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The uptake of kynurenine, a tryptophan metabolite, into mouse brain

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Kynurenine, a liver tryptophan metabolite, itself reduces brain tryptophan uptake (Green & Curzon, 1970). Since 5-HT synthesis depends on brain tryptophan levels (Carlsson & Lindqvist, 1978) kynurenine would be expected to reduce 5-HT turnover. This has been reported to occur 2 h after low (0.5 mg/kg) but not after higher (5-20 mg/kg) doses of (\pm)-kynurenine in the mouse (Gould & Handley, 1978). In order to investigate this anomaly, brain uptake of kynurenine has been examined.

(\pm)-Kynurenine (0.5-20 mg/kg) was injected intraperitoneally into male mice (BK/W, 23-27 g). Plasma and brain kynurenine was determined after Joseph,

Baker & Lawson (1978). Doses are expressed as base equivalent.

Peak plasma kynurenine occurred at 30 min (table 1) and had returned to normal by 2 h except after 20 mg/kg when levels were still significantly raised at 2 h.

Brain kynurenine generally followed plasma kynurenine. The two values showed a strong linear correlation ($r = +0.969$, $P < 0.01$) and a rather constant proportion (about 25%) of plasma kynurenine entered brain. The process of entry could not be distinguished from passive diffusion. However during the secondary peaks 2 h after the two lower doses, the linear correlation no longer held and the brain/plasma ratio was much higher (42-48%). This probably represents slower, carrier-assisted uptake. It is likely that kynurenine, a neutral alpha amino-acid, would use the same carrier as tryptophan (see Christensen, 1975); accounting for its inhibition of tryptophan uptake.

The effects of the various doses on 5-HT turnover 2 h after kynurenine (Gould & Handley, 1978) were

Table 1 Plasma and brain kynurenine concentrations after injection of various doses of (\pm)-kynurenine

Pretreatment	Time after injection (min)	Kynurenine ($\mu\text{g/ml} \pm \text{s.e. mean}$)	
		Plasma	Brain
Saline		0.674 \pm 0.020 (12)	0.166 \pm 0.009 (22)
Kynurenine (0.5 mg/kg i.p.)	30	0.869 \pm 0.110 (5)*	0.217 \pm 0.028 (7)*
	60	0.733 \pm 0.040 (6)	0.188 \pm 0.024 (6)
	120	0.754 \pm 0.095 (7)	0.314 \pm 0.044 (10)**
Kynurenine (5.0 mg/kg i.p.)	30	1.412 \pm 0.131 (7)***	0.278 \pm 0.025 (9)***
	60	0.949 \pm 0.080 (6)**	0.235 \pm 0.026 (8)**
	120	0.641 \pm 0.052 (10)	0.308 \pm 0.020 (11)***
Kynurenine (20.0 mg/kg i.p.)	30	3.416 \pm 0.223 (6)***	0.865 \pm 0.137 (6)***
	60	1.503 \pm 0.138 (5)***	0.512 \pm 0.072 (6)***
	120	0.893 \pm 0.130 (11)*	0.289 \pm 0.033 (11)**

n of determinations given in brackets. Significance of increase above saline controls: * $P < 0.05$; ** $P < 0.01$;

*** $P < 0.001$. Student's 't' test.

not paralleled by significant differences in brain kynurenine at this time. The fluxes during the intervening period may have more important effects on turnover than the actual brain levels at 2 h.

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