

Effects of tryptophan and portocaval anastomosis on activity and brain tryptophan metabolism

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Chronic portocaval anastomosis in the rat increases brain tryptophan and tyrosine, and thus 5-hydroxytryptamine (5-HT) (Curzon, Kantamaneni, Fernando, Woods & Cavanagh, 1975) and octopamine synthesis

anastomosis also showed significantly less ambulation than sham-operated animals, and midbrain tryptophan, 5-HT and 5-HIAA were all significantly raised. Ambulation by anastomosed rats was not significantly decreased further by tryptophan, although midbrain tryptophan and 5-HT (but not 5-HIAA) rose significantly. Ambulation was significantly decreased and all biochemical measures significantly increased in tryptophan-treated anastomosed rats when compared with the sham-operated group given saline. Brain tryptophan rose more strikingly in anastomosed rats than in sham-operated animals given tryptophan.

These results are suggestive of an association between raised brain tryptophan, and/or 5-HT turnover, and central disturbances in liver failure.

Table 1 Effects of tryptophan and portocaval anastomosis on activity and midbrain tryptophan metabolism

Group	Rats	Injected	Ambulation	Tryptophan	Midbrain 5-HT µg/g wet wt	5-HIAA
1	Sham (7)	0.9% NaCl	73 ± 16	4.28 ± 0.26	1.15 ± 0.04	1.25 ± 0.14
2	Sham (7)	Tryptophan	18 ± 8	5.73 ± 0.41	1.26 ± 0.03	1.63 ± 0.16
3	PCA (6)	0.9% NaCl	29 ± 11	9.76 ± 1.05	1.37 ± 0.03	3.37 ± 0.26
4	PCA (7)	Tryptophan	24 ± 7	16.23 ± 1.92	1.59 ± 0.06	4.58 ± 0.56
Group 1 v. Group 2		<i>p</i>	<0.005	<0.05	n.s.	n.s.
Group 1 v. Group 3		<i>p</i>	<0.05	<0.001	<0.01	<0.001
Group 3 v. Group 4		<i>p</i>	n.s.	<0.05	<0.05	n.s.
Group 1 v. Group 4		<i>p</i>	<0.05	<0.001	<0.01	<0.001

PCA = portocaval anastomosis. Singly-housed rats were injected with 0.9% NaCl or L-tryptophan (20 mg/kg i.p.), placed in an open field and their behaviour observed by closed circuit television between 15 and 95 min after injection, a method based on that of Taylor (1976). They were then killed and determinations made as described by Curzon *et al.* (1975). Number of rats shown in parentheses. Results are expressed as mean ± s.e. mean. The number of areas entered (ambulation) were counted and values compared by the Mann-Whitney *U* test. Midbrain determinations were compared by Student's *t* test.

(James, Hodgman, Funovics & Fischer, 1976). These changes may be responsible for central disturbances in human liver failure (for review of evidence see Curzon & Knott, 1977). The role of tryptophan was investigated by giving the amino acid to rats with portocaval anastomosis.

Anastomosis or sham operation was performed on male Sprague-Dawley rats (mean body weight ± s.d. (*n*) 341 g ± 27 (28)) using the method of Funovics, Cummings, James, Shuman & Fischer (1975). Animals were caged singly 3 weeks after the operation and the experiment indicated in Table 1 was performed 4 weeks later.

Tryptophan (20 mg/kg i.p.) significantly decreased ambulation (but not rearing, turning, head-lifting or grooming) in sham-operated rats and significantly increased midbrain tryptophan (Table 1). 5-HT and its metabolite 5-hydroxyindoleacetic acid (5-HIAA) did not rise significantly. Rats with portocaval

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