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The effects of chronic lithium administration on the metabolism of L-tryptophan in the rat forebrain

K.J. COLLARD* & M.H.T. ROBERTS

Department of Physiology University College Cardiff

We have investigated the effect of lithium (Li^+) on the accelerated production of 5-hydroxyindoles induced by a large dose of L-tryptophan. Male Albino Wistar rats (124) weighing 150-250 g were divided into two groups of 62 animals. One group received an i.p. injection of isotonic (0.15 M) LiCl (0.75 mequiv/kg) each day for 10 days, whilst the control group received injections of saline. Twenty-four hours after the last dose of Li^+ or saline, half of the animals in each group received a single injection of L-tryptophan (100 mg/kg i.p.)

the injection, was significantly reduced in the Li^+ group, and the concentration of 5-HIAA was correspondingly increased.

There is evidence that the increase in 5-HIAA concentration induced by a loading dose of L-tryptophan results from the deamination of the increased amount of free cytoplasmic 5-HT which is accessible to monoamine oxidase (Moir & Eccleston, 1968). The results of this study may therefore indicate that Li^+ increases the deamination of free cytoplasmic 5-HT, possibly by inhibiting the transport of newly synthesized 5-HT into, or the binding of 5-HT within the storage compartment of 5-HT neurones. Alternatively, Li^+ may divert the metabolism of L-tryptophan away from the production of 5-HT, and towards the production of 5-hydroxyindolepyruvic acid through the 5-HTP aminotransferase pathway (Millard & Gal, 1971).

Table 1 The effect of Li^+ pretreatment on L-tryptophan-induced changes in forebrain 5-hydroxyindoles measured 30, 60, and 90 min after the i.p. injection of L-tryptophan (100 mg/kg). Results are expressed as the mean \pm s.e. of mean 8, 13, and 10 pairs respectively. Statistical analysis is by paired *t* test

Change in 5-HT concentration (ng/g wet weight)				
Time after L-tryptophan	Control	Lithium	Lithium minus control	P
30 min	+ 145 \pm 50	+ 142 \pm 52	- 3 \pm 77	NS
60 min	+ 283 \pm 59	+ 132 \pm 71	- 151 \pm 64	<i>P</i> < 0.05
90 min	+ 202 \pm 53	+ 72 \pm 80	- 130 \pm 96	NS
Change in 5-HIAA concentration (ng/g wet weight)				
Time after L-tryptophan	Control	Lithium	Lithium minus control	P
30 min	+ 75 \pm 19	+ 117 \pm 15	+ 42 \pm 24	NS
60 min	+ 201 \pm 39	+ 280 \pm 23	+ 79 \pm 35	<i>P</i> < 0.05
90 min	+ 254 \pm 30	+ 235 \pm 47	- 19 \pm 39	NS

whilst others received an equivalent volume of saline. Pairs of animals (one tryptophan treated and one control) from each group were killed 30, 60 and 90 min after the injection of tryptophan or saline, and the forebrain concentration of 5-HT and 5-HIAA measured fluorimetrically (Collard & Roberts, 1974).

Li^+ pretreatment had no effect on the changes in forebrain 5-HT and 5-HIAA measured 30 or 90 min after the injection of L-tryptophan (Table 1). However, the maximum increase in 5-HT concentration which occurred 60 min after

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