Role of tryptamine in the behavioural changes caused by a monoamine oxidase inhibitor and L-tryptophan

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Giving L-tryptophan (L-TP) to rats pretreated with the monoamine oxidase (MAO) inhibitor tranylcypromine causes behavioural changes including hyperactivity, reciprocal forepaw treading, head weaving, Straub tail and hind limb abduction which depend on 5-hydroxytryptamine (5-HT) synthesis as they are prevented by tryptophan hydroxylase inhibition (Grahame-Smith, 1971). As brain tryptamine also increases when L-TP is given after MAO inhibition (Saavedra & Axelrod, 1973; Marsden & Curzon, 1974) it could also be involved and its role was therefore investigated.

In experiment 1 (Table 1) the increase of locomotor activity after tranylcypromine was greatly enhanced by L-TP, 50 mg/kg (+94% v. tranylcypromine alone). Addition of tryptamine (0.75 mg/kg) increased this further (+30% v. tranylcypromine + L-TP) but increased the behaviour score more strikingly (+76%). Brain 5-HT and tryptamine rose after L-TP (+56%, +64% respectively v. tranylcypromine alone) and tryptamine rose further when it was also given (+128% v. tranylcypromine + L-TP). These results suggest that the tryptamine changes after giving tranylcypromine + L-TP are sufficient to influence behaviour.

This is also supported by experiment 2 (Table 1) in which increasing the L-TP dose to 100 mg/kg increased locomotor activity slightly (+21% v. tranylcypromine + L-TP, 50 mg/kg) but the behavioural score considerably (+159%) in association with slight (+23%) and considerable (+107%) rises of brain 5-HT and tryptamine respectively.

Therefore, increased brain tryptamine on given L-TP after tranylcypromine may alter behaviour. However, this effect of tryptamine requires 5-HT as in confirmation of Foldes and Costa (1975) we find the behavioural effects of tranylcypromine (20 mg/kg) + tryptamine (1 mg/kg) are partly prevented by the tryptophan hydroxylase inhibitor *p*-chlorophenylalanine (3 × 100 mg/kg).

Table 1 Behavioural and biochemical effects of L-tryptophan (L-TP) and tryptamine in tranylcypromine (TCP) treated rats

	Behaviour		*Biochemical determinations*		
Treatment	*Locomotor activity*	*Behaviour score*	*L-TP*	*5-HT Brain (μg/g wet wt.)*	*Tryptamine*
Exp. 1					
Control (0.9% saline)	1224 ± 329(4)	ND	2.3 ± 0.5(9)	0.64 ± 0.08(9)	ND
TCP (20 mg/kg)	3765 ± 917(7)‡	ND	2.5 ± 0.3(15)	0.97 ± 0.14(15)‡	0.11 ± 0.03(6)
TCP (20 mg/kg) + L-TP (50 mg/kg)	7279 ± 433(8)‡	13.0 ± 1.8(8)	17.7 ± 2.8(18)‡	1.51 ± 0.23(18)‡	0.18 ± 0.05(6)*
TCP (20 mg/kg) + L-TP (50 mg/kg) + Tryptamine (0.75 mg/kg)	9507 ± 844(4)‡	35.9 ± 3.4(4)‡	16.4 ± 2.4(12)	1.51 ± 0.16(12)	0.41 ± 0.06(6)‡
Exp. 2					
TCP (20 mg/kg) + L-TP (50 mg/kg)	6434 ± 510(4)	12.3 ± 2.4(4)	23.8 ± 5.4(10)	1.26 ± 0.15(10)	0.15 ± 0.05(5)
TCP (20 mg/kg) + L-TP (100 mg/kg)	7767 ± 576(4)*	31.8 ± 1.3(4)‡	45.9 ± 4.8(12)‡	1.56 ± 0.17(12)†	0.31 ± 0.08(6)†

All injections were i.p. Tranylcypromine was injected 30 min before other drugs and rats killed 60 min after the second injection. Locomotor activity is total counts (Animex) during these 60 min. Behaviour was scored (head weaving, forepaw treading, hind limb abduction, Straub tail) every 15 min during the 60 min (the total score is given). Tryptophan and 5-HT determined in single brains (Marsden & Curzon, 1974) and tryptamine on bulked extracts of two brains (Sloan, Martin, Clements, Buchwald & Bridges, 1975). Figures in brackets are number of values obtained; each behavioural value is on a cage of three rats. Values given as mean ± s.d. * $P < 0.05$, † $P < 0.01$, ‡ $P < 0.001$ all with respect to corresponding value on preceding line. ND = not done.

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Monoamine oxidase activity at different levels of rat spinal cord

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Monoamine oxidase (MAO) exists in at least two forms, 'A' and 'B' which exhibit different substrate affinities and inhibitor susceptibilities (Squires, 1972). Rat spinal cord MAO exhibits 80% type A activity and 20% type B activity (George & Jones, 1976). In this study, MAO activity was investigated in different regions of rat spinal cord. Male rats 200–250 g were anaesthetized and the spinal cord was divided, *in situ*, into its cervical, lumbar, thoracic and sacral segments. The MAO activity of homogenates of each cord region was determined as previously described by George & Jones (1976). Each homogenate sample was incubated with [^{14}C]-tyramine (0.3 μCi) which is a substrate for both MAO types. The protein concentration of each homogenate sample was determined as described by Lowry, Roseborough, Farr & Randall (1951) and the MAO activity was expressed as ng product mg protein^{-1} h^{-1}. By separate assays, the percentage inhibition of MAO produced by clorgyline (1×10^{-7} M) a specific type A inhibitor and pargyline (1×10^{-7} M) a specific type B inhibitor was determined for homogenates of each spinal region.

George & Jones (1976) have demonstrated that the ratio of type A/B MAO in rat brain is 1.5:1. The present results show that for whole spinal cord the ratio was 4:1 while for the thoracic section it was 9:1. A ratio of 9:1 has been demonstrated in sympathetic ganglia (Goridis & Neff, 1971).

It is suggested that differences in MAO ratios between regions of the spinal cord may be related to the distribution of efferent pathways and neurotransmitters in the cord.

Table 1 Differential MAO inhibition in spinal cord

	% Inhibition of MAO activity		*Ratio type A/B MAO activity*
Tissue	*Clorgyline (1×10^{-7} M)*	*Pargyline (1×10^{-7} M)*	
Whole cord	81.9%	23.2%	4:1
Cervical cord	70.7%	28.9%	2.3:1
Thoracic cord	90.7%	9.8%	9:1
Lumbar cord	61.3%	39.4%	1.5:1
Sacral cord	82.5%	21.2%	4:1

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