypothesized that the glucoregulatory responses to IE after a mixed meal (as close to the “real life” scenario as possible) would be similar to those observed during glucose infusion, in that the Ra response would still occur and be highly correlated to the catecholamine response despite the PP preexercise suppression of endogenous Ra. To test this, it would be desirable to trace glucose originating both from the meal and endogenously. This would require labeling the carbohydrate in a mixed meal and being able to interpret the markedly non-steady-state data. We reasoned that if the huge IE Ra response were preserved, it would be improbable that it would be from the meal, and one intravenous label would give informative data. In studies of moderate exercise, the following conditions have been shown with glucose “meals” only: postabsorptive splanchnic blood flow decreases (35),...
and postprandially glucose absorption either does not increase (13, 14, 34) or progressively decreases, with intensities ≤ 64% VO₂max (31), or increases but only after 30 min. at 71% VO₂max (27). IE has not been studied. We therefore studied fit, lean, young males who exercised for 14–15 min at > 84% VO₂max. 8 starting 3 h after a mixed meal of 412 kcal (PP) and 10 in the postabsorptive state (PA). Results of these studies have been presented in part in abstract form (24).

METHODS

Two groups of subjects were studied: one, a postprandial (PP) group of 8 subjects, and the other a postabsorptive (PA) control group of 10 subjects. Participants in the study were 18 lean, weight-stable, fit men aged 18–35 yr. All engaged in regular activity such as running, cycling, soccer, and/or rowing, and some combined this activity with resistance training. Anthropometric and exercise data are presented in Table 1. Screening before the study included medical history, physical examination, and the laboratory investigations previously detailed (37–39). Subjects gave consent as prescribed by the institutional human ethics committee.

VO₂max was determined with breath-by-breath analysis during an incremental workload (20 W/min) test on an electrically braked cycle ergometer (Collins Metabolic Cart, Collins, Braintree, MA), as previously detailed (37–39). Then each subject underwent a test without blood sampling at 50% for 30 s, followed by ~80% of his maximum workload, to become familiar with the workload protocol and to assure a uniform 12- to 15-min duration and assurance that he would reach ~85% VO₂max within 6–7 min. These workloads were used for the glucose turnover study that began between 0800 and 0900, with subjects in the 12-h overnight-fasted state. The protocols are shown graphically in Fig. 1. Cannulas (Criticon Canada, Markham, ON, Canada) were inserted into veins in both arms for sampling and infusion. A priming bolus of 22 µCi of high-performance liquid chromatography-purified [3-3H]glucose tracer (Du Pont-NEN, Billerica, MA) was followed by a constant infusion of 0.22 µCi/min [3-3H]glucose in 0.9% saline for 150 min in both groups (starting at ~150 min in PA and ~330 min in PP). Blood was sampled at seven 10-min intervals before time 0 (beginning of exercise) in PA, and to time ~180 (meal) in PP. Additional postmeal samples were drawn in PP to define the total Ra response. PP subjects ate a meal of 412 kcal [54.2 g (49%) carbohydrate (43% fructose, 57% glucose), 30.6 g (30%) protein, 9.5 g (21%) fat, 4.1 g dietary fiber] consisting of two Power 8 Thermobars (Bariatrax International, Lachine, QC, Canada) over 12.8 ± 1.8 min, with water.

Glucose specific activity (SA) was adequately maintained by increasing and decreasing the tracer infusion incrementally (maximum 7.5-fold) during the exercise and the immediate recovery periods (25, 26, 36–39) to assure validity of glucose turnover calculations (12). Blood samples were drawn at intervals, as seen from the data in Figs. 1–6. Samples for glucose turnover measurements were placed into tubes containing heparin and sodium fluoride and were processed as described previously (26). Heparinized plasma was collected with aprotinin (Trasylol, FBA, New York, NY) for subsequent insulin (IRI), glucagon (IRG), and free fatty acid (FFA) assays. For catecholamine measurements, blood was added to EGTA- and reduced glutathione-containing tubes, and the plasma was frozen at –70°C until assay. One aliquot of blood was added to cold 10% (wt/vol) perchloric acid and then frozen at –20°C for later lactate and pyruvate assays.

Glucose was measured by the glucose oxidase method (GlucoseAnalyzer II, Beckman, Fullerton, CA); blood lactate and pyruvate were measured by enzymatic microfluorometric methods, plasma IRI and IRG by radiomunnoassays, and FFAs by a radiometric assay, all previously detailed (25, 37–39). Plasma norepinephrine and epinephrine concentrations were measured using a radiometric technique (sensitivity < 50 pmol/l) (10). The intra- and interassay coefficients of variation for all assays were <10% for the enzymatic assays, they were <5%. Glucose Ra and glucose disappearance or utilization (Rd) were calculated from the variable isotope infusion protocols according to the one-compartment model (33), with data systematically smoothed using the OOPSEG (optimized optimal segments) program (5). Glucose metabolic clearance rate (MCR) was calculated by dividing Rd by the plasma glucose concentration.

Baseline characteristics were analyzed using one-way ANOVA. The metabolic variables were analyzed by ANOVA for repeated measures. Intergroup differences found to be significant (P < 0.05) were subsequently analyzed by the independent t-test at specific times. Paired t-tests were used for analysis of some differences within the same group over time. Linear correlations were calculated using the Pearson

| Table 1. Subject anthropometric and exercise data |
|---|---|---|
| PA | PP |
| n | 10 | 8 |
| Age, yr | 22.7 ± 1.7 | 21.6 ± 0.8 |
| Height, cm | 175 ± 3 | 181 ± 3 |
| Weight, kg | 71.3 ± 2.6 | 73.7 ± 3.8 |
| BMI, kg/m² | 23.2 ± 0.6 | 22.4 ± 0.8 |
| VO₂max, l/min | 4.4 ± 0.22 | 4.42 ± 0.24 |
| ml·kg⁻¹·min⁻¹ | 62.5 ± 3.4 | 60.4 ± 2.8 |
| Study VO₂, l/min | 3.88 ± 0.23 | 4.01 ± 0.16 |
| Study VO₂/VO₂max, % | 86.2 ± 5 | 92 ± 3 |
| Workloads | |
| Max, W | 332 ± 19 | 320 ± 16 |
| Study, W | 261 ± 13 | 262 ± 12 |
| Study/max, % | 78 ± 2 | 82 ± 4 |
| Exercise duration, min | 14.2 ± 0.3 | 14.7 ± 0.3 |
| HR at exhaustion, beats/min | 180 ± 3 | 170 ± 5 |

Data are means ± SE. PA, postabsorptive; PP, postprandial; BMI, body mass index; VO₂ and VO₂max, O₂ uptake and maximum O₂ uptake, respectively; HR, heart rate.
correlation coefficient. Individual correlation coefficients were calculated using all nine data points for each individual, at which catecholamines were measured in the stated interval. This correlation coefficient was then treated as a continuous variable on which means and SE were calculated, and intergroup differences were assessed using one-way ANOVA, repeated-measures ANOVA, and the Student-Newman-Keuls tests. The SAS-STAT software package (SAS Institute, Cary, CA), SPSS-Windows Release 6.0 software package (SPSS, Chicago, IL), Microsoft Excel 5.0 Analysis ToolPak (GreyMat International, Cambridge, MA), and Primer Biostats (McGraw-Hill, New York, NY) were used. Data are presented as means ± SE.

RESULTS

The subjects of the two groups were comparable (Table 1). No untoward effects were experienced. Glucose SAs were constant before the meal and during exercise, although at a slightly lower level in PP preexercise. No changes during or after exercise exceeded 25% (data not shown). The principal findings in PP were that 1) IE-related hyperglycemia was delayed and diminished, and in recovery was of shorter duration and smaller magnitude; 2) the $R_a$ response remained rapid, marked, and significantly correlated with plasma catecholamines; 3) both $R_a$ and $R_d$ were higher than in PA preexercise and part of the recovery period; 4) in PP, insulin was much higher and FFA were lower before and during exercise, and glucagon responses were similar.

Glycemia (Fig. 2) rose ($P < 0.001$) postprandially from 4.78 ± 0.13 mM to a peak of 5.57 ± 0.13 mM at 30 min and then returned to baseline by 60 min. Preexercise glycemia were the same (PP: 4.98 ± 0.10, PA: 5.01 ± 0.13 mM), but exercise responses differed ($P = 0.037$). In PA, glycemia rose from the onset of exercise to 5.21 ± 0.11 mM at 4 min ($P = 0.027$) and to 6.43 ± 0.24 mM at exhaustion, and it peaked at 7.47 ± 0.38 mM at 4 min of recovery. In PP it declined to 4.66 ± 0.26 mM at 8 min, was 5.84 ± 0.51 mM at exhaustion, and peaked at 6.84 ± 0.50 mM at 4 min of recovery. The first value different from preexercise was at 2 min of recovery ($P = 0.018$). It took 30 min to return to baseline in PP but 50 min in PA, being lower in PP from 8 to 40 min of recovery ($P = 0.042$).

Total glucose $R_a$ (Fig. 3A) rose postprandially, remaining higher ($P = 0.009$) than in PA for 60 min preexercise (2.60 ± 0.23 vs. 2.02 ± 0.09 mg·kg\(^{-1}\)·min\(^{-1}\), $P = 0.044$). $R_a$ rose markedly and rapidly in both groups during exercise, significantly by 2 min ($P < 0.005$). Total $R_a$ change in $R_a$ ($\Delta R_a$: $R_a$ minus preexercise baseline $R_{a0}$ not shown), peak $R_a$ at exhaustion (PP: 11.51 ± 1.39, PA: 13.79 ± 1.40 mg·kg\(^{-1}\)·min\(^{-1}\)), and peak $R_a$ (PP: 8.92 ± 1.31, PA: 11.77 ± 1.39 mg·kg\(^{-1}\)·min\(^{-1}\)) values were not significantly different. Total $R_a$ did not differ in early recovery but from 20 min on was higher in PP ($P < 0.001$), as it rose again ($P < 0.05$), whereas it continued to fall slightly in PA ($P < 0.001$), becoming less than at preexercise baseline at 30 min ($P = 0.024$).

Glucose $R_d$ (Fig. 3B) also rose in PP after the meal, remaining higher than in PA for 60 min preexercise ($P = 0.016$). $R_d$ rose rapidly in both groups during exercise, significantly by 2 min ($P < 0.02$), and did not differ during exercise. It peaked in recovery at 2 min in PA (9.29 ± 0.75 mg·kg\(^{-1}\)·min\(^{-1}\)) and at 4 min in PP [7.96 ± 0.61 mg·kg\(^{-1}\)·min\(^{-1}\), $P = 0.044$].
R_d fell rapidly in both groups in recovery, approaching preexercise values by 20–30 min but reaching them only at 80–100 min. R_d was higher (P = 0.009) in PP from 20 min onward. Trends for MCR (not shown) followed those of R_d. MCR rose in PP after the meal, was significantly higher in the 60 min preexercise (P = 0.032) and from 20–120 min of recovery (P = 0.001), but was not different during exercise, at peak, or in early recovery.

In PP, IRI increased threefold (P < 0.001) to peak at 30 min after the meal (Fig. 4A) and then returned to 1.5-fold premeal values (P < 0.001) until exercise and was thus higher than in PA preexercise (P = 0.032). The slight decline during exercise was not significant, and IRI remained higher in PP throughout exercise (P = 0.02). IRI increased during the early recovery period, although it did not differ between groups, but it took 40 min to return to baseline in PA vs. 15 min in PP.

IRG rose and remained elevated in response to the meal (P < 0.001), although preexercise values were not significantly different between groups (Fig. 4B). It did not change significantly during exercise, and neither exercise nor recovery values differed between groups. Glucagon/insulin (Fig. 4C) fell (P = 0.003) in PP 30 min after the meal and then remained lower (P = 0.003) than premeal values until exercise. It was not significantly different between groups at preexercise baseline or during exercise. It rose slightly but not significantly with exercise in PA (20%, P = 0.12) and PP (23%, P = 0.07). It was not different between groups during recovery.

Plasma catecholamines (NE, Fig. 5A and Epi, Fig. 5B) did not change after the meal. Neither NE nor Epi differed significantly between groups at preexercise baseline, during exercise, at their peak values, or during recovery. Both underwent rapid and marked increases in both groups during exercise, peaking at exhaustion, falling rapidly early in recovery, and reaching baseline values by 40 min. Peak NE was 33.38 ±
3.70 nM in PP (16.0-fold increase) and 36.38 ± 7.16 nM in PA (12.6-fold increase), and Epi was 5,684 ± 1,281 pM in PP (13.2-fold increase) and 5,243 ± 986 pM (12.0-fold increase) in PA. The mean correlation coefficients of NE and Epi with $R_a$ in each group from preexercise baseline until 40 min of recovery were highly significant: in PA, $R_a$ vs. NE, $r^2 = 0.86$, $P < 0.02$; $R_a$ vs. Epi, $r^2 = 0.76$, $P < 0.03$; in PP, $R_a$ vs. NE, $r^2 = 0.73$, $P < 0.02$; $R_a$ vs. Epi, $r^2 = 0.60$, $P < 0.05$.

Blood lactate and pyruvate in PP were both slightly higher ($P = 0.025$ and 0.003, respectively) at the preexercise than the premeal baseline (data not shown). Lactate was higher ($P = 0.021$) in PP than in PA preexercise, but pyruvate was not. Both rose markedly during the exercise, peaking at or soon after exhaustion (at 11–13 mM for lactate and 0.4 mM for pyruvate) and slowly returning toward baseline in recovery. There were no significant intergroup differences during exercise, at exhaustion, or during recovery. FFA levels (Fig. 6) dropped postprandially ($P < 0.001$) and were lower ($P = 0.007$) than in PA at preexercise baseline. Premeal levels in PP were also lower ($P = 0.022$) than preexercise PA baseline. During exercise, FFAs were lower and unchanged in PP ($P = 0.004$), despite a marked fall in PA ($P = 0.017$), and remained lower ($P = 0.040$) for 10 min of recovery. Respiratory exchange ratio (RER) was significantly higher in PP at preexercise baseline (0.89 ± 0.05 vs. 0.75 ± 0.02), increased to ~1.0 throughout exercise in both groups ($P = 0.001$), but did not differ between groups (Table 2).

**DISCUSSION**

We have demonstrated that the marked glucose $R_a$ response to IE is preserved in the postprandial state after a mixed meal, the “real life” situation under which most exercise is performed. At the onset of exercise, PP demonstrated hyperinsulinemia, relative to premeal and to the PA subjects, and an increased $R_a$ in the circulation, indicative of a portion of it coming from the gastrointestinal tract. Hepatic glucose production has been shown to be suppressed 50–67% for >3 h after the administration of similar carbohydrate loads (11, 32). Thus generating the marked rises in endogenous $R_a$ of PA intense exercise in the PP state would require a rapid reversal of the liver’s metabolic orientation.

Because our method could not distinguish between endogenous and exogenous contributions to $R_a$, we cannot prove that the majority of the increment in total $R_a$ was from the liver (± kidney) rather than the gut. We consider the latter to be improbable, but there might have been sufficient intraluminal carbohydrate to supply the requisite glucose. From 70 to 100% of a glucose load is absorbed by 180 min (11, 21). The PP subjects consumed a mixed meal (which slows absorption) and had higher $R_a$ and $R_0$ than those of PA that persisted into recovery, suggesting that enough glucose remained in the gut at the time of exercise to make it theoretically possible for absorption to have increased. However, splanchnic blood flow is reduced considerably at even moderate workloads in the PA state (35). We could find no data on splanchnic blood flow during PP exercise. During moderate-intensity exercise, glucose absorption did not decrease (13, 14, 34), likely due to local blood flow autoregulation in the small intestine (15), but it did not increase either. One study of glucose ingestion during exercise did show decremental contributions of exogenous glucose to carbohydrate oxidation at intensities up to 64% $V_{O2max}$ (31). A study of 60 min of 71% $V_{O2max}$ exercise starting 30 min after 75 g of labeled oral glucose showed 1) interruption of the progressive increase in absorption for 30 min, followed by an increase up to 60 min of exercise, and 2) a sustained rise in endogenous $R_a$ despite prior complete suppression (27). Absorption of glucose has not been reported in intense exercise, but the fed pattern of intestinal motor activity was frequently interrupted at 90% $V_{O2max}$, as opposed to rarely at 80% $V_{O2max}$ (40). It therefore seems more likely that the gut-derived contribution to the total $R_a$ in our PP subjects either fell or remained constant during the 15 min of IE, and it is highly improbable that it rose enough to contribute more than a small part of the increment. A further, albeit indirect, finding in support of this is the midrecovery rise of $R_a$ seen only in PP subjects, which would be consistent with returning to higher rates of gut-derived glucose influx.

We have hypothesized that catecholamines are likely the principal mediators of the $R_a$ response to intense exercise in the PP state, as in other settings. We have argued previously (23, 37–39) that the IRI, IRG, and IRG-to-IRI ratio (IRG/IRI) responses in intense exercise in the PA state are insufficient to account for the marked $R_a$ response. Our PP subjects demonstrated trends toward similar responses, with the decrease in IRI (18% at its nadir), rise in IRG (8% at its peak), and

<table>
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<th>Group</th>
<th>Baseline</th>
<th>4 min</th>
<th>10 min</th>
<th>Exhaustion</th>
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<tr>
<td>PA</td>
<td>0.75 ± 0.02</td>
<td>1.06 ± 0.04</td>
<td>0.98 ± 0.04</td>
<td>0.99 ± 0.05</td>
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<tr>
<td>PP</td>
<td>0.89 ± 0.05*</td>
<td>1.10 ± 0.01</td>
<td>1.02 ± 0.02</td>
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Data are presented as means ± SE. *$P < 0.05$ vs. PA.

**Fig. 6.** Plasma free fatty acid (FFA) levels during baseline, intense exercise, and recovery periods. Data are means ± SE for 10 PA and 8 PP subjects.

**Table 2.** Respiratory exchange ratios
rise in IRG/IRI (23% at its peak) not reaching statistical significance. Notably, none of these changes occurred in a consistent and progressive fashion that corresponded to the rise in $R_a$. Furthermore, their changes would need to be more pronounced during the PP than during the PA state to overcome the preexercise hepatic $R_a$ suppression. It is the portal venous IRI and IRG that regulate hepatic metabolism, and these undergo greater changes during exercise than do systemic levels (42). However, given their peripheral venous changes, portal responses of sufficient magnitude to cause the $R_a$ effect observed seem highly improbable, although the small changes likely contributed. The most compelling argument for the portal IRG/IRI changes being of secondary importance is that their portal levels were probably equal to peripheral levels during our islet cell clamp study, which showed a rapid and large $R_a$ response (37). As in previous studies in the PP state, the pattern of $R_a$ increment followed those of both the NE and Epi responses and were highly correlated with them. This is consistent with (but does not prove) catecholamines being important mediators of glucoregulation in IE during the PP state.

As reviewed previously (23), glucose labeled with tritium on the third carbon could lead to an underestimation of the increment of endogenous glucose production if label were incorporated into glycogen in the preexercise period and subsequently released. The metabolic setting that would favor this is present in both glucose-infused and PP subjects, but not in PA control subjects. Thus the apparent attenuation in endogenous $R_a$ in the glucose-infused subjects may have been overestimated (23). The portoarterial glucose gradient, such as occurs postprandially (1, 30), is of prime importance in hepatic glycogen accumulation. However, because the PP and PA $R_a$ responses were the same, tritium radiolabeling of glycogen could not create a significant source of interpretive error. If we did underestimate endogenous $R_a$ responses, this would provide yet more support to our inference that IE is able to overcome PP suppression of endogenous hepatic glucose output.

The responses to our mixed meal were noteworthy. First, the hyperglycemic response was small, and total $R_a$ was less than that reported after a carbohydrate load (11). These responses are likely due to the mixed composition of the meal (2) and its glucose content of only 30.9 g. The 23.3 g of fructose in the meal is largely removed by the liver on first pass (22), unlike glucose, whose first pass uptake is 5–25% (21, 22). Fructose produces only 20% of the glycemic response of glucose (2) and would only be measured as $R_a$ if converted to glucose and not incorporated into glycogen. Fructose may also have contributed to the higher preexercise lactate levels (22). Second, IRI remained elevated despite glycemia returning to baseline, and IRG also remained elevated. These are likely due to the high protein content of the meal (30 g), which can cause simultaneous hyperinsulinemia and hyperglucagonemia during normoglycemia, both presumably stimulated by the sustained hyperaminoacidemia (9). Third, the lower preexercise FFA level in the PP group was an expected effect of the sustained hyperinsulinemia.

The glycemic responses differed between the PA and PP groups. The PA hyperglycemia during IE and early recovery is well documented (6, 20, 23, 26, 39) and consistent with a feedforward mechanism (20, 44), whose “overshoot,” along with hyperinsulinemia, may be viewed as providing substrate for rapid replenishment of muscle glycogen stores. In the PP group the hyperglycemia was delayed and attenuated. This may have been due to the higher preexercise and exercise insulin levels as well as the need to reverse hepatic $R_a$ suppression. The glucose-infused subjects also had a diminished glycemic response compared with controls (23). The lesser PP glycemic response to IE does not detract from the theory of a feedforward mechanism as primary contributor, but it constitutes evidence against an IRG/IRI-based feedback mechanism. In moderate-intensity PP exercise, glycemia declines 15–25% (7, 29, 43). If this decline were related to the need to reverse the postprandial IRG/IRI, one would predict that a greater decline (due to greater $R_a$) would be present during PP IE, but we and others (28) have shown that the opposite occurs. This is consistent with a separate feedforward, perhaps catecholamine-driven mechanism, capable of overriding and/or adding to the IRG/IRI effects. The higher recovery period $R_a$ in the PP group would be consistent with an enhanced ability to rapidly replenish glycogen.

In our study the RER was not different during exercise between PA and PP. This contrasts with five of six studies of caloric ingestion before or during moderate exercise that showed increased carbohydrate oxidation and/or increased RER (4, 7, 8, 19, 28, 43). These findings in moderate exercise could be due to greater glucose availability in the PP state and/or to lower FFA level and lipolysis (8, 19, 43). The lack of such a finding in IE is consistent with the lesser contribution of FFAs as fuel substrates (16), although RER must be interpreted cautiously in IE. We did note a much greater drop in FFA levels in the PA group during exercise, possibly due to greater uptake in the non-leg muscles exercising at lower intensities during the cycling, and/or to decreased release due to decreased adipose tissue blood flow in IE (cited in Ref. 16).

In summary, this study has shown that the marked $R_a$ response to intense exercise is present and unchanged in the PP state after a mixed meal despite the need to overcome the physiological suppression of hepatic glucose output in this setting. The patterns of plasma catecholamine responses are suggestive of a major regulatory function in the endogenous $R_a$ response, whereas the patterns and magnitudes of insulin and glucagon changes suggest a lesser role for them. Recovery period hyperglycemia is reduced in the PP setting, yet $R_a$ is enhanced in PP IE, and this could be associated with glycogen repletion in muscle. If so, it could potentially translate into improved performance in repeated bouts of IE after a meal.

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GLUCOREGULATION IN POSTPRANDIAL INTENSE EXERCISE

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