Effects of plasma epinephrine on fat metabolism during exercise: interactions with exercise intensity

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Mora-Rodriguez, Ricardo, and Edward F. Coyle. Effects of plasma epinephrine on fat metabolism during exercise: interactions with exercise intensity. Am J Physiol Endocrinol Metab 278: E669–E676, 2000.—This study determined the effects of elevated plasma epinephrine on fat metabolism during exercise. On four occasions, seven moderately trained subjects cycled at 25% of peak oxygen consumption (V\(_{\text{O}_2}\) peak) for 60 min. After 15 min of exercise, subjects were intravenously infused with low (0.96 ± 0.10 nM), moderate (1.92 ± 0.24 nM), or high (3.44 ± 0.50 nM) levels (all P < 0.05) of epinephrine to increase plasma epinephrine above control (Con; 0.59 ± 0.10 nM). During the interval between 35 and 55 min of exercise, lipolysis [i.e., rate of appearance of glycerol] increased above Con (4.9 ± 0.5 µmol·kg\(^{-1}·\)min\(^{-1}\)) with low, moderate, and high (6.5 ± 0.5, 7.1 ± 0.8, and 10.6 ± 1.2 µmol·kg\(^{-1}·\)min\(^{-1}\), respectively; all P < 0.05) levels of epinephrine despite simultaneous increases in plasma insulin. The release of fatty acid into plasma also increased progressively with the graded epinephrine infusions. However, fatty acid oxidation was lower than Con (11.1 ± 0.8 µmol·kg\(^{-1}·\)min\(^{-1}\)) during moderate and high levels (8.7 ± 0.7 and 8.1 ± 0.9 µmol·kg\(^{-1}·\)min\(^{-1}\), respectively; P < 0.05). In one additional trial, the same subjects exercised at 45% V\(_{\text{O}_2}\) peak without epinephrine infusion, which produced a plasma epinephrine concentration identical to low levels. However, lipolysis was lower (11.8 ± 0.6 vs. 6.5 ± 0.5 µmol·kg\(^{-1}·\)min\(^{-1}\); P < 0.05). In conclusion, elevations in plasma epinephrine concentration during exercise at 25% of V\(_{\text{O}_2}\) peak progressively increase whole body lipolysis but decrease fatty acid oxidation. Last, increasing exercise intensity from 25 to 45% V\(_{\text{O}_2}\) peak attenuates the lipolytic actions of epinephrine.

stable isotopes; indirect calorimetry; lipolysis; free fatty acid kinetics

EPINEPHRINE has been used in many situations as a tool to stimulate fat metabolism (12). Intravenous epinephrine infusion has been used to test differences in lipolysis between genders or between fat depots in the same individual (20). Epinephrine has also been used to determine if endurance training increases lipolytic sensitivity (17) and to test if obesity is caused by a reduction in hormonal stimulation of lipolysis (40). The information derived from those studies has greatly helped understanding of the hormonal regulation of lipolysis in humans. However, all of these studies have been conducted on resting humans. Surprisingly, little is known about the whole body lipolytic response to epinephrine administration during exercise.

The increase in lipolysis within subcutaneous adipose tissue with the transition from rest to mild exercise appears to be stimulated by epinephrine through beta receptor activation (2) and by the lowering of plasma insulin (15). However, the pattern with which whole body lipolysis increases with increased exercise intensity (11) and the mechanisms by which triglyceride stored within adipose tissue and within muscle fibers is hydrolyzed remain unclear. It is well known that fatty acid oxidation increases when exercise intensity increases from low to moderate levels and that it declines with intense exercise in association with accelerated carbohydrate metabolism (8, 33). It is logical that lipolysis might follow the same pattern. Raising exercise intensity from 25 to 65% maximal oxygen consumption (V\(_{\text{O}_2}\) max) appears to increase lipolysis in association with increasing plasma epinephrine concentrations (33). This association suggests that the increases in plasma epinephrine might be responsible for the increases in lipolysis when exercise is increased from low to moderate intensities. However, when exercise intensity increases from 65 to 85% V\(_{\text{O}_2}\) max, lipolysis plateaus despite further large increases in plasma epinephrine concentration (33).

This last observation suggests that either 1) lipolysis is maximally stimulated by the plasma epinephrine levels achieved at 65% of V\(_{\text{O}_2}\) max or 2) epinephrine stimulation of lipolysis is counteracted by increases in exercise intensity that somehow suppress lipolysis. No study, to our knowledge, has directly quantified lipolysis when increasing plasma epinephrine levels during exercise. Furthermore, a possible interaction between plasma epinephrine levels as a stimulator of lipolysis and exercise intensity as an inhibitor of lipolysis has not been considered.

The main aim of the present study was to determine the effect of graded elevations of plasma epinephrine concentration on lipolysis, the rate of appearance (R\(_{a}\)) of free fatty acid (FFA), and fatty acid oxidation during low-intensity exercise. The effect of increasing plasma epinephrine levels on reesterification (i.e., nonoxidative lipolysis) was also determined. To make these determinations, we performed three intravenous epinephrine infusion trials at increasing doses (low, moderate, and
To raise plasma epinephrine concentrations progressively yet within physiological values observed during aerobic exercise at ~45, 65, and 85% of peak oxygen consumption \( (\text{VO}_2\text{peak}) \). The exercise intensities used in this investigation (i.e., 25 and 45% of \( \text{VO}_2\text{peak} \)) correspond to those which people typically choose when exercising for health and body fat reduction.

Another aim of the present study was to separate the lipolytic effects of increasing plasma epinephrine from the lipolytic effects of increasing exercise intensity. The hypothesis tested was that increases in exercise intensity attenuate the lipolytic effects of raising plasma epinephrine concentrations.

**METHODS**

Subjects. Seven moderately trained men \( (n = 4) \) and women \( (n = 3) \) participated in this experiment. Subjects were healthy and were not taking any medication. The women were premenopausal and were not taking oral contraceptives. In the women, testing was performed in the follicular phase. The subject’s mean age, \( \text{VO}_2\text{peak} \), peak heart rate while cycling, body weight, and percent body fat were 29 ± 7 yr, 52.2 ± 5 ml·kg\(^{-1}\)·min\(^{-1}\), 187 ± 10 beats/min, 68.6 ± 11 kg, and 15.9 ± 7%, respectively. Each of the seven subjects participated in five treatments. A subset sample of five male subjects was recruited and participated in only two treatments. These subjects were recruited to enlarge our sample and be able to test differences that we found close to significance after testing the seven original subjects. Their characteristics were similar to the original subjects. Mean age, \( \text{VO}_2\text{peak} \), peak heart rate while cycling, body weight, and percent body fat were 27 ± 8 yr, 63.8 ± 8 ml·kg\(^{-1}\)·min\(^{-1}\), 189 ± 9 beats/min, 74.6 ± 10 kg, and 13.4 ± 4%, respectively. Before participation in the testing, subjects were informed of the possible risks involved and signed a consent form approved by the Internal Review Board of the University of Texas at Austin.

Preliminary testing, diet, and training. \( \text{VO}_2\text{peak} \), was determined while subjects cycled an ergometer (model 819; Monark, Varberg, Sweden) using an incremental protocol lasting 7–10 min. Two days before the first experimental trial, subjects performed a standardized training bout (40 min of cycling at 45% \( \text{VO}_2\text{peak} \)) to ensure homogeneity of the last exercise bout. Subjects exactly replicated the last meal before each test and restrained from training during the 24 h before the trials.

Experimental procedure. Subjects arrived at the laboratory in the morning, after an overnight fast (i.e., 12 h). Teflon catheters were inserted in an antecubital vein in each arm for infusion and blood sampling. A heating pad was affixed to the sampling forearm to obtain arterialized blood. After 60 min of resting isotope infusion (see below), subjects pedaled a cycle ergometer (Jaeger-Ergotest) for 60 min at either low or moderate intensity.

Epinephrine infusion. Fifteen minutes into the exercise period, epinephrine (Adrenalin, Chloride Solution; Parke-Davis) was infused at a constant rate until the end of the exercise period at 60 min. Four of the experimental trials only differed in the rate of epinephrine infusion: 0.005 µg·kg\(^{-1}\)·min\(^{-1}\) (LOW), 0.015 µg·kg\(^{-1}\)·min\(^{-1}\) (MID), 0.045 µg·kg\(^{-1}\)·min\(^{-1}\) (HIGH), or no epinephrine infusion (CON 25%). These four trials were performed at an intensity that elicited 25% of the subject \( \text{VO}_2\text{peak} \). One additional trial was performed at 45% of \( \text{VO}_2\text{peak} \) without epinephrine infusion (CON 45%). During all five trials, electrocardiogram tracing was monitored throughout the testing period to confirm that normal sinus rhythm was maintained. Trials were separated by at least 48 h, and the order of the trials was randomized.

Isotope infusion. Upon catheterization, blood was sampled (4 ml) for determination of background isotopic enrichment. Next, a primed constant-rate infusion of \([2\text{H}_5]\)glycerol (prime = 3.7 µmol/kg; constant = 0.25 µmol·kg\(^{-1}\)·min\(^{-1}\); Isotec, Miamisburg, OH) and [1-1\(^{3}\text{C}\)]palmitate (Cambridge Isotope Laboratories, Andover, MA) bound to 5% human albumin (0.04 µmol·kg\(^{-1}\)·min\(^{-1}\); no prime) was started using calibrated syringe pumps (Harvard Apparatus, South Natick, MA). These stable isotope infusions were delivered during 60 min of rest to achieve isotopic equilibrium and maintained at their constant rate throughout exercise. During the CON 45% trial, \([2\text{H}_5]\)glycerol was the only stable isotope infused.

Blood sampling and analysis. For determination of resting glycerol and palmitate kinetics, blood samples were withdrawn 5 min before and immediately before exercise. During exercise, blood samples (−14 ml) were collected every 10 min. After collection, blood samples were divided into four different prechilled tubes according to the constituents to be analyzed. For each tube, plasma was separated in tubes containing 0.2 ml of EDTA (25 mg/ml) and were analyzed for isotopic enrichment of the hepatofluorobutyric anhydride derivative of glycerol (13) and the methyl ester derivative of palmitate (14) using gas chromatography-mass spectrometry (Hewlett-Packard 5989). Five milliliters of plasma were placed in tubes containing 0.25 ml of EDTA (25 mg/ml) for determination of plasma glycerol (fluorometric assay; see Ref. 9) and plasma FFA (colorimetric assay; see Ref. 30). Three milliliters of blood were mixed in a tube containing 0.3 ml of a solution of reduced glutathione (4.5 mg), sodium heparin (50 IU), and 20 µl of 0.24 M EGTA for determination of epinephrine and norepinephrine concentration (HPLC with electrochemical detection; see Ref. 16). The final 2 ml of each blood sample were placed in a test tube containing 0.2 ml of an EDTA (24 mg/ml)-aprotinin (0.5 tissue inhibitor units/ml) solution and were analyzed for plasma insulin concentration (RIA; Linco Research, St. Charles, MO).

Measurements of gas exchange. Periodically, during rest and exercise, subjects inhaled through a two-way Daniels mask while inspired air volume was measured with a Parkinson-Cowan CD4 dry gas meter (Rayfield Equipment, Waitsfield, VT). The expired gases were continuously sampled from a mixing chamber and were analyzed for oxygen (Applied Electrochemistry, SA3; Ametek, Pittsburgh, PA) and carbon dioxide (LB2; Beckman, Schiller Park, IL). These instruments were interfaced to a computer for calculation of the rate of oxygen consumption and rate of carbon dioxide production.

Calculations. Plasma glycerol and palmitate kinetics were calculated using the one-pool model non-steady-state equations of Steele (38) modified for use with stable isotopes

\[
R_a = \left[ F - V_a/(C/(1 + E_1 + E_2/2)) \times ([E_2 - E_j]/(t_2 - t_j))\right]/(E_1 + E_j)/2
\]

\[
R_d = R_a - \left[ V_d/(C_2 - C_1)/(t_2 - t_1)\right]
\]

where \( F \) is the isotope infusion rate, \( V_a \) is the effective volume of distribution, \( R_d \) is the rate of disposal, \( C \) is the plasma concentration of the trace, and \( (E_2 - E_j)/(t_2 - t_j) \) is the change in enrichment (i.e., \( E = \text{tracer-to-tracer ratio} \)) between two consecutive samples \( (t_2 - t_1 \approx 10 \text{ min}) \). \( V_a \) was assumed to be 230 ml/kg for glycerol and 40 ml/kg for palmitate based on previous reports (33). The rate of appear-
Table 1. Plasma concentration of epinephrine, norepinephrine, and insulin after 60 min of exercise at 25% \( V_{\text{O2peak}} \) without (CON 25%) or with intravenous epinephrine infusion at rates of LOW, MID, and HIGH or at 45% \( V_{\text{O2peak}} \).

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Plasma epinephrine, nM</th>
<th>Plasma norepinephrine, nM</th>
<th>Plasma insulin, ( \mu U/ml )</th>
</tr>
</thead>
<tbody>
<tr>
<td>CON 25%</td>
<td>0.59 ± 0.10</td>
<td>1.8 ± 0.3</td>
<td>4.4 ± 0.7</td>
</tr>
<tr>
<td>LOW</td>
<td>0.96 ± 0.10*</td>
<td>1.7 ± 0.3</td>
<td>5.9 ± 0.9</td>
</tr>
<tr>
<td>MID</td>
<td>1.92 ± 0.24†</td>
<td>2.2 ± 0.5</td>
<td>6.8 ± 1.0*</td>
</tr>
<tr>
<td>HIGH</td>
<td>3.44 ± 0.50‡</td>
<td>2.2 ± 0.4</td>
<td>7.2 ± 1.4†</td>
</tr>
<tr>
<td>CON 45%</td>
<td>0.96 ± 0.10*</td>
<td>3.6 ± 0.9†</td>
<td>4.1 ± 0.5</td>
</tr>
</tbody>
</table>

Values are means ± SE for \( n = 7 \) subjects. \( V_{\text{O2peak}} \), peak oxygen consumption; CON 25%, 25% \( V_{\text{O2peak}} \) with no epinephrine infusion; LOW, 0.005 \( \mu g \cdot kg^{-1} \cdot min^{-1} \) epinephrine infusion; MID, 0.015 \( \mu g \cdot kg^{-1} \cdot min^{-1} \) epinephrine infusion; HIGH, 0.045 \( \mu g \cdot kg^{-1} \cdot min^{-1} \) epinephrine infusion; CON 45%, 45% of \( V_{\text{O2peak}} \) with no epinephrine infusion. *Significantly different from CON 25%, \( P < 0.05 \); †significantly higher than LOW, \( P < 0.05 \); ‡significantly higher than MID, \( P < 0.05 \).

Fig. 1. The rate of glycerol appearance (\( R_a \) glycerol) during exercise at 25% \( V_{\text{O2peak}} \) without (CON 25%) or with intravenous epinephrine (Epi) infusion beginning at 15 min at rates of LOW, MID, and HIGH (0.005, 0.015, and 0.045 \( \mu g \cdot kg^{-1} \cdot min^{-1} \), respectively). Values are means ± SE for \( n = 7 \) subjects. *Significantly higher than CON 25%, \( P < 0.05 \); †significantly higher than LOW, \( P < 0.05 \); ‡significantly higher than MID, \( P < 0.05 \).
and high substantially increased Ra FFA above all of the other trials (22.1 ± 3.6 μmol·kg⁻¹·min⁻¹; all P < 0.05). Plasma glycerol concentration responded similarly to Ra glycerol.

A stable Ra FFA was observed during the interval between the 35 and 55 min of exercise in all trials (Fig. 2). LOW modestly elevated Ra FFA above CON (12.3 ± 1.7 vs. 10.1 ± 1.2 μmol·kg⁻¹·min⁻¹, respectively; P < 0.05). MID clearly increased Ra FFA above CON and LOW (15.7 ± 2.1 μmol·kg⁻¹·min⁻¹; P < 0.05), and HIGH substantially increased Ra FFA above all of the other trials (22.1 ± 3.6 μmol·kg⁻¹·min⁻¹; all P < 0.05). Plasma FFA concentration responded similarly to Ra FFA with progressive elevations from CON (0.41 ± 0.10 mM at 60 min) during LOW, MID, and HIGH (0.57 ± 0.04, 0.62 ± 0.10, and 0.89 ± 0.10 mM, respectively; P < 0.05). Ra FFA also increased above CON (9.8 ± 1.2 μmol·kg⁻¹·min⁻¹) gradually with LOW, MID, and HIGH (12.0 ± 1.6, 14.8 ± 2.0, and 20.1 ± 3.2 μmol·kg⁻¹·min⁻¹, respectively; P < 0.05).

Fatty acid oxidation during exercise at 25% VO₂peak.

During the first 10 min of epinephrine infusion, fatty acid oxidation declined below CON (9.9 ± 0.3 μmol·kg⁻¹·min⁻¹) gradually with LOW, MID, and HIGH (8.1 ± 0.6, 3.6 ± 0.9, and 1.5 ± 0.9 μmol·kg⁻¹·min⁻¹, respectively; P < 0.05; Fig. 3). During the interval between 35 and 55 min of exercise, fatty acid oxidation increased in all trials but remained lower than CON (11.1 ± 0.8 μmol·kg⁻¹·min⁻¹) during MID and HIGH (8.7 ± 0.7 and 8.1 ± 0.9 μmol·kg⁻¹·min⁻¹, respectively; P < 0.05). In contrast, during LOW, fatty acid oxidation returned to CON levels and even tended to increase above CON (11.7 ± 0.7 μmol·kg⁻¹·min⁻¹, n = 7; P < 0.08). When five additional subjects were added to the original data set (i.e., n = 12), fatty acid oxidation during LOW was significantly higher than during CON for the last 30 min of exercise (12.9 ± 1.0 vs. 11.4 ± 1.0 μmol·kg⁻¹·min⁻¹, respectively, n = 12; P < 0.05).

Reesterification during exercise at 25% VO₂peak.

During the interval between the 35 and 55 min of exercise, total reesterification of fatty acid (i.e., Ra glycerol × 3 – fatty acid oxidation) increased progressively above CON (3.6 ± 0.2 μmol·kg⁻¹·min⁻¹) with the graded LOW, MID, and HIGH epinephrine infusions (7.8 ± 0.6, 12.6 ± 0.7, and 23.7 ± 1.1 μmol·kg⁻¹·min⁻¹, respectively; P < 0.05; Fig. 4). During CON and LOW, calculated minimal plasma FFA reesterification (i.e., Ra FFA – FFA oxidation) was nearly zero since the rates of Ra FFA matched total fatty acid oxidation rates. However, minimal plasma FFA reesterification increased above CON during MID and HIGH (6.6 ± 0.5 and 12.9 ± 0.9 μmol·kg⁻¹·min⁻¹, respectively; P < 0.05).

Fat metabolism during exercise at 25 vs. 45% VO₂peak.

At a similar plasma epinephrine concentration, lipolysis was lower during CON 45% VO₂peak than during LOW 25% VO₂peak (5.5 ± 0.6 vs. 6.5 ± 0.5 μmol·kg⁻¹·min⁻¹, respectively; P < 0.05; Fig. 5). However, fatty acid oxidation was higher during CON 45% VO₂peak, and thus total reesterification was lower during CON 45% VO₂peak than during LOW 25% VO₂peak (i.e., 2.1 ± 0.1 vs. 7.8 ± 0.6 μmol·kg⁻¹·min⁻¹, respectively; P < 0.05; Fig. 6). Without epinephrine infusion, increases in exercise intensity from 25 to 45% of VO₂peak increased lipolysis and fatty acid oxidation similarly. As a consequence, total reesterification remained similar during 25 and 45% VO₂peak exercise (3.6 ± 0.2 vs. 2.1 ± 0.1 μmol·kg⁻¹·min⁻¹, respectively; Fig. 6). However, the excessive elevation of plasma epinephrine during LOW 25% resulted in a large increase in total reesterification due to the simultaneous increase in lipolysis and reduction in fatty acid oxidation.

**DISCUSSION**

The first major finding of the present experiment is that graded epinephrine infusion progressively increased lipolysis (i.e., Ra glycerol) and the release of fatty acid into plasma (i.e., Ra FFA) during low-intensity exercise (i.e., 25% of VO₂peak). Lipolysis re-
sponded to small (i.e., LOW) and large (i.e., HIGH) elevations in plasma epinephrine without an apparent plateau response (Fig. 4). In contrast, when plasma epinephrine concentrations are elevated to levels similar to HIGH (i.e., ~3 nM) by increasing exercise intensity (i.e., from 65 to 85% VO2 max), lipolysis plateaus (33) and Rd FFA is reduced (22). This led to the speculation that an increase in exercise intensity attenuates epinephrine stimulation of lipolysis.

To directly test this hypothesis, lipolysis was presently compared during exercise at 45% of VO2 peak with that at 25% of VO2 peak with epinephrine infusion, so as to match plasma epinephrine levels (i.e., LOW; see Fig. 5). The second major finding of the present study was that at the same plasma epinephrine concentration (i.e., 0.96 ± 0.10 nM), lipolysis was significantly lower at 45 than at 25% of VO2 peak. However, the mechanism by which increasing exercise intensity reduces epinephrine stimulation of lipolysis is unclear.

Fatty acid oxidation declines when exercise intensity is increased from moderate to high levels (8, 20, 33, 37), and it would seem appropriate for the concomitant large increases in plasma epinephrine concentration to be somehow restrained from progressive stimulation of lipolysis. Otherwise, an excess of fatty acids would be made available during intense exercise, a condition that appears to actively limit fatty acid oxidation in association with a high glycolytic flux (7, 37). Fatty acids released in lipolysis can only be oxidized or reesterified. To prevent the accumulation of FFA in plasma and in the interstitial space, of which there is only a very limited storage capacity, it therefore seems possible for some factor associated with increasing exercise intensity to restrain epinephrine from excessive stimulation of lipolysis.

During CON 25% VO2 peak and during LOW, the rates of plasma Rd FFA were equal to FFA oxidation. Because these rates matched, it is possible that fatty acid oxidation was supplied exclusively by plasma Rd FFA.
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V˙O2 peak clearly increased total and minimal plasma epinephrine response during exercise at 25% intensity (Fig. 4). In contrast, increases in epinephrine concentration by increasing exercise intensity (i.e., CON 25% and CON 45% of VO2 peak) stimulated lipolysis simultaneously with fatty acid oxidation, and thus total reesterification was maintained at low levels (Fig. 6).

Any amount of epinephrine infused that increased plasma epinephrine concentration above normal control levels (i.e., LOW, MID, and HIGH) increased total reesterification rates (Fig. 4). This implies that, in these young, healthy, and moderately trained subjects, their normal plasma epinephrine response to exercise is appropriate for matching lipolysis to fatty acid oxidation, thus minimizing total reesterification. An excessive epinephrine response during exercise at 25% of VO2 peak clearly increased total and minimal plasma FFA reesterification (Fig. 4). Therefore, an excessive epinephrine response during low-intensity exercise does not seem beneficial for stimulating fat oxidation and increases the mobilization of fatty acid in plasma (i.e., Ra FFA), whose fate is reesterification rather than oxidation.

The increased plasma epinephrine concentration with increased exercise intensity serves numerous metabolic and cardiovascular functions (e.g., increased cardiac output and liver gluconeogenesis), and it certainly functions to stimulate lipolysis during exercise (2). The present results further indicate that epinephrine, per se, stimulates lipolysis during exercise to a level that is in excess of fatty acid oxidation. It appears, therefore, that some other factors associated with increased exercise intensity beneficially attenuate the epinephrine stimulation of lipolysis and thus minimize reesterification. Excessive lipolysis during exercise has been observed in the elderly and untrained population, who are also characterized as having elevated plasma catecholamine levels (27, 32). It is possible that the excessive lipolysis observed in these populations is originated by the overproduction of catecholamines. In addition, during aging and in obesity, the antilipolytic effect of insulin is reduced, which may also contribute to the unrestrained lipolysis (21, 23). It has been suggested that excessive lipolysis and reesterification may contribute to the high-risk blood lipid profile observed in patients with diabetes or obesity (5). Interventions that reduce the catecholamine response to exercise (i.e., aerobic training) have been shown to reduce reesterification (32, 36).

It is becoming evident that adipose tissue blood flow (ATBF) is involved in the regulation of lipolysis (3). It has been shown that vasoconstriction of adipose tissue is accompanied by a decreased rate of lipolysis in adipocytes (1). In rats, increases in exercise intensity to high levels result in a redistribution of blood flow away from noncontracting muscle and adipose tissue (25). In humans, increases in exercise intensity can reduce conductance to the skin (39), the splanchnic area (34), and likely adipose tissue. Reductions in ATBF could prevent epinephrine from stimulating lipolysis and might possibly explain our observation that a given plasma epinephrine concentration reduced whole body lipolysis as exercise intensity increases from 25 to 45% VO2 peak. However, it is unknown if the mild elevation in exercise intensity from 25 to 45% of VO2 peak would be enough stimulus to reduce ATBF.

At rest, adipose tissue lipolysis is inhibited by α-adrenergic stimulation (2). Epinephrine and norepinephrine bind to α-adrenergic receptors, which could reduce their own stimulatory effect on lipolysis. Although epinephrine levels were similar during CON 45% and LOW 25% VO2 peak, norepinephrine levels were significantly elevated at the higher exercise intensity (CON 45%, Table 1). The higher plasma norepinephrine levels during CON 45% VO2 peak could have counteracted epinephrine lipolytic effects. However, during moderate-intensity exercise, α-adrenergic blockade does not appear to affect lipolysis in subcutaneous adipose tissue (2). The role of α-adrenergic receptors in whole body lipolysis during exercise remains unclear.

MID and HIGH epinephrine infusion elevated plasma insulin (i.e., 2.8 μU/ml, P < 0.05) above control levels (Table 1) in association with increases in plasma glucose levels (28). Lipolysis is very sensitive to increases in plasma insulin (4, 18), and reductions in lipolysis might occur with insulin elevation of only 2–3 μU/ml such as those observed during MID and HIGH. However, the elevation in plasma insulin levels during MID and HIGH did not prevent graded epinephrine infusion from progressively increasing lipolysis. Therefore, the potent antilipolytic effect of insulin in the present study was overwhelmed by the increase in plasma epinephrine concentration that apparently created the overall effect of progressively stimulating lipolysis. Nevertheless, the increasing levels of plasma insulin with the graded epinephrine infusion may have modulated the full effect of epinephrine-stimulated lipolysis.

Recent reports have suggested that Ra glycerol may underestimate whole body lipolysis due to utilization of glycerol within inactive muscle (19, 24). However, the low activity of glycerol kinase in mammalian skeletal muscle (29) makes large muscle glycerol utilization unlikely. During rest and low-intensity exercise, adipose tissue (rather than skeletal muscle) accounts for most of the lipolysis (24, 37). Although glycerol utilization by skeletal muscle is possible, glycerol utilization by adipose tissue it very unlikely. Human adipose tissue does not take up glycerol (6, 35), likely due to the low activity of glycerol kinase (26) and the inability of this tissue to utilize glycerol. It is unlikely that skeletal muscle glycerol utilization measurably affects plasma Ra glycerol during low-intensity exercise.

In the present experiment, the differences in Ra glycerol between trials were significant and large, occurred within a few minutes of epinephrine infusion, and were graded in accordance with the graded epinephrine infusion rates. Therefore, although Ra glycerol may not be an exact quantitative measure of whole body lipolysis, it appears to be sensitive to the increases
in plasma epinephrine concentration. A possible error incurred by the use of R\textsubscript{a} glycerol as a measurement of lipolysis should be similar in all trials, and thus the comparison among treatments and the conclusions derived should remain valid.

Elevations in lipolysis above CON levels by LOW rates of epinephrine infusion significantly increased fatty acid oxidation (i.e., 13\%, n = 12; Fig. 3) in association with increased plasma FFA concentration. After 15 min of LOW, epinephrine stimulation of carbohydrate oxidation decreased, which likely allowed the available fatty acid to be oxidized. It has been reported that increases in glycolytic flux directly impair the oxidation of plasma FFA during exercise (7, 37). During moderate-intensity exercise, increases in plasma epinephrine concentrations to high but physiological levels increase muscle glycogen utilization (10) and thus glycolytic flux. Apparently, epinephrine infusions that stimulated carbohydrate oxidation (i.e., MID and HIGH) did not permit increases in fatty acid oxidation despite high plasma FFA availability. This suggests that, when plasma epinephrine stimulates both lipolysis and glyco- genolysis, carbohydrate oxidation predominates over fatty acid oxidation that is reduced.

In summary, during low-intensity exercise (25% \(V\dot{O}_2\text{peak}\)), graded epinephrine infusion progressively stimulates lipolysis and plasma FFA mobilization. However, increases in exercise intensity (i.e., from 25 to 45% \(V\dot{O}_2\text{peak}\)) somehow counteract epinephrine from stimulating lipolysis. This creates a better match between lipolysis and fatty acid oxidation rates and thus reduces total reesterification.

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