Glucose administration before exercise modulates catecholaminergic responses in glycogen-depleted subjects

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Glucose administration before exercise modulates catecholaminergic responses in glycogen-depleted subjects. J. Appl. Physiol. 82(1): 248–256, 1997.—In glycogen-depleted subjects (GD) a nonlinear increase in epinephrine (Epi) and norepinephrine (NE) parallels blood lactate (La) during graded exercise. The effect of glucose (Glc) supplementation and route of administration on these relationships was studied in 26 GD athletes who were randomly assigned to receive 1.3 g/kg Glc by slow intravenous infusion (IV; n = 9), oral administration (PO; n = 9), or artificially sweetened placebo in 1 liter of water (Asp; n = 8) in the 2 h preceding a graded maximal exercise. Performance and La were similar among the three groups in normal glycogen (NG) or GD conditions. However, slightly improved performances were observed in GD compared with NG and were associated with a shift to the right in La curves. Blood Glc concentrations were higher in IV and PO before exercise, but they rapidly decreased to lowest levels in IV, gradually decreased over time in PO, and remained stable in Asp or NG. Insulin concentrations were highest in IV and lowest in Asp and NG at onset of exercise, rapidly decreasing in IV and PO although remaining at higher levels than in Asp or NG. In contrast, higher serum levels of free fatty acids were measured during exercise in Asp with no significant differences in glucagon or glycerol among the three groups. Free and sulfated NE increases were smaller in IV than in PO and Asp on exhaustion. In contrast, free and conjugated Epi were most increased in IV, with smallest increases in Asp. Dopamine levels were most increased in IV at exhaustion. We conclude that the changes of Epi and NE concentrations, associated with the activation of glucoregulatory mechanisms, including hyperinsulinemia, display different magnitude and time courses during exercise in GD subjects who receive oral vs. intravenous load of Glc before exercise. We speculate that the magnitude of insulin surge after acutely increased Glc before exercise in GD subjects may exert dissociative effects on adrenal-dependent glycogenolysis and on sympathetic responses.

autonomic system; gluconeogenesis; norepinephrine; epinephrine; dopamine

During high-intensity exercise, the catecholamines (CAs), epinephrine (Epi), and norepinephrine (NE) have been implicated, via their action on α-adrenergic receptors, in the well-known increase of muscle glycogenolysis and inhibition of glycogen synthase during contraction (39). Elevated levels of Epi may induce increased rates of muscle glycogen breakdown during exercise and consequent increases in lactate (La) production (28). Thus a causal relationship between the inflection in plasma Epi concentrations during a graded exercise test and the La threshold (T_La) has been postulated (20). Such relationship is further suggested by decreased plasma La and CA concentrations at similar workloads during graded exercise in glycogen-depleted (GD) subjects, even though maximal work rates and maximal O2 uptake (V̇O2max) remain unaffected (26).

A major regulatory role has also been ascribed to CA with respect to glucose (Glc) production during exercise. Indeed, light-to-moderately heavy exercise in which Glc production is tightly matched to utilization is usually not associated with significant changes in either CA or blood Glc concentrations (4, 8). Significant decreases in plasma insulin (Ins) levels and modest increases in glucagon (Glu) accompany these exercises, indicating that at such exercise intensities basal glucoregulatory mechanisms are sufficient and that no significant autonomic recruitment occurs. However, during heavy exhaustive exercise, CA secretion is markedly increased and may become the preponderant regulator of Glc availability. Indeed, immediately after an exercise bout leading to marked enhancements in CA concentrations, a hyperglycemic rebound occurs, suggesting that Glc levels are preserved during intense exercise by substantial adrenal and sympathetic discharges. The causal relationship between CA and Glc is further suggested by a recent study by Marliss and colleagues (19), who demonstrated that during a second bout of steady-state exercise at 80–100% V̇O2max leading to exhaustion and performed 60 min after the first bout, i.e. after GD, more circulating Glc was utilized and that significant correlations between Glc production and CA existed.

Such findings support the notion that a more important sympathetic recruitment may be necessary in GD conditions. GD was deleterious to performance during prolonged submaximal exercise, and administration of Glc reversed such effect (15). Short-lasting exercise performances were not affected by GD conditions (26, 19, 20).
morning. until beginning of third experimental exercise the following
the GD protocol was completed, subjects were allowed access for 2 min, immediately followed by 1-min rest periods. After
METHODS

regulatory mechanisms.

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male exercise in GD athletes may influence both Glc-Ins
relationshipsand performance. Indeed, Glc utilization
for readily available carbohydrate shortly before a maxi-
We hypothesized that ingestion of small quantities of
administration of Glc during the immediate preexer-
38). However, in GD subjects, the effect of Glc adminis-
exercise has not been previously assessed.

experiment in GD athletes may influence both Glc-Ins
relationships and performance. Indeed, Glc utilization
patterns were markedly affected by administration of
oral Glc during strenuous exercise (21). Similarly, route of
Glc administration (oral vs. intravenous) modified Glc uptake and glycogen synthesis after exercise (3).

Thus we sought to examine whether administration of
Glc to GD subjects in the 2 h preceding an incremental exercise would elicit differing sympathetic and adrenal
responses to exercise or affect performance. In addition,
we wished to establish whether oral or intravenous administration of Glc during the immediate preexercise period would induce differential activation of gluco-

regulatory mechanisms.

Subjects.

Twenty-six male athletes, members of various national Cameroonian teams encompassing track and field, handball, volleyball, and judo, were included in the study. Before their involvement, each subject was informed of the methods and possible risks associated with the study and signed a written informed consent. This study was approved by the Institutional Review Board of the National Institute for Youth and Sports of Yaoundé.

Subjects were randomly assigned to one of the three experimental groups, and their mean characteristics, which were similar across groups, were as follows: age, 23.5 ± 0.7 (SE) yr; height, 177.1 ± 1.3 cm; weight, 74.3 ± 1.5 kg; and VO_{2max}, 58.6 ± 14.4 mL·min^{-1}·kg^{-1}.

Experimental protocol. Subjects were requested to partici-
pate in three graded exercise tests on a mechanically braked ergometer (Ergomeca) after they underwent a series of three to six preliminary sessions of familiarization with ergocycle pedaling at various loads, during which VO_{2max} was measured. One week later, the subjects underwent the first stepwise incremental graded exercise test. After 2-min warm-up at zero load, loads were increased every 4 min by 35 W. During this first test, blood La was sampled during the last minute of each step and individual T_{La} was determined. It should be stressed at this point that the 4-min step duration at each workload may lead to underestimation of VO_{2max} although it improves T_{La} determination (46). In addition, in 8 of the 26 subjects, additional blood samples were drawn at various times as described below. This test was performed after an overnight fast and was considered to represent normal glycogen (NG) conditions.

The second exercise portion of the study entailed a previ-
ously well-documented exercise schedule designed to achieve muscle GD (11). In brief, subjects reported to the laboratory 3 h after their last meal of the day and were assigned to pedal until volitional fatigue at 60–70 revolutions/min (rpm) at a power output just below their T_{La}. This procedure lasted ~90–100 min. After a 2-min rest, subjects subsequently underwent a series of six exercise bouts, consisting of pedaling at 70 rpm at a power output of 120% of the individual T_{La} for 2 min, immediately followed by 1-min rest periods. After the GD protocol was completed, subjects were allowed access to water but otherwise remained under fasting conditions until beginning of third experimental exercise the following morning.

This third stage consisted of an identical incremental test as described above. However, in the 2 h before beginning of exercise, subjects were randomly assigned to receive the following: 1) intravenous Glc group (IV): intravenous administration of a 1-liter water solution containing 10% Glc, i.e., 100 g of Glc (intravenous), or ~1.3 g/kg; 2) oral Glc group (PO): oral administration of 100 g of Glc in 1 liter of water; 3) placebo group (Asp): oral administration of 1 liter of water sweetened with 1.5 g of aspartame.

Blood La measurements. Whole blood La was assayed by an electrochemical-enzymatic sensor technique with a LA 640 LA analyzer (Roche Kontron) according to the method of Geys-
sant et al. (10). Duplicate measurements were made on 10-µl blood samples diluted 1:20 with 190 µl of buffer solution (phosphate buffer 0.2 mmol/l at pH 7.20; penthanil 0.085 mmol/l). I immediate erythrocyte hemolysis was obtained by a saponin dry residue present in the special hemolyzing tubes (10 µl of a 90 g/l saponin-water solution evaporated to dryness). Calibration and linearity of the instrument were routinely carried with 5 and 10 mmol/l solutions. T_{La} was defined as the load at which a nonlinear increase in blood La was measured (37, 46).

Glc, Ins, and Gluc assays. Blood Glc concentrations were assayed by the glucose oxidase method with a commercially available enzymatic assay (BioMérieux, Marcy-l’Etoile, France) from blood samples stored for up to 4 h at 4°C in tubes containing fluorocarbon.

Plasma Ins and Gluc assays were performed by using commercial radioimmunoassay reagent kits, with intrassay coefficients of variation of 1.7 and 2.5%, respectively. The Ins kit was obtained from CIS Biointernational (Gif-sur-Yvette, France), whereas the Gluc kit was obtained from Biodata (Rome, Italy).

FFA and Glyc measurements. Serum FFA concentrations were measured with a commercially available kit (Unipath, Dardilly, France) according to Novack (24). Serum Glyc concentrations were assayed enzymatically (Boehringer Mannheim, Meylan, France).

Free and sulfated CAs. Blood samples were immediately transferred to ice-chilled heparinized tubes and centrifuged at 2,000 g for 10 min. Plasma samples were frozen and stored at −70°C until assay. Plasma Ca concentrations were determined by using high-performance liquid chromatography with electrochemical detection. Extraction was performed as previously described (30). The sensitivity of this method is 0.03, 0.05, and 0.01 pmol for NE, Epi, and DA, respectively.

Data analysis. Data are presented as means ± SD. Re-
sponse curves were obtained by linear interpolation between successive observations. Average response curves in the three experimental conditions were compared by means of the nonparametric method developed by Zerbe (48). Statistical significance was assessed at 0.05 critical level by the use of an
Table 1. Peak power exercise performances, lactate threshold, and peak blood lactate concentrations in normal glycogen or in glycogen-depleted subjects receiving intravenous glucose, oral glucose, or placebo during 2 h before graded exercise test

<table>
<thead>
<tr>
<th>Group</th>
<th>Peak Performance, W</th>
<th>T_{La}, W</th>
<th>Peak Blood Lactate, mmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>NG</td>
<td>316.2 ± 9.4*</td>
<td>133.8 ± 7.5†</td>
<td>12.0 ± 0.4†</td>
</tr>
<tr>
<td>GD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>335.8 ± 12.8</td>
<td>155.6 ± 8.1</td>
<td>8.8 ± 0.6</td>
</tr>
<tr>
<td>PO</td>
<td>369.1 ± 14.9</td>
<td>140.9 ± 6.8</td>
<td>10.1 ± 0.6</td>
</tr>
<tr>
<td>Asp</td>
<td>348.8 ± 13.2</td>
<td>189.9 ± 8.2</td>
<td>9.6 ± 0.5</td>
</tr>
</tbody>
</table>

Values are means ± SD. T_{La}, lactate threshold; NG, normal glycogen; GD, glycogen depleted; IV, intravenous glucose; PO, oral glucose; Asp, placebo. NG vs. GD: *P < 0.05; †P < 0.01.

approximate F-test of which degrees of freedom depend on the sample size and the time period considered (i.e., 0–10th min of recovery). In addition, in each experiment, the Newman-Keuls (47) test was performed to compare the values measured during exercise with the value obtained at time 0. When appropriate, statistically significant differences between NG, PO, IV, and Asp for blood La, Glc, Hct, plasma CA, Ins, FFA, and Glyc were determined by two-way analysis of variance (ANOVA) for repeated measures followed by summary t-tests, using the BMDP386 statistical software program (6).

RESULTS

Mean overall performances were significantly improved in all GD groups compared with their previous performances in the NG state (P < 0.04; Table 1). Peak performances during the incremental test used for V\textsubscript{O\textsubscript{2}max} measurement and during the test considered as representative of exercise in NG conditions were similar [P = not significant (NS)], suggesting that no significant training effect was present. Indeed, the difference between the load at which the anaerobic threshold (AT; determined from plots of the CO\textsubscript{2} production-to-O\textsubscript{2} consumption ratio) occurred and the load corresponding to T_{La} from the La curve during the NG exercise bout did not exceed 20 W for any given subject [mean 11.7 ± 3.7 (SD) W]. Furthermore, no significant differences in performance were observed among the three GD groups (Table 1). However, a shift to the right in La-power relationships occurred in all GD subjects (NG vs. IV, PO, and Asp: P < 0.01 ANOVA; Table 1, Fig. 1). Of note, higher heart rates were measured in the IV group during exercise compared with either Asp or NG (Table 2).

Glc concentrations were similar in both NG and GD groups before Glc administration (T\textsubscript{0–2}). At exercise onset, Glc concentrations were highest in IV and lowest in both NG and Asp (Fig. 2A). In NG and Asp subjects, exercise was associated with minimal changes in Glc over time. In contrast, rapid decreases in Glc to levels below those measured at T\textsubscript{0–2} occurred in IV (P < 0.01). Similar, although slower, decreases were measured in the PO group such that nadir Glc occurred at T\textsubscript{0} (Fig. 2A). Plasma Ins concentrations were similar in all groups at T\textsubscript{0–2} and were significantly increased at T\textsubscript{0} in IV and PO. Ins levels decreased over time in all groups during exercise but remained significantly above Asp in both IV and PO despite concomitant lower Glc concentrations (Fig. 2B). Thus Glc/Ins ratios were markedly reduced in subjects receiving Glc (Fig. 2D). Glc concentrations increased with exercise intensity (P < 0.03), but no significant differences occurred among groups (Fig. 2D). FFA concentrations were similar at T\textsubscript{0–2} in all groups but were markedly increased at T\textsubscript{0} in Asp (P < 0.01) and decreased in both IV and PO during the period from T\textsubscript{0} to T_{La} (Table 3). At exercise loads above T_{La}, FFA decreased in Asp and increased in IV and PO (Table 3). Overall, Gly increases occurred during early exercise in all groups, reaching peak levels at T_{La} after which similar declines were measured (P = NS; Table 3).

Significant increases in sulfoconjugated and free Epi and NE occurred in all GD groups after reaching T_{La} with increasing exercise loads (Table 4, Fig. 3). However, Epi concentrations were significantly higher at T\textsubscript{e} in IV (P < 0.004), midrange in PO (P < 0.01 vs. IV; P < 0.02 vs. Asp or NG), and lowest in Asp and NG (Table 4). Conversely, free NE concentrations were highest in NG, Asp, and PO and lowest in IV (P < 0.003 vs. IV; Table 4, Fig. 3). Thus Epi/NE ratios were significantly higher in IV compared with any other group (P < 0.0001; Figs. 3 and 4). In addition, Epi/NE ratios were higher in Asp (0.30 ± 0.03) compared with NG (0.20 ± 0.02; P < 0.02). Free and conjugated DA levels increased at high-intensity loads. Such increases were particularly prominent in IV and PO at T\textsubscript{e} (Fig. 5, Table 4).

Nonlinear curve fitting of free Epi and NE vs. blood La concentrations revealed significant relationships for each subject within each treatment group, with mean squared regression coefficients ranging between 0.95 and 0.99 (Fig. 6). However, at any La concentrations >2 mmol/L, higher Epi would be predicted in IV compared with PO (P < 0.006) and Asp (P < 0.001). Conversely, lower NE would be expected in IV compared with Asp (P < 0.03) or PO (P < 0.006).

![Fig. 1. Blood lactate concentrations plotted against power in normal glycogen (NG; ○) or in glycogen-depleted subjects receiving intravenous glucose (IV; □), oral glucose (PO; △), or placebo (Asp; ■) during 2 h before a graded exercise test. Values are means ± SD. Nonlinear individual curve-fitting procedures revealed mean best fit curves as expressed by the following equations (NG vs. IV, PO, and Asp: P < 0.001). NG: y = 1.97 – 0.0152x + 0.00014x^2; r^2 = 0.99. IV: y = 1.67 – 0.0149x + 0.00011x^2; r^2 = 0.96. PO: y = 1.79 – 0.0156x + 0.00011x^2; r^2 = 0.98. Asp: y = 1.44 – 0.0134x + 0.0001x^2; r^2 = 0.99.](http://jap.physiology.org/)
DISCUSSION

In this study, intravenous administration of Glc in GD subjects in the 2 h preceding a graded maximal exercise was associated with marked alterations in Glc homeostasis characterized by lower blood Glc concentrations, relative hyperinsulinemia, and differential adrenergic and sympathetic activity recruitment. Thus Epi plasma concentrations were highest while NE plasma concentrations were lowest in IV on exhaustion.

Increased muscle glycogen content is associated with improved performances in prolonged submaximal exercise (1, 2, 15). However, glycogen depletion does not appear to modify performance or even electromyogram frequency characteristics during short-duration high-intensity exercise (12, 38). Current data further suggest that administration of a readily available carbohydrate, i.e., intravenous or oral Glc, to GD athletes does not incur modification of their maximal working capacity in a graded incremental test. Although our methodological approach, which included several familiarization sessions, does not completely exclude some potentially concealed training effect with certainty, the mechanisms underlying improved performances observed in GD athletes, irrespective of carbohydrate administration, are currently unclear. Nonetheless, because similar improvements in performance occurred in all GD treatment groups, differences in the pattern of plasma CA responses cannot be explained by the GD effect on performance.

Glc administration in GD subjects induced marked alterations of glycemic homeostasis. Before critical examination of potential mechanisms underlying such alterations, several points deserve comment. First, GD alone has been shown to alter Ins ability to stimulate muscle Glc transport (23, 42) and to enhance Glc transport by Ins-independent mechanisms, i.e., the contractile activity-dependent pathway (27). Second, NG athletes with a high and sustained level of training, such as those participating in this study, are more likely to demonstrate relative exercise-induced hyperglycemia, possibly mediated by increased adrenomedullary responsiveness and elevated Epi secretion (16). Such training-related adaptations will enhance mobili-

Table 2. Heart rates during a graded exercise test and at 10 min of recovery in normal glycogen athletes and in glycogen-depleted athletes receiving either oral or intravenous glucose or placebo in 2 h preceding exercise onset

<table>
<thead>
<tr>
<th>Condition</th>
<th>T0-2</th>
<th>T0</th>
<th>T8</th>
<th>TL8</th>
<th>Te</th>
<th>R'10</th>
</tr>
</thead>
<tbody>
<tr>
<td>GD</td>
<td>52.4 ± 4.7</td>
<td>62.2 ± 4.7</td>
<td>112.8 ± 15.0</td>
<td>143.5 ± 14.7</td>
<td>185.3 ± 13.9</td>
<td>79.9 ± 6.7</td>
</tr>
<tr>
<td>Asp</td>
<td>53.2 ± 5.1</td>
<td>59.5 ± 4.8</td>
<td>116.6 ± 11.2</td>
<td>151.6 ± 11.4</td>
<td>190.7 ± 10.4</td>
<td>87.5 ± 5.9</td>
</tr>
<tr>
<td>PO</td>
<td>51.8 ± 5.4</td>
<td>62.8 ± 4.9</td>
<td>122.4 ± 7.9*</td>
<td>158.5 ± 10.3*</td>
<td>194.9 ± 11.1*</td>
<td>94.2 ± 6.4*</td>
</tr>
<tr>
<td>IV</td>
<td>52.2 ± 4.9</td>
<td>63.1 ± 6.2</td>
<td>110.3 ± 9.8</td>
<td>146.3 ± 12.6</td>
<td>187.9 ± 14.8</td>
<td>82.9 ± 7.2</td>
</tr>
<tr>
<td>NG</td>
<td>52.2 ± 4.9</td>
<td>63.1 ± 6.2</td>
<td>110.3 ± 9.8</td>
<td>146.3 ± 12.6</td>
<td>187.9 ± 14.8</td>
<td>82.9 ± 7.2</td>
</tr>
</tbody>
</table>

Values are means ± SE given in beats/min. T0–2, 2 h before exercise onset; T0, exercise onset; T8, second 4-min exercise step; Te, time of exhaustion; R'10, 10-min passive recovery. *P < 0.05 vs. Asp or NG.

Fig. 2. Serum glucose levels (A), plasma insulin concentrations (B), glucose-to-insulin ratios (C), and plasma glucagon concentrations (D) during a graded exercise test. Values are means ± SD. ○, NG conditions (when available); ▲, PO subjects; ■, Asp subjects. T0–2, 2 h before exercise onset; T0, exercise onset; T8, second 4-min exercise step; TL8, lactate threshold; Te, time of exhaustion; R'10, 10-min passive recovery. Glucose: IV vs. NG or Asp: P < 0.001 at T0, T8, TL8, and Te and T0 vs. PO vs. NG or Asp: P < 0.01 at T0 and Te. Insulin: IV and PO vs. NG or Asp: P < 0.001 at T0, T8, TL8, T0, and R'10. Glucose-to-insulin ratios: IV and PO vs. NG or Asp: P < 0.001 at T0, TL8, and T0, and R'10. Glucagon: T0 vs. Te: P < 0.03 in Asp, IV, and PO; at T0: Asp vs. PO: P = 0.12; Asp vs. IV: P = 0.051.
during the 2 h preceding exercise

everything else indicated that the use of identical training and exercise parameters in our three GD groups, the use of identical exercise protocols, and the similar work achieved during graded exercise rule out the possibility that these factors might have influenced any of the potential regulatory mechanisms discussed above. The only obvious differences among the GD groups are in the administration of Glc supplements and the route of administration. Thus our primary explanation for the differing glucoregulation in IV, PO, and Asp probably lies in the dysregulatory effect induced by introduction of carbohydrate within 2 h of exercise. Our results confirm and further extend on previous work by Montain et al. (22), indicating that enhanced susceptibility to hypoglycemia is likely in the early period after carbohydrate loading and that this phenomenon is not modified by muscle glycogen content. In addition, for identical carbohydrate loads, the magnitude of hyperglycemia and associated residual hyperinsulinemia determined by the route of carbohydrate administration appear to potentiate the effect of early exercise on Glc homeostasis (22).

The important role played by CA in adjustment processes to dynamic homeostatic disturbances induced by variable intensity exercise is now firmly established (4, 7). The close similarity between inflections of blood La and CA concentrations during graded exercise further suggests that a causal relationship between these two measures may be in place (18, 20). In contrast with Epi, NE plays a dual role as a neurotrans-

ization of hepatic gluconeogenesis and decrease muscle Glc uptake (14, 43). Third, both carbohydrate oxidation and adipose tissue lipolysis and FFA concentrations during exercise are extremely sensitive to prior fasting duration. Indeed, shorter latencies and FFA differences between meals and exercise bouts elicited lower blood Glc concentrations in conjunction with plasma Ins reductions of smaller magnitude, thus creating inappropriately high Ins, which in turn might further exacerbate hypoglycemia by increasing Glc transport into the cell. The more severe reduction in Glc levels would also elicit further adrenomedullary recruitment to preserve circulating Glc levels (22, 34). Interestingly, decreases in blood Glc early after a meal were more pronounced in trained compared with untrained subjects and demonstrated a clear exercise-intensity dependency (22). Finally, activation of mechano- and metaboreceptors and corresponding nerve afferents in exercising muscle may also provide neural feedback inputs allowing for fine hormonal and metabolic adjustments of Glc regulation (40). The similarity of training and endurance characteristics in our three GD groups, the use of identical exercise protocols, and the similar work achieved during graded exercise rule out the possibility that these factors might have influenced any of the potential regulatory mechanisms discussed above. The only obvious differences among the GD groups are in the administration of Glc supplements and the route of administration. Thus our primary explanation for the differing glucoregulation in IV, PO, and Asp probably lies in the dysregulatory effect induced by introduction of carbohydrate within 2 h of exercise. Our results confirm and further extend on previous work by Montain et al. (22), indicating that enhanced susceptibility to hypoglycemia is likely in the early period after carbohydrate loading and that this phenomenon is not modified by muscle glycogen content. In addition, for identical carbohydrate loads, the magnitude of hyperglycemia and associated residual hyperinsulinemia determined by the route of carbohydrate administration appear to potentiate the effect of early exercise on Glc homeostasis (22).

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Table 4. Free and sulfoconjugated plasma catecholamine concentrations at various times points during graded exercise in glycogen-depleted subjects who received either oral glucose, intravenous glucose, or placebo during the 2 h preceding exercise

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mitter in the sympathetic nervous system and as a hormone. Thus high-intensity exercise will induce a substantial sympathetic response resulting in NE spill-over to the systemic circulation (17) and will also elicit Epi release from the adrenal medulla (18, 31). Interestingly, despite their relatively different roles, NE and Epi do exhibit similar relationships with La in both NG and GD subjects (26). Such concordance was also found in this study for NG, PO, and Asp. However, in IV, preferential activation of adrenal mechanisms with concurrent diminution of sympathetic recruitment induced disproportionately higher Epi/NE ratios, such that the linear relationships between Epi and La and NE and La were significantly altered. The disproportionate elevation of Epi is considered to be representative of adrenomedullary secretion, an assumption that is further strengthened by the enhanced elevation of DA levels in IV. Although the exact origin of plasma DA in exercise remains elusive, the adrenal glands remain the major source of DA, with or without potential contributions from neural crest-derived tissue (25, 35). Our findings, therefore, suggest that the dose relationships between CA and La may be either dependent on, or at least modified by, concurrent activation patterns of the various mechanisms responsible for Glc homeostasis. In other words, we postulate that the primary stimulus leading to Epi secretion is the need to increase metabolic substrate availability to muscle during intense exercise. Such Epi response will in turn exert secondary effects, i.e., increased glycogenolysis, and the enhanced Glc delivery to the circulation will favor La production from glycolysis (28). Indeed, continuous Glc administration during exercise reduces Epi secretion (8). An additional consideration, particularly when exercise occurs at work rates above the AT, resides in...
increased hepatic sensitivity to Gluc by exercise-induced falls in Ins has been demonstrated and could counterbalance potential differences in Gluc secretion across treatment groups (43), such that lower Gluc levels would be expected with lower Ins concentrations. Indeed, such a trend was present (Fig. 2).

The disparity in FFA levels between Asp and groups receiving Glc may indicate the restraining role exerted by Ins on adipocyte lipolysis and consequent oxidation of fatty acids in the muscle (Glc-FFA cycle) (9, 41). Conversely, the increase in FFA toward exhaustion could indicate a more preponderant CA role during intense exercise or muscular fatigue.

The Epi/NE ratios at T_e in NG were significantly lower than in GD Asp. We interpret this finding as indicative of a diminished NE response in GD conditions. This reduced NE spill to the peripheral circulation probably results from lower La levels leading to an attenuation of metabotropic receptor activation and type III/IV afferent fiber stimulation and consequent reductions in exercise-induced sympathetic outflow (32). Thus it is conceivable that increased Ins sensitivity induced by GD conditions (23) and higher Ins levels elicited by intravenous Glc administration may rapidly act to create a propensity for the development of hypoglycemia, which, in turn, triggers adrenal catecholaminergic recruitment to enhance glycogenolysis and gluconeogenesis. Further support for this hypothesis stems from recent findings by Davis and colleagues (5) that CA secretion is amplified and hepatic Glc production is maintained during equivalent hypoglycemia, when a greater increase in physiological levels of Ins is allowed.

The overall trend of sulfonconjugated CA changes was similar to that observed with free CA, such that both conjugated and free Epi and NE increased in each treatment group at loads greater than or equal to T_La. However, increases in free CA were markedly larger than those of conjugated CA (Table 4). Such changes in CA as a result of short-lasting high-intensity exercise have been previously reported for NE but not for Epi or DA (36), and their significance during acute exercise remains unclear.

According to several recent studies (20, 26, 45), La concentrations should have been modified by such cascade of events; i.e., higher elevations of free Epi in IV should have induced La enhancements, at least at Epi concentrations >220–250 pg/ml (45). However, such increased La responses did not occur. We submit the hypothesis that NE may provide a more accurate, although indirect, indicator of intramuscular metabolic events, i.e., La efflux, leading to type III/IV fibers (29) afferent sympathetic reflex pathways activation. In contrast, Epi concentrations may preferentially point to adrenomedullary activation as a function of Glc homeostasis. The close correlation between Epi and La may not indicate a causal relationship as previously suggested (20) and could reflect an epiphenomenon instead.

In summary, we have demonstrated that intravenous administration of a relatively modest carbohydrate load to GD athletes immediately before a maximal
exercise exerts profound and differential modifications of catecholaminergic recruitment patterns during exercise compared with the administration of a similar oral Glc load. A relative hyperinsulinemic state induced by intravenous Glc leads to preferential adrenomedullary recruitment and Epi secretion without parallel NE elevations. These findings suggest that the magnitude of hyperinsulinemia at exercise onset exerts dissociative effects on glucoregulatory and sympathetic activating responses.

The assistance of Jean Marie Lechevalier and the technical help of Both Louha during the exercise protocol and of R. M. Cottet-Emard, B. Sempore, A. Vouillarmet, and D. Desplanches in the performance of plasma assays is greatly appreciated.

This work was supported in part by a grant from the Programme Pluriannuel de Recherche, Région Rhône-Alpes, France. D. Gozal is supported by National Institute of Child Health and Human Development Grant HD-01072 and Maternal and Child Health Bureau Grant supported by National Institute of Child Health and Human Development.


