

Uptake of Individual Amino Acids by the Human Brain¹ (36994)

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(Introduced by P. J. Mulrow)

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Previous studies from our laboratories have examined the pattern of exchange of individual amino acids across the splanchnic bed (1, 2), forearm muscle (3), exercising leg (4), and kidney (1), in intact man. With regard to amino acid exchange across the brain, uptake of amino acids by brain tissue has been demonstrated in experimental animals by means of *in vitro* studies with tissue slices (5) as well as by *in vivo* investigations involving intra-arterial injection of tracer amounts of radiolabeled amino acids (6). Data on amino acid uptake in human brain is not however, available. The present study was undertaken to examine the pattern of amino acid exchange in human brain by determining the differences in concentration of amino acids in arterial and jugular venous blood.

Materials and Methods. The subjects were eight healthy adult volunteers. They had no history or evidence of neurologic impairment or cerebrovascular disease. The studies were carried out after a 12–14 hr overnight fast. Teflon catheters were placed percutaneously in a brachial artery and in an antecubital vein. The latter catheter was advanced under fluoroscopic observation to the internal jugular bulb, where its position was repeatedly checked with image intensification fluoroscopy. Two sets of simultaneous arterial and jugular venous blood samples were obtained from each subject with an interval of 30 min between the two sets of blood samples. The blood was centrifuged in the cold, the plasma was de-

proteinized with sulfosalicylic acid, (7), and the protein-free supernatants were stored at -20° until analyzed by the automatic ion-exchange chromatographic technique (8).

Results and Discussion. Table I shows the mean arterial concentrations and the mean arterio-jugular venous differences for the group of subjects. The results indicate that for virtually all of the amino acids measured there is a significantly higher concentration in arterial than in jugular venous blood. Thus in the postabsorptive condition there is a net uptake of amino acids by the human brain.

Although it is recognized that the amino acid pool in brain tissue is derived in part by transport from the blood, it is generally believed that the nonessential amino acids are largely formed within the substance of the brain, their carbon skeletons being derived from glucose (9). The current data indicate that under the conditions of our experiments a net uptake by the brain of plasma amino acids is demonstrable for the nonessential as well as the essential amino acids. With regard to the latter group, it is of interest that the A–V difference for valine exceeded that of all other amino acids. Inasmuch as valine is released in significant amounts from peripheral muscle (3, 10), yet is neither extracted (1, 2, 4) nor metabolized by the liver (11) the brain may be an important site of valine disposal in the postabsorptive state.

It should be noted that blood flow measurements were not obtained in the current study. Accordingly conclusions regarding the absolute rate of amino acid uptake across the brain can not be drawn from the present data. Nevertheless the consistently positive A–V differences indicate a net extraction of amino

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TABLE I. Arterial Concentrations and Arterial-Jugular Venous (A-V) Concentration Differences of Plasma Amino Acids (Mean \pm SE of Mean).

Amino acid	Arterial concn (μ mole/liter)	A-V Difference (μ mole/liter)	p^a
Taurine	43.1 \pm 2.6	1.8 \pm 1.1	.2
Aspartic acid	20.0 \pm 2.0	1.6 \pm 0.8	.05 $< p < .1$
Threonine	124.1 \pm 4.5	8.8 \pm 3.0	$< .025$
Serine	131.6 \pm 7.7	9.8 \pm 3.1	$< .02$
Proline	182.4 \pm 18.0	18.5 \pm 7.8	$< .05$
Citrulline	36.4 \pm 2.1	4.8 \pm 1.8	$< .05$
Glycine	226.1 \pm 12.9	13.0 \pm 5.4	$< .05$
Alanine	248.8 \pm 36.4	11.1 \pm 5.7	.05 $< p < .1$
α -Aminobutyric acid	24.9 \pm 3.1	2.5 \pm 0.7	$< .005$
Valine	221.8 \pm 10.5	19.3 \pm 5.5	$< .02$
Cystine	97.8 \pm 5.2	9.0 \pm 4.2	.05 $< p < .1$
Methionine	17.5 \pm 1.2	1.8 \pm 0.7	$< .05$
Isoleucine	52.5 \pm 2.5	5.4 \pm 1.3	$< .005$
Leucine	112.3 \pm 6.0	10.5 \pm 2.0	$< .005$
Tyrosine	41.0 \pm 3.0	2.8 \pm 1.1	$< .05$
Phenylalanine	43.8 \pm 1.6	3.8 \pm 1.4	$< .05$

^a Significance of A-V difference (Student's *t* test).

acids by the brain in intact man.

Summary. Individual plasma amino acids were determined in simultaneously drawn arterial and jugular venous blood samples obtained from healthy postabsorptive subjects. Consistently positive A-V differences were observed for virtually all amino acids, indicating a net uptake of essential and nonessential amino acids by the brain in intact man.

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