Elevation of Plasma Epinephrine Concentrations Inhibits Proteolysis and Leucine Oxidation in Man via β-Adrenergic Mechanisms

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Abstract

The role of elevated plasma epinephrine concentrations in the regulation of plasma leucine kinetics and the contribution of β-receptors were assessed in man. Epinephrine (50 ng/kg per min) was infused either alone or combined with propranolol (β-blockade) into groups of six subjects fasted overnight; leucine flux, oxidation, and net plasma leucine forearm balance were determined during 180 min. Constant plasma insulin and glucagon concentrations were maintained in all studies by infusing somatostatin combined with insulin and glucagon replacements. Plasma leucine concentrations decreased from baseline during epinephrine infusion by 27±5 μmol/liter ($P < 0.02$) due to a 22±6% decrease in leucine flux ($P < 0.05$ vs. controls receiving saline) and to an increase in the metabolic clearance rate of leucine ($P < 0.02$). Leucine oxidation decreased by 36±8% ($P < 0.01$ vs. controls). β-Blockade abolished the effect of epinephrine on leucine flux and oxidation. Net forearm release of leucine increased during epinephrine ($P < 0.01$), suggesting increased muscle proteolysis; the fall of total body leucine flux was therefore due to diminished proteolysis in nonmuscle tissues, such as splanchnic organs. Nonoxidative leucine disappearance as a parameter of protein synthesis was not significantly influenced by epinephrine. Plasma glucose and FFA concentrations increased via β-adrenergic mechanisms ($P < 0.001$). The results suggest that elevation of plasma epinephrine concentrations similar to those observed in severe stress results in redistribution of body proteins and exerts a whole body protein-sparing effect; this may counteract catabolic effects of other hormones during severe stress.

Introduction

Sympathoadrenal activation during physical and emotional stress results in release of epinephrine and norepinephrine into the circulation (1). Heavy exercise and trauma have been reported to result in a 10–20-fold elevation of plasma epinephrine concentrations above resting values (2–4). Increased plasma catecholamine concentrations are associated with well-recognized changes in glucose (5), fat (6), and ketone body (7, 8) metabolism. Regarding the effects of catecholamines on protein metabolism, little is known from studies performed in humans in vivo. Epinephrine administration resulted in decreased plasma concentrations of branched-chain amino acids in normal and diabetic subjects (9). Miles et al. (10) demonstrated recently that epinephrine infusion into normal subjects decreased whole body proteolysis studied by tracer infusions of amino acids. However, epinephrine infusion resulted in increased plasma insulin concentrations which may have confounded epinephrine's effects.

The present study was designed to (*a*) determine the effect of hyperepinephrinemia on leucine plasma flux, oxidation, and nonoxidative disappearance using 1-[^{13}C]leucine infusions; (*b*) assess the contribution of muscle proteins in epinephrine's effect on whole body leucine kinetics by measuring net plasma leucine balance across the forearm; (*c*) determine the role of β-receptors in mediating epinephrine's effect on leucine kinetics; and (*d*) eliminate confounding effects of altered insulin and glucagon concentrations by administration of somatostatin with replacement infusions of the two pancreatic hormones.

Methods

Subjects and procedures. Written informed consent was obtained from 18 healthy male volunteers aged 20–25 yr; all were within 10% of ideal body weight (Metropolitan Life Insurance Tables). Glucose tolerance and laboratory screening for renal or hepatic disease were normal before study. None was on medication or performed vigorous exercise. After a 12-h overnight fast a teflon cannula was placed into a left forearm vein and a constant infusion of 1-[^{13}C]leucine (0.04 μmol/kg per min) was started after the subjects received intravenous priming doses of 2 μmol/kg 1-[^{13}C]leucine and 0.3 mg/kg NaH[^{13}C]O_3 (11). After a 2-h tracer equilibration period, arterialized blood samples were obtained in 10–15-min intervals from a superficial hand vein using a thermostatically controlled heat box at a temperature of 60–62°C (12). Deep venous blood was sampled from a teflon cannula inserted retrogradely into the left antecubital vein, draining blood from the forearm muscle of the contralateral arm. Blood was collected in tubes containing EDTA as an anticoagulant. Plasma was rapidly obtained by refrigerated centrifugation and stored at −70°C for later assay. Partial oxygen pressure in arterialized blood was 74.5±2.3 mmHg, and in deep venous blood 32.6±2.0 mmHg. Left forearm blood flow was measured by mercury strain-gauge plethysmography (EC4; Hokanson, Issaquah, WA) (13). A pediatric blood pressure cuff was applied to the wrist and inflated to 300 mmHg 2 min before each blood sampling point for measurement of forearm flow, excluding the blood draining the hand. Expired air was collected from a valve attached to a mouthpiece after a 3-min breathing equilibration period into gas-tight 100-ml glass flasks for later [^{13}C]O_2-analysis. Expired air was also collected at 10–15-min intervals in Douglas bags for determination of CO_2 production (V_{CO_2}) and O_2 consumption (V_{O_2}) by infrared gas analysis (E. Jäger, Würzburg, FRG). Respiratory volume per unit time was measured using a respirometer (Hewlett-Packard Co., Palo Alto, CA).

Materials and infusions. 99% enriched L-1-[^{13}C]leucine and 90% enriched sodium 1-[^{13}C]bicarbonate were obtained from Kor Isotopes (Cambridge, MA); they were determined to be pyrogen free, and passed through a filter (0.22 μm; Millipore/Continental Water Sys-

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tems, Bedford, MA) before use. Insulin (Actrapid-HM) and glucagon were from Novo (Bagsvaerd, Denmark), and somatostatin (Stilamin) was a gift from Serono (Freiburg, FRG). Epinephrine (Streuli, Uznach, Switzerland) was prepared in 0.9% saline to which 25 mg ascorbic acid (Redoxon; Roche, Basel, Switzerland) was added. Human albumin (Swiss Red Cross) was added to the infusions of epinephrine, insulin, and glucagon to a final concentration of 0.5%. After a baseline period of 30 min there was a 180-min infusion period during which either saline (controls, $n = 6$), epinephrine (50 ng/kg per min, $n = 6$), or the same dose of epinephrine plus propranolol (5 mg i.v. injection at 25 min, followed by 80 μg/min; ICI-Pharma, Lucerne, Switzerland) were infused continuously using Harvard syringe pumps. During the 180-min infusion period of all three groups, somatostatin (100 ng/kg per min) was infused combined with insulin (100 μU/kg per min) and glucagon 0.8 ng/kg per min. The study protocol was approved by the Human Ethics Committee of the University Hospital, Basel.

Analytical methods. Plasma concentrations and ^{13}C-enrichments of leucine and α-ketoisocaproate (α-KIC)[1] were measured by selected ion-monitoring gas chromatography mass spectrometry (model 5890; Hewlett Packard Co.) using D10-leucine and D3-α-KIC, respectively, as internal standards (14). [^{13}C]O_2-content in expired air was measured by isotope ratio mass spectrometry (251 spectrometer; Finnigan MAT, Bremen, FRG). From all ^{13}C-enrichments determined during 1-[^{13}C]-leucine infusions in air and plasma, background measurements obtained before start of the tracer infusion were subtracted. Plasma catecholamines were measured by a radioenzymatic method (15), insulin and glucagon by RIAs as described previously (16), plasma glucose using hexokinase, and FFA using a radiochemical method (17).

Calculations. Steady state was present during the basal period (0–30 min) and during the last 60 min of the infusion period (150–210 min) as determined by the absence of significant changes of plasma concentrations and ^{13}C-enrichment of leucine and α-KIC over time, assessed by analysis of variance with repeated measures. Plasma leucine flux and oxidation rates were calculated during these periods. Leucine plasma appearance was calculated by dividing the isotope infusion rate by the steady-state plasma 1-[^{13}C]leucine enrichment (mole% excess; MPE) and subtracting the tracer infusion rate (18). Whole body leucine flux was calculated the same way but using [^{13}C]α-KIC in the calculation.

The metabolic clearance rate (MCR) of leucine was calculated by dividing leucine plasma appearance by the prevailing arterialized plasma leucine concentration. The rate of leucine oxidation was calculated using the equation:

leucine oxidation (micromoles/kilogram per minute)

$$= \frac{IECO_2 \times \dot{V}CO_2}{MPE_{\alpha\text{-KIC}} \times 0.8},$$

where $\dot{V}CO_2$ was the rate of CO_2 production and $MPE_{\alpha\text{-KIC}}$ the ^{13}C-enrichment in arterialized plasma α-KIC (19), the deaminated product of leucine that equilibrates with intracellular α-KIC (19). The factor 0.8 corrected for CO_2-fixation and other losses (18). Nonoxidative leucine flux was the difference between whole body leucine flux and leucine oxidation. Net forearm leucine balance was calculated by multiplying the leucine concentration differences between arterialized hand-venous blood and forearm deep-venous blood by forearm blood flow (20).

Statistical analyses. Statistical analyses were performed using statistical software (BMDP, Los Angeles, CA); analysis of variance with repeated measures (program 2V) was used to determine effects of protocols and time. Differences between individual protocols were examined by Bonferroni t tests (program 5D). All data are expressed as mean±SEM.

1. *Abbreviations used in this paper:* α-KIC, α-ketoisocaproate; MCR, metabolic clearance rates; MPE, mole% excess.

Results

Plasma catecholamines, insulin, and glucagon concentrations (Table I). Epinephrine infusion alone resulted in plasma epinephrine levels of 689±31 pg/ml after 210 min, representing a 13-fold elevation above basal values. Epinephrine concentrations were increased when propranolol was administered ($P < 0.01$ vs. epinephrine alone), indicating β-adrenoceptor-mediated degradation of epinephrine, in agreement with a previous study (21). Plasma norepinephrine and insulin concentrations did not change in any protocol. Plasma glucagon was slightly higher during the period of replacement infusions than during the basal period without significant differences between the three protocols.

Effect of epinephrine and β-blockade on leucine kinetics (Fig. 1, Table II). Plasma leucine concentrations decreased during epinephrine infusion by 28% and reached mean levels of 69±6 μmol/liter during the last hour of infusion ($P < 0.02$ vs. basal values, Fig. 1). In contrast, epinephrine infusion with β-blockade resulted in a slight (13±3%) increase in plasma leucine concentrations, similar to that observed in controls (12±5%). The changes in plasma leucine concentrations during epinephrine infusion were significantly different compared with controls ($P < 0.001$) and β-blockade ($P < 0.05$). Isotopic enrichment of plasma leucine during the basal period was 2.4±0.1% MPE in the saline control protocol, and similar in the other studies. Leucine ^{13}C-enrichment increased significantly during epinephrine ($P < 0.05$ vs. controls) but remained unchanged during saline; it increased transiently during epinephrine and β-blockade, reaching values at the end of the infusion similar to those in the control study. Table II demonstrates that epinephrine infusion resulted in a significant decrease in leucine flux from 1.77±0.14 μmol/kg per min during the basal period to 1.37±0.08 μmol/kg per min during epinephrine ($P < 0.05$), representing a 22±6% decrease from basal ($P < 0.05$ vs. controls). Saline infusion and epinephrine combined with β-blockade had no significant effect on leucine flux (−7.3±5 and −14±7%, respectively). Epinephrine infusion increased the MCR of leucine by 0.8±1.2 ml/kg per min compared with a decrease in the MCR in controls (−2.1±0.6 ml/kg per min, $P < 0.01$ vs. basal period; epinephrine vs. controls, $P < 0.02$); it decreased also during β-blockade (−2.3±0.8 ml/kg per min, $P < 0.01$ vs. basal period). The fall in plasma leucine concentration and leucine flux was continuous and largest at the end of the study. The ratio of the ^{13}C-enrichments of α-KIC and leucine in the epinephrine and saline protocols were 0.73±0.08 and 0.71±0.09 during the basal period, and 0.61±0.09 and 0.66±0.09 during the infusion periods, respectively. Leucine oxidation decreased during epinephrine by 36±8% from 0.67±0.1 to 0.43±0.1 μmol/kg per min ($P < 0.05$ compared with basal period), but it remained unchanged in control subjects and during β-blockade; the differences between epinephrine, saline controls, and β-blockade were statistically significant ($P < 0.01$ and $P < 0.02$, respectively). Nonoxidative leucine flux was nearly twice the leucine oxidation rate; it did not change significantly during epinephrine but increased during β-blockade ($P < 0.05$ vs. basal period).

Effect of epinephrine and β-blockade on net leucine forearm balance (Fig. 2). Forearm blood flow was 3.1±0.2 ml/100 ml per min in the basal period of control subjects. It increased during epinephrine infusion from similar values to 13±1

Table I. Effect of Epinephrine without and with β-Blockade and of Saline (controls) on Plasma Epinephrine, Norepinephrine, Insulin, and Glucagon

	Basal period	90 min	210 min	*P* vs. controls	*P* vs. basal
Epinephrine (*pg/ml*)					
Controls	61±13	51±14	69±18		NS
Epinephrine	56±5	608±59	689±31	<0.005	<0.005
E + β-blockade	169±29	1,706±575	1,338±353	<0.02	<0.02
Norepinephrine (*pg/ml*)					
Controls	183±51	177±39	158±37		NS
Epinephrine	80±20	94±13	98±10	NS	NS
E + β-blockade	205±63	454±223	228±92	NS	NS
Insulin (*μU/ml*)					
Controls	15.1±1.7	15.8±1.7	15.7±1.7		NS
Epinephrine	13.8±2.3	14.2±2.0	19.7±2.5	NS	NS
E + β-blockade	15.2±2.3	19.2±1.8	19.2±2.1	NS	NS
Glucagon (*pg/ml*)					
Controls	184±55	185±52	186±65		NS
Epinephrine	99±24	127±32	147±32	NS	NS
E + β-blockade	168±37	195±38	180±33	NS	NS

$n = 6$ in each group; mean±SEM.

ml/100 ml per min ($P < 0.001$) but remained unchanged during saline and β-blockade. During the control studies the net forearm leucine balance was −26±9 nmol/100 ml per min in the infusion period, whereas it increased significantly from −28±9 to −115±36 nmol/100 ml per min ($P < 0.01$ vs. controls; $P < 0.01$ vs. β-blockade) during epinephrine infusion. The increase in forearm blood flow and net leucine release during epinephrine persisted throughout the infusion period; both were prevented by β-blockade. The relatively large variability of the net leucine balance data was due to the small arteriovenous concentration gradients of leucine (average: 7 μmol/liter during the basal period).

Plasma glucose and FFA concentrations (Fig. 3). Epinephrine infusion resulted in a sustained increase in plasma glucose concentrations from 96±6 mg/dl to 227±27 mg/dl after 90 min ($P < 0.001$ vs. controls and β-blockade). Saline infusion and β-blockade did not affect plasma glucose. Epinephrine infusion also increased plasma FFA levels, with a maximal effect after 30 min (1,316±175 μmol/liter vs. 585±110 μmol/liter during the basal period, $P < 0.005$); thereafter, plasma FFA declined gradually but remained elevated until the end of the studies ($P < 0.01$). Plasma FFA did not change in controls and during β-blockade.

Hemodynamic effects and respiratory parameters (Table III). Epinephrine administration resulted in a significant increase in heart rate ($P < 0.005$). β-Blockade resulted in a decrease of the heart rate from 67±5 to 55±3 beats/min ($P < 0.05$), documenting the efficacy of β-blockade. There were slight but insignificant increases in blood pressure, oxygen consumption, and CO_2 production during epinephrine infusion without significant differences between protocols. Systolic and diastolic blood pressure did not change significantly. The respiratory quotient was 0.90±0.07 in controls, 0.85±0.09 during epinephrine, and 0.88±0.06 during β-blockade at 210 min (NS).

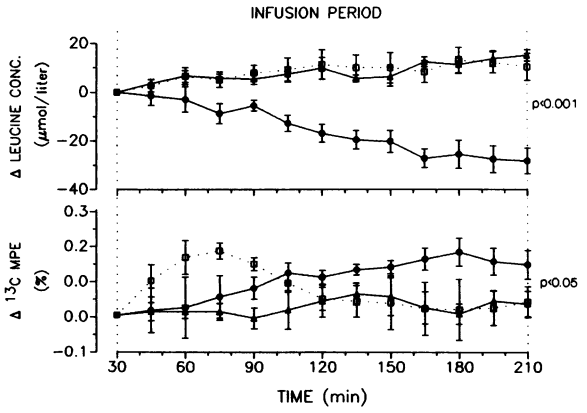

Figure 1. Changes of leucine plasma concentrations and of ^{13}C mole% excess from basal levels during infusion of epinephrine (50 ng/kg per min) without and with β-blockade, and of saline (controls). *P* refers to differences between protocols (two-way analysis of variance with repeated measures; $n = 6$ in each group; results are mean±SEM). ●, Epinephrine; ▲, controls; □, epinephrine + β-blockade.

Discussion

The present data demonstrate that elevation of plasma epinephrine to concentrations as observed during severe stress (2–4) decreases whole body leucine flux. As the only source of this essential amino acid in the postabsorptive state is endogenous protein, this finding indicates that total body protein breakdown is inhibited by epinephrine. Furthermore, the data demonstrate that hyperepinephrinemia decreases leucine oxidation, whereas nonoxidative leucine flux is not affected in spite of the fall in leucine plasma disappearance. The effects of epinephrine on leucine flux and oxidation are mediated via β-adrenergic receptors.

β-Stimulation has been reported to inhibit amino acid release from skeletal muscle (22, 23). These data and those of the present study are consistent with an insulin-like effect of epinephrine (24). The present finding that isolated α-stimulation produced by epinephrine administration combined with β-blockade resulted in increased nonoxidative leucine disappearance even suggested an increase in protein synthesis (25), in

Table II. Effect of Epinephrine without and with β-Blockade and of Saline (Controls) on Leucine Kinetics

	Basal period (0–30 min)	Infusion period (165–210 min)	Change from basal (165–210 min)	*P* vs. controls*	*P* vs. basal
Leucine concentration (*μmol/liter*)					
Controls	104±10	117±11	+13±3		NS
Epinephrine	95±11	69±6	−27±5	<0.001	<0.02
E + β-blockade	89±4	101±8	+11±5	NS	NS
Leucine plasma appearance (*μmol/kg per min*)					
Controls	1.12±0.08	1.04±0.07	−0.08±0.06		NS
Epinephrine	1.28±0.10	0.99±0.06	−0.28±0.07	<0.05	<0.05
E + β-blockade	0.93±0.05	0.80±0.05	−0.13±0.07	NS	NS
Whole body leucine flux (*μmol/kg per min*)					
Controls	1.55±0.11	1.43±0.09	−0.12±0.08		NS
Epinephrine	1.77±0.14	1.37±0.08	−0.37±0.09	<0.05	<0.05
E + β-blockade	1.21±0.07	1.03±0.06	−0.17±0.09	NS	NS
Leucine MCR (*ml/kg per min*)					
Controls	11.3±1.3	9.3±0.9	−2.1±0.6		NS
Epinephrine	14.3±1.7	15.3±1.5	+0.8±1.2	<0.02	NS
E + β-blockade	10.4±0.5	8.2±0.7	−2.3±0.8	NS	<0.05
Leucine oxidation (*μmol/kg per min*)					
Controls	0.44±0.04	0.45±0.05	+0.01±0.04		NS
Epinephrine	0.67±0.09	0.42±0.04	−0.23±0.06	<0.01	<0.05
E + β-blockade	0.50±0.03	0.53±0.06	+0.03±0.07	NS	NS
Nonoxidative leucine flux (*μmol/kg per min*)					
Controls	1.12±0.09	0.98±0.07	−0.13±0.05		NS
Epinephrine	1.10±0.08	0.94±0.06	−0.13±0.07	NS	NS
E + β-blockade	0.71±0.07	0.51±0.07	−0.20±0.04	NS	<0.05

n = 6 in each group; mean±SEM. * Comparison of changes from basal period.

agreement with a previous study in rat myocardial cells (26). However, they are in contrast to previous data reporting diminished protein synthesis in rat diaphragm (27) and submandibular gland (28), and diminished branched-chain amino acid oxidation in liver during α-stimulation (29). Whether these differences are due to organ specificity or species variability remains to be answered.

Epinephrine infusion resulted in a significant increase in leucine MCR when compared with controls. This effect augmented the fall of plasma leucine concentration induced by diminished proteolysis. It may have been due to a direct effect of epinephrine on leucine clearance, possibly indicating increased efficiency of utilization when the contribution of oxidation to total disappearance decreased. Alternatively, disappearance of leucine was nonlinear with increasing concentrations (25), and the fall in plasma leucine concentration during epinephrine was the reason for the increase in leucine clearance.

The forearm technique was used in the present studies to assess the contribution of muscle to whole body leucine me-

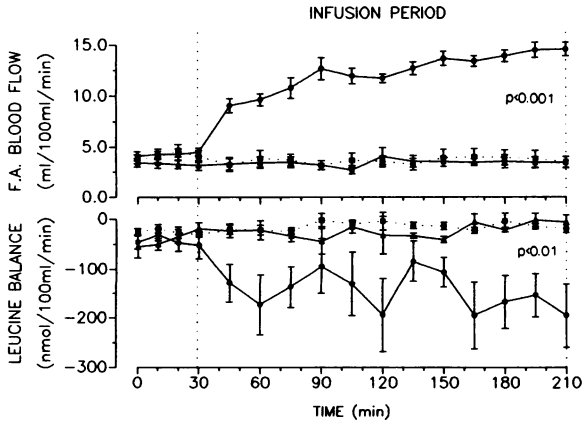

Figure 2. Forearm blood flow and net forearm leucine balance during infusion of epinephrine without and with β-blockade, and of saline (controls). *P* refers to differences between protocols (n = 6 in each group; results are mean±SEM). ●, Epinephrine; ▲, controls; □, epinephrine + β-blockade.

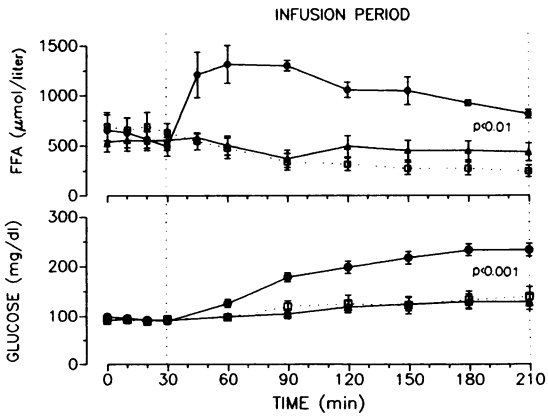

Figure 3. Plasma FFA and glucose concentrations during infusion of epinephrine without and with β-blockade, and of saline (controls). During the 180-min infusion period of all protocols, somatostatin (100 μg/kg per min) was infused combined with insulin (100 μU/kg per min) and glucagon (0.8 ng/kg per min) (n = 6 in each group; results are mean±SEM). ●, Epinephrine; ▲, controls; □, epinephrine + β-blockade.

Table III. Effect of Epinephrine without and with β-Blockade and of Saline (Controls) on Hemodynamic and Respiratory Parameters

	Basal period (0–30 min)	165–210 min	*P* vs. controls	*P* vs. basal
Systolic blood pressure (*mmHg*)				
Controls	133±11	133±12		NS
Epinephrine	130±11	141±7	NS	NS
E + β-blockade	139±8	145±7	NS	NS
Heart rate (*beats/min*)				
Controls	58±3	57±3		NS
Epinephrine	55±7	90±4	<0.005	<0.005
E + β-blockade	67±5	55±3	NS	<0.05
CO_2 production (*μmol/kg per min*)				
Controls	118±6	123±8		NS
Epinephrine	154±9	171±10	NS	NS
E + β-blockade	146±9	149±14	NS	NS
O_2 production (*μmol/kg per min*)				
Controls	135±8	130±8		NS
Epinephrine	184±11	214±19	NS	NS
E + β-blockade	175±15	171±16	NS	NS

$n = 6$ in each group; mean±SEM.

tabolism (30). The data demonstrated that elevation of plasma epinephrine concentrations resulted in increased net leucine release from the forearm. This finding seemed paradoxical, as one would expect the opposite in view of the decrease in whole body leucine flux. However, it has been reported that only ~ 35% of total plasma leucine flux is derived from muscle, either as net contribution or as exchanged leucine (31); the remaining leucine originates from other tissues such as splanchnic organs.

Assuming that forearm muscle is representative of other skeletal muscles in the body, the contribution of muscle to total body leucine flux can be calculated from the forearm data. During basal conditions, net leucine release by the forearm was ~ 30 nmol/100 ml forearm per min; if forearm leucine was released solely by muscle, if 100 ml forearm consisted of 40% muscle (32), and if total muscle mass was 23% of body weight, total body net muscle leucine release was 170 nmol/kg per min, representing 14% of total body leucine flux (1.2 μmol/kg per min). During epinephrine infusion, net forearm leucine release increased threefold, suggesting that the 22% fall of total body leucine flux during epinephrine was the result of a considerably greater fall of leucine appearance from nonmuscle tissues such as splanchnic organs. These respond to epinephrine with no appreciable increase in local blood flow (33).

The effect of epinephrine on forearm blood flow agrees with a previous paper (34), and largely explains the increase in net leucine forearm balance. Since it is not known whether skeletal muscle blood flow in other parts of the body responds to epinephrine similarly to forearm, the overall contribution of muscle proteins to leucine flux cannot be determined from the present data. Epinephrine infusion resulted in a significant increase in plasma glucose concentrations. This effect was mediated via β-adrenergic receptors, in agreement with a previous study (5).

Earlier data on the effect of hyperglycemia on leucine metabolism demonstrated increased leucine oxidation in diabetic rat diaphragm (35). Hyperglycemia per se increased leucine flux in insulin-deficient subjects (36), but decreased leucine appearance modestly in normal human volunteers during hyperglycemia (37). Therefore, epinephrine-induced hyperglycemia decreased leucine flux and oxidation, but an important effect is unlikely. Hyperepinephrinemia also resulted in a significant increase in plasma FFA concentrations due to its lipolytic effect (6, 7). This effect was also β-receptor mediated, in agreement with previous data (38). Elevation of plasma FFA in dogs decreased leucine plasma flux, oxidation, and concentration (39). Therefore, it is possible that the inhibitory effect of epinephrine on proteolysis observed in the present study was at least in part mediated through the increase in FFA. Previous studies demonstrated that epinephrine administration results in increased circulating plasma insulin concentrations in man (10, 16). These may have decreased plasma leucine flux (40) and amino acid concentrations (9). To exclude the confounding effect of insulin the present studies were performed using somatostatin with insulin and glucagon replacements to maintain constant plasma insulin and glucagon concentrations.

The present data on protein anabolic effects of epinephrine are difficult to reconcile with the well-recognized protein-catabolic response of the body to severe stress. Sepsis and trauma result in marked acceleration of leucine turnover and leucine oxidation (41), the increase in flux exceeding that of protein synthesis. The present data are incompatible with the hypothesis that epinephrine reduces protein synthesis by virtue of its stimulatory effect on branched-chain amino acid oxidation (42). The results suggest, therefore, that other stress hormones or mediators are responsible for the increase in net protein breakdown during severe stress. A previous study in humans emphasized the protein catabolic effect of elevated plasma cortisol concentrations; catecholamines were able to counteract increased concentrations of glucagon (43).

Thus, the present data suggest that acute hyperepinephrinemia results in redistribution of amino acids. While muscles such as those of forearm release amino acids, protein breakdown is inhibited in other tissues. All effects of epinephrine were independent of alternations in plasma insulin and glucagon concentrations. Whether prolonged β-adrenergic stimulation or blockade influence whole body protein metabolism remains to be determined.

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