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# EFFECT OF ISOPRENALINE INFUSION ON THE DISTRIBUTION OF TRYPTOPHAN, TYROSINE AND ISOLEUCINE BETWEEN BRAIN AND OTHER TISSUES

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**Abstract**—Intravenous infusion of anaesthetized rats with the β-adreno-receptor agonist isoprenaline decreased plasma total tryptophan concentration and increased both plasma free and brain tryptophan concentrations. Muscle tryptophan and also tyrosine concentrations showed moderate significant decreases, but concentrations in liver and kidney did not alter significantly. Plasma tyrosine concentration fell and brain tyrosine concentration rose, but these changes were less marked than those of tryptophan. Isoprenaline infusion considerably increased egress of $^{14}$C-tryptophan from plasma and moderately increased egress of $^{14}$C-isoleucine, but did not alter egress of $^{14}$C-tyrosine. However, 5 min after pulse injection of any of the above $^{14}$C-labelled amino acids, the isoprenaline-infused rats had higher brain counts than control animals. Results are consistent with previous evidence that increased availability of tryptophan to the brain can occur in stressful situations.

Many factors can influence brain tryptophan concentration and because tryptophan hydroxylase is unsaturated with substrate at physiological concentrations [1,2], they can influence 5HT synthesis.

For example, increased insulin secretion can lead to increased brain tryptophan concentration by decreasing the plasma concentration of neutral aromatic and branched chain amino acids which compete with tryptophan for entry to brain [3]. However, the effects of drugs altering insulin secretion suggest that only large insulin changes comparable with those occurring after food intake alter the disposition of tryptophan (and other aromatic amino acids) between plasma and brain [4]. Another influence on brain tryptophan concentration results from most of the plasma tryptophan being bound to albumin [5]. Thus brain tryptophan concentration and 5HT synthesis are increased by drugs which displace tryptophan from albumin [6] or which increase lipolysis because unesterified fatty acids decrease tryptophan binding to albumin [7].

Lipolysis may be increased by stimulation of adrenergic β receptors in fat cells [8] and hence is influenced by sympathetic activity. It has been shown that disturbance caused by removal of 24 hr fasted rats from cages is sufficient to rapidly increase plasma unesterified fatty acid in remaining cage-mates and is associated with an increase of the percentage of plasma free tryptophan. Concurrently, plasma total tryptophan falls, suggesting a shift of tryptophan into cells and/or increased tryptophan catabolism [9]. In some experiments there is an associated increase of brain tryptophan [10]. These changes appear to depend on stimulation of β receptors as they are prevented by propranolol. Similar changes occur on injecting human subjects with adrenaline [11].

The purpose of the present study was to investigate the effect of β-adrenergic stimulation on the disposition of tryptophan and other amino acids in more detail. Anaesthetized rats were infused with the β-adrenergic receptor agonist isoprenaline and changes of tryptophan concentration in plasma, brain and other tissues studied. The fate of intravenously injected tracer amount of labelled tryptophan was also determined. Similar investigations were also made on tyrosine and isoleucine disposition.

## METHODS

*Animals.* Male Sprague–Dawley rats (Anglia Laboratory Animals, Huntingdon, England) were fed on ALGH diet (Grain Harvesters) and tap water *ad lib.*

*Isoprenaline infusion.* Rats weighing 180–220 g were anaesthetized with Nembutal (60mg/kg i.p.) (Abbot Laboratories) and left for 15 min before commencing surgery. Cannulae were made from polythene tubing (Portex PP50) with 23 g × 1 3/16in. disposable needles (Gillette Sabre) inserted into one end and the other end drawn out. A cannula (length 30 cm) was tied into the right jugular vein for infusion of isoprenaline (144 μg/ml at 0.0388 ml/min for either 15 min or 1 hr) using a Harvard infusion pump. Another cannula (length 10 cm) was tied into the left carotid for withdrawal of blood samples. Between samplings this was filled with 0.9 per cent sodium chloride w/v. At the end of the infusion period the rats were decapitated, tissues removed and stored at −20° until determinations were made.

*Tissue radioactivity.* This was determined by extracting the labelled amino acids as previously described for tryptophan and tyrosine in brain [12]. Thus, after tissues were homogenized in 10 vol. of acidified butanol, the amino acids were back extracted into 0.1N HCl containing 0.1 per cent

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Table 1. Effect of anaesthesia and surgery on plasma and brain tryptophan*

| Treatment | Plasma tryptophan Total (μg/ml) | Plasma tryptophan Free (μg/ml) | Free (%) | Brain tryptophan (μg/g) |
|---|---|---|---|---|
| Unanaesthetized (6) | 15.81 ± 0.73 | 6.22 ± 0.32 | 39.62 ± 2.26 | 2.80 ± 0.12 |
| Sagatal (60 mg/kg i.p.) 15 min (6) | 11.12 ± 0.98§ | 4.28 ± 0.36§ | 39.32 ± 3.50 | 2.28 ± 0.24 |
| Nembutal (60 mg/kg i.p.) 15 min (6) | 10.88 ± 1.62† | 4.28 ± 0.55‡ | 40.59 ± 3.55 | 2.53 ± 0.12 |
| Sagatal (60 mg/kg i.p.) 25 min + sham operations (5) | 9.81 ± 1.32§ | 4.68 ± 0.47‡ | 50.08 ± 7.30 | 2.10 ± 0.17§ |

* Results given as mean ± 1 S.E. Nos. of determinations in brackets. See Methods section for details.
§ Differences from values for unanaesthetized rats: †$P < 0.05$, ‡$P < 0.02$, ‡$P < 0.01$.

cysteine. Samples (0.5 ml) of the HCl extract were transferred to scintillation vials and 0.5 ml 0.1N HCl added followed by 15 ml scintillant (6 g 2,5-diphenyloxazole (PPO), 1 litre toluene, 500 ml Triton X100) and counted in a scintillation counter (Packard Tricarb.).

*Packed cell volume.* This was determined after 1 hr infusion using a haematocrit reader (Gelman-Hawksley Ltd., Lancing, Sussex, England).

*Blood and plasma volumes.* These were determined after 55 min of infusion with isoprenaline or 0.9 per cent sodium chloride. $^{131}$I-Human serum albumin (50 μCi) in 0.1 ml saline (Radiochemical Centre, Amersham) was injected into the venous cannula followed by 0.2 ml of saline and the rats were killed 5 min later. Blood samples (0.1 and 0.2 ml) were immediately removed for counting and the remainder used for the preparation of plasma from which samples were also taken for counting. Blood and plasma volumes (ml/100 g wt of rat) were calculated from the following equation:

$$\frac{\text{c.p.m. for 0.1 ml injected } ^{131}\text{I-albumin}}{\text{c.p.m. for 0.1 ml blood or plasma}} \times \frac{100}{\text{wt of rat.}}$$

*Egress of amino acids from plasma.* The removal of labelled tryptophan, tyrosine or isoleucine from the plasma was determined following the intravenous injection of 1 μCi of the appropriate amino acid. L-Methylene-1-$^{14}$C tryptophan s.a. 52 mCi/mmole; L-U-$^{14}$C tyrosine s.a. 495 mCi/mmole and L-U-$^{14}$C-isoleucine s.a. 10 mCi/mmole were all obtained from the Radiochemical Centre, Amersham, England. Amino acids were injected in 0.1 ml 0.9 per cent sodium chloride followed by 0.2 ml 0.9 per cent sodium chloride. Total injection time was 35 sec.

Blood samples were then withdrawn at intervals into heparinized syringes, centrifuged immediately in 0.75 ml polythene tubes (Sarstedt, Leicester) and plasma collected and prepared for scintillation spectrometry [13]. Plasma samples (50 μl) were transferred to scintillation vials and solubilized by 1.1 ml Soluene 350 (Packard) followed by 50 μl of glacial acetic acid to neutralize and prevent chemiluminescence. After adding 15 ml of scintillant (5 g 2,5-diphenyloxazole (PPO), 0.3 g 1, 4 bis 2 (4-methyl-5-phenyloxazolyl benzene) (dimethyl POPOP), 1 litre toluene) samples were counted in the scintillation counter.

*Biochemical determinations.* After decapitation, brain, liver, kidney, muscle and plasma concentrations of tryptophan and tyrosine were determined as previously described [12]. Plasma free tryptophan was determined using ultrafiltration at pH 7.4 [14]in the experiment shown in Table 1, and Amicon CF50 membrane cones without pH control [15] in the experiment shown in Table 4.

## RESULTS

*The influence of anaesthesia and surgery on plasma and brain tryptophan concentrations.* Rats were

Table 2. Effect of isoprenaline infusion on blood, plasma and packed cell volume*

| Infused | Blood volume (ml/100g body wt) | Plasma volume (ml/100g body wt) | Packed cell volume (as % of blood volume) |
|---|---|---|---|
| 0.9% sodium chloride (1 hr) (6) | 5.10 ± 0.16 | 3.06 ± 0.15 | 36.8 ± 0.69 |
| Isoprenaline (1 hr) (6) | 5.30 ± 0.32 | 3.28 ± 0.18 | 35.5 ± 0.67 |
| % change | +4 | +7 | −4 |
| P | NS† | NS | NS |

* Results given as means ± 1 S.E. Nos. of determinations in brackets. See Methods section for details.
† NS: not significant.

injected with Nembutal (60 mg/kg, i.p.) or Sagatal (60 mg/kg i.p.) (pentobarbitone preparations used in subsequent experiments) and killed 15 min later. An additional group of rats was subjected to sham operation in which carotid cannulae were inserted 10 min after giving Nembutal and the rats killed 15 min later. Table 1 shows the effects of these procedures on plasma and brain tryptophan. Anaesthetized rats had significantly lower plasma total and free tryptophan concentrations than untreated animals. Sham operation has no significant additional effect. Mean brain tryptophan concentrations in the anaesthetized groups were lower than in the unanaesthetized group, but this difference was significant only for the anaesthetized and sham operated group.

*Effect of isoprenaline infusion on blood, plasma and packed cell volumes.* Isoprenaline infusion might have affected blood or plasma volume by its cardiovascular action and hence altered concentrations of blood and plasma metabolites. However, results in Table 2 show that infusing rats with isoprenaline for 1 hr did not significantly alter blood, plasma or packed cell volumes.

*Effect of isoprenaline infusion on the rate of egress of tryptophan, tyrosine and isoleucine from plasma.* Before investigating the effect of isoprenaline on removal of pulse injected labelled tryptophan from plasma, it was necessary to determine if the rate of binding of tryptophan to albumin (or other blood constituents) influenced its removal rate. Therefore, rates of removal of labelled tryptophan injected in 0.9 per cent sodium chloride and injected after preincubation with blood were compared as follows: Blood (0.9 ml) was withdrawn from the carotid artery into a heparinized syringe containing 1 $\mu$Ci of L-methylene-$^{14}$C tryptophan in 0.1 ml 0.9 per cent sodium chloride and rapidly reinjected 5 min later through the venous cannula. Arterial blood samples (0.1 ml) were withdrawn at 15, 30, 45, 60 and 120 sec, plasmas collected and samples taken for radioactive counting. This procedure was followed using 3 rats and in 3 additional animals 0.1 ml tryptophan solution was injected directly, followed immediately by 0.2 ml 0.9% sodium chloride. Egress of tryptophan from plasma was essentially identical for both groups (Fig. 1a). Therefore, in subsequent experiments $^{14}$C-tryptophan in 0.9% sodium chloride was injected. It was noted that the logarithmic decrease of plasma radioactivity was linear for about 60 sec and that subsequent egress rate was reduced. Therefore, samples for counting were taken at times up to 60 sec after injection. The elimination half-life ($t_{\frac{1}{2}}$) was calculated from the slope of the egress curve [16].

The effects of isoprenaline infusion for 10 min on the egress of tryptophan and isoleucine from plasma are shown in Figs. 1b and d, respectively. Logarithmic decreases of radioactivity were linear for 60 sec in both saline and isoprenaline infused rats. The infusion of isoprenaline significantly increased the slope of the regression line for tryptophan so that the elimination half life was significantly reduced, but isoleucine egress was not significantly altered.

Longer periods of isoprenaline infusion (55 min) significantly increased the egress of tryptophan and isoleucine but not tyrosine (Figs. 1 c,e,f). The elimination of both tryptophan and isoleucine in rats infused with saline for 55 min was slower than in rats infused for 10 min. This is not readily explicable. Conceivably it may have been a consequence of the second injection of Nembutal given after 30 min to maintain anaesthesia.

Tyrosine egress after 55 min infusion was not significantly altered by isoprenaline infusion. Although the intercept of the regression line on the $y$ axis was somewhat lower for isoprenaline treated than for control animals, values were not significantly different.

*Effect of isoprenaline infusion on the accumulation of labelled tryptophan tyrosine and isoleucine by tissues.* Results in Table 3 show that brain radio-activity 5 min after intravenous injection of $^{14}$C-tryptophan was slightly, but significantly, increased by infusion of isoprenaline over the previous 15 min. Mean brain radioactivity was comparably increased after similar injection of $^{14}$C-isoleucine but not to a significant extent. After infusion of isoprenaline for 1 hr, brain radioactivities following intravenous injections of $^{14}$C-tryptophan, $^{14}$C-tyrosine and $^{14}$C-isoleucine were more markedly increased and significantly so for all three amino acids. The percentage increase was greatest for tryptophan and least for tyrosine. Isoprenaline infusion for 1 hr had little effect on radioactivities of other organs, except after $^{14}$C-tryptophan injection when liver radioactivity was significantly decreased.

*Effect of isoprenaline infusion on plasma and tissue concentrations of tryptophan and tyrosine.* Isoprenaline infusion for both 15 min and 1 hr significantly reduced plasma total tryptophan concentration (Table 4). Plasma free tryptophan concentration was determined after 1 hr infusion only, and shown to be considerably and significantly increased. After 15 min infusion brain tryptophan concentration was not significantly raised, but by 1 hr there was a considerable and significant increase approximately in proportion to that of plasma free tryptophan. Liver and kidney concentrations were not significantly altered, but muscle tryptophan was moderately but significantly reduced after 1 hr infusion. Plasma and brain tyrosine concentrations were not significantly altered after 15 min, but by 1 hr they were reduced and increased, respectively, although the magnitudes and significances of the changes were smaller than for tryptophan. Muscle tyrosine concentration was unaltered by 15 min infusion, but by 1 hr it was significantly reduced about in proportion to the tryptophan change. Liver tyrosine concentration was unaltered.

## DISCUSSION

Preliminary experiments showing that anaesthesia decreased both plasma total and free tryptophan concentrations in the rat agree with results in man [17], though in the latter case only the change of total tryptophan was significant. The additional fall of plasma total tryptophan after infusing rats with isoprenaline for 1 hr is consistent with the effect of subcutaneous isoprenaline [18] when plasma total tryptophan concentration fell in association with rises of unesterified fatty acid concentration and of the

Table 3. Effect of isoprenaline infusion on distribution of $^{14}$C-tryptophan, $^{14}$C-tyrosine and $^{14}$C-isoleucine

| Injected | Infused | Radioactivity (c.p.m./g tissue) | | | |
|---|---|---|---|---|---|
| | | Brain | Liver | Kidney | Muscle |
| $^{14}$C-Tryptophan | 0.9% Sodium chloride (15 min) | 4128 ± 302 (7) | ND | ND | 2930 ± 250 (7) |
| | Isoprenaline (15 min) | 5028 ± 290 (7) | ND | ND | 3446 ± 58 (7) |
| | % change | + 22 | | | + 18 |
| | P | < 0.05 | | | NS |
| $^{14}$C-Tryptophan | 0.9% Sodium chloride (1 hr) | 3066 ± 357 (5) | 4386 ± 2695 (5) | 6335 ± 687 (7) | 2441 ± 146 (7) |
| | Isoprenaline (1 hr) | 5144 ± 514 (7) | 3313 ± 221 (7) | 5245 ± 283 (7) | 2672 ± 277 (7) |
| | % Change | +68 | − 25 | − 17 | + 9 |
| | P | < 0.02 | < 0.02 | NS | NS |
| $^{14}$C-Isoleucine | 0.9% Sodium chloride (15 min) | 2016 ± 186 (6) | ND | ND | 1664 ± 185 (6) |
| | Isoprenaline (15 min) | 2359 ± 342 (6) | ND | ND | 1705 ± 330 (6) |
| | % Change | + 17 | | | +2 |
| | P | NS | | | NS |
| $^{14}$C-Isoleucine | 0.9% Sodium chloride (1 hr) | 3047 ± 307 (7) | ND | ND | 3080 ± 427 (8) |
| | Isoprenaline (1 hr) | 4437 ± 360 (7) | ND | ND | 2708 ± 257 (7) |
| | % Change | + 45 | | | − 12 |
| | P | <0.02 | | | NS |
| $^{14}$C-Tyrosine | 0.9% Sodium chloride (1 hr) | 4336 ± 121 (7) | 1932 ± 170 (7) | 4427 ± 656 (7) | 3513 ± 197 (7) |
| | Isoprenaline (1 hr) | 5787 ± 585 (7) | 1490 ± 200 (7) | 3209 ± 502 (7) | 3249 ± 417 (7) |
| | % Change | + 33 | − 23 | − 28 | − 8 |
| | P | < 0.05 | NS | NS | NS |

* After infusing with 0.9% sodium chloride or isoprenaline (28 μg/kg body wt/min) for either 10 min or 55 min 1 μCi of the amino acid was injected i.v., infusion continued for 5 min and rats killed. Results given as means ± 1 S.E. Nos. of determinations in brackets.

† NS: not significant. See Methods section for details.

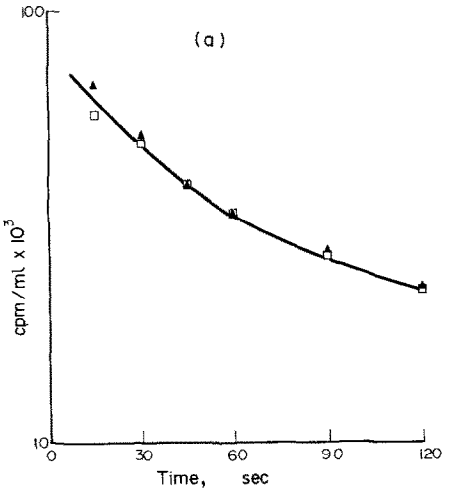
Table 4. Effect of isoprenaline infusion on distribution of tryptophan and tyrosine

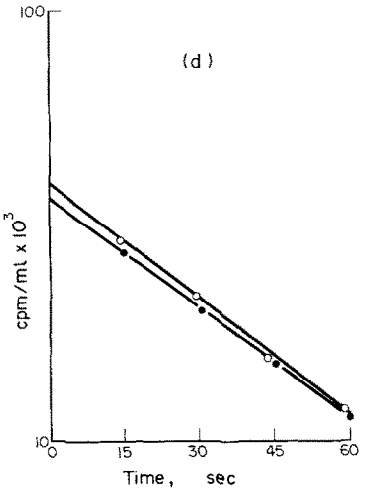
| Infused | Plasma (μg/ml) Total | Plasma (μg/ml) Free | Brain (μg/g) | Liver (μg/g) | Kidney (μg/g) | Muscle (μg/g) |
|---|---|---|---|---|---|---|
| **TRYPTOPHAN** | | | | | | |
| 0.9% Sodium chloride (15 min) | 6.66 ± 0.54 (6) | ND† | 5.48 ± 0.29 (13) | ND | ND | 5.26 ± 0.42 (13) |
| Isoprenaline (15 min) | 4.59 ± 0.36 (6) | ND | 6.13 ± 0.36 (13) | ND | ND | 4.62 ± 0.15 (13) |
| % change | − 31.1 | | + 12 | | | − 12 |
| P | <0.001 | | NS‡ | | | NS |
| 0.9% Sodium chloride (1 hr) | 9.51 ± 0.47 (14) | 2.51 ± 0.34 (14) | 4.55 ± 0.35 (10) | 8.57 ± 0.34 (14) | 31.88 ± 2.88 (14) | 6.18 ± 0.47 (14) |
| Isoprenaline (1 hr) | 5.77 ± 0.36 (15) | 4.07 ± 0.36 (15) | 6.87 ± 0.32 (10) | 7.76 ± 0.50 (14) | 28.71 ± 2.53 (14) | 4.91 ± 0.34 (14) |
| % change | − 39 | + 62 | + 51 | − 9 | − 10 | − 21 |
| P | <0.001 | <0.01 | <0.001 | NS | NS | <0.05 |
| **TYROSINE** | | | | | | |
| 0.9% Sodium chloride (15 min) | 12.49 ± 0.45 (6) | | 16.27 ± 0.80 (13) | ND | ND | 19.06 ± 1.26 (12) |
| Isoprenaline (15 min) | 12.06 ± 0.54 (6) | | 16.81 ± 1.01 (13) | ND | ND | 17.83 ± 0.63 (13) |
| % change | − 3.4 | | + 3 | | | − 6.5 |
| P | NS | | NS | | | NS |
| 0.9% Sodium chloride (1 hr) | 13.97 ± 1.09 (13) | | 13.86 ± 0.39 (14) | 25.94 ± 1.11 (14) | ND | 27.57 ± 1.16 (13) |
| Isoprenaline (1 hr) | 10.85 ± 0.74 (14) | | 16.31 ± 0.87 (14) | 24.45 ± 1.26 (14) | ND | 20.59 ± 1.21 (14) |
| % change | − 22 | | + 18 | − 6 | | − 25 |
| P | < 0.05 | | < 0.05 | NS | | <0.001 |

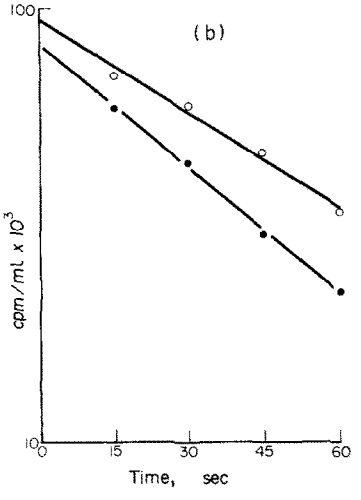
* After infusing with 0.9% sodium chloride or isoprenaline (28 μg/kg body wt/min), rats were killed and determinations made as described in Methods section. In the 1 hr infusion experiments plasma and brain values were determined on one group of animals and liver, kidney and muscle values were determined on another group. Results given as ± 1 S.E. Nos. of determinations in brackets.

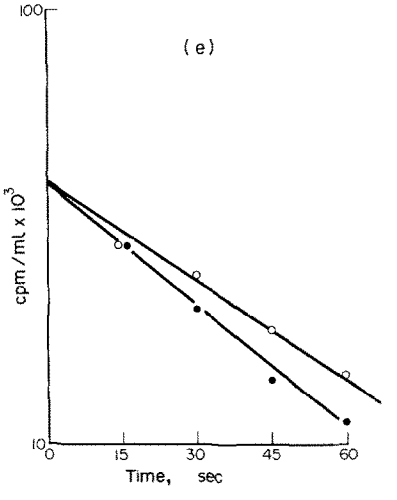
† ND: not determined.

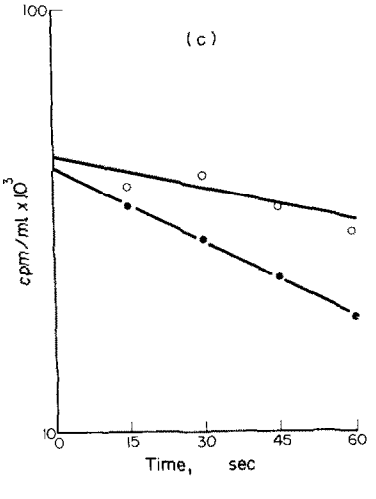
‡ NS: not significant.

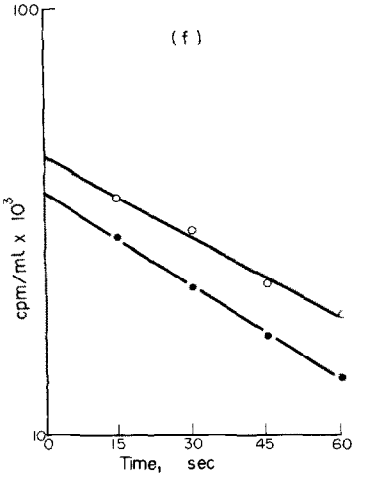



*(Figure legend opposite)*

percentage of plasma tryptophan in the free state. Subcutaneous injection of adrenaline into human subjects had similar effects [11].

In the present work, isoprenaline caused a moderate fall of plasma tyrosine concentration as well as a larger fall of tryptophan. Furthermore, both amino acids were similarly redistributed between the tissues, inasmuch as there were comparable decreases of their concentrations in muscle and also increases in brain, though the latter change was more marked for tryptophan than for tyrosine. Results suggest that the changes in muscle are due to release of muscle amino acid stores and not to decreased transport of amino acids from plasma to muscle, as isoprenaline pretreatment did not significantly affect muscle radioactivity on intravenous injection of the $^{14}C$ amino acids. The increased brain tryptophan and tyrosine concentrations after isoprenaline infusion, however, probably reflect increased transport from plasma, as brain radioactivity 5 min after intravenous injection of the above $^{14}C$ labelled amino acids (or isoleucine) was greater in isoprenaline treated than in control rats.

The above brain tryptophan changes occured together with an increased rate of its egress from plasma, but brain tyrosine changes were smaller and not associated with altered egress from plasma. These differences may result from specific changes of plasma tryptophan binding, from different effects of isoprenaline on tryptophan and tyrosine metabolism or from effects on their transport into other tissues. However, differences of transport are not indicated by any clear differences between the effects of isoprenaline on the radioactivities of liver, kidney or muscle.

The rate of egress of $^{14}C$-tryptophan from plasma was essentially identical whether it was injected in sodium chloride solution or after pre-equilibrating with blood. This suggests either that the binding of tryptophan to plasma albumin is very rapid or that its rate of egress from plasma is unaffected by binding. This is not the case for transport of tryptophan from plasma to brain, as recent work using a modified version of the Oldendorf method in which $^{14}C$-tryptophan uptake by brain was measured 6 sec after intracarotid injection indicates that uptake into brain is appreciably influenced by binding [19]. However, evidence is against a similar effect in other tissues (Tables 3 and 4).

Results in general agree with the previous finding that in stress situations [10] the freeing of plasma tryptophan from binding to albumin results in increased availability of tryptophan to the brain, but that this is partly opposed, possibly by egress of plasma tryptophan to other unknown sites or by increased tryptophan metabolism. The slight increase of brain tyrosine concentration even though plasma tyrosine was decreased agrees with other experiments in which brain tyrosine values tended to be maintained even though plasma concentrations fell, e.g. after aminophylline [20] or amphetamine [21] injection. Rat brain tyrosine hydroxylase is reported to be normally unsaturated with tyrosine [22,23]. Therefore, mechanisms whereby brain tyrosine concentrations are maintained could safeguard against possible impairment of catecholamine synthesis.

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Fig. 1. Effect of isoprenaline infusion on the egress from plasma of tryptophan, isoleucine and tyrosine following intravenous injection of the labelled amino acids. Values on figures given as means of determinations of numbers of rats shown below in brackets.
(a) Egress of $^{14}C$ from plasma following intravenous injection of 1 $\mu$Ci $^{14}C$-tryptophan ▲, after 5 min pre-equilibration with blood (3); □, in 0.9% sodium chloride (3).

| Infusion | Amino acid | $t_{½}$ (sec) | P |
|---|---|---|---|
| (b) ○, 10 min sodium chloride (7) | $^{14}C$-tryptophan | 44 ± 3 | |
| ●, 10 min isoprenaline (6) | $^{14}C$-tryptohan | 32 ± 1 | <0.01 |
| (c) ○, 55 min sodium chloride (5) | $^{14}C$-tryptophan | 110 ± 12 | |
| ●, 55 min isoprenaline (6) | $^{14}C$-tryptophan | 60 ± 9 | <0.01 |
| (d) ○, 10 min sodium chloride (5) | $^{14}C$-isoleucine | 36 ± 3 | |
| ●, 10 min isoprenaline (5) | $^{14}C$-isoleucine | 34 ± 2 | NS |
| (e) ○, 55 min sodium chloride (7) | $^{14}C$-isoleucine | 44 ± 4 | |
| ●, 55 min isoprenaline (6) | $^{14}C$-isoleucine | 33 ± 2 | <0.05 |
| (f) ○, 55 min sodium chloride (6) | $^{14}C$-tyrosine | 49 ± 3 | |
| ●, 55 min isoprenaline (6) | $^{14}C$-tyrosine | 46 ± 6 | NS |

Infusions were continued for 5 min after the $^{14}C$-amino acids were injected. Rats were then immediately killed and tissues removed and processed for scintillation counting.

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