The non-specificity of diethyldithiocarbamate

When an inhibitor of tyrosine hydroxylase, 3-iodo-L-tyrosine (3-IT) (200 mg/kg, s.c.), is injected into rats, there is a reduction in the concentration of noradrenaline in the brain. Sodium diethyldithiocarbamate (DDC) (500 mg/kg, s.c.) causes a greater reduction in brain noradrenaline than does 3-IT. If these same doses of 3-IT and DDC are administered simultaneously, the depletion of noradrenaline is significantly less than that obtained with DDC alone (Goodchild, 1969). The interpretation of these results depended on the fact that the decrease in noradrenaline after DDC has previously been attributed to inhibition of dopamine-β-hydroxylase (Collins, 1965; Carlsson, Lindqvist & others, 1966). I have now measured the level of tyrosine in the brains of rats treated with DDC with the object of challenging the utilization of tyrosine in the brain.

Adult, male white rats (150–200 g) were injected with DDC (500 mg/kg, s.c.) killed at various times after injection and the brain tyrosine levels estimated (Waalkes & Udenfriend, 1957). The results are shown in Table 1.

Table 1. *The effects of DDC on rat brain tyrosine levels.* Tyrosine levels are expressed as the percentage of uninjected controls. The figures in parentheses are the standard errors of the means (each value represents the mean of 5 determinations). The absolute value for the tyrosine level in control brains was 11·49 μg/g.

Time after injection of DDC	% Tyrosine	Significance value
20 min	102 (±4)	N.S.
30 min	120 (±2)	$P < 0{\cdot}02$
1 h	135 (±5)	$P < 0{\cdot}01$
2 h	134 (±6)	$P < 0{\cdot}01$
3 h	123 (±8)	N.S.

There was a significant increase in brain tyrosine levels 30 min after injection and this persisted for a further 90 min. This increase could arise from an increased availability of tyrosine, or from an inhibition of its enzymic degradation. Taylor, Stubbs & Ellenbogen (1969) have recently reported that DDC can inhibit tyrosine hydroxylase *in vitro*. Thus it appears that in addition to its inhibitory action on the conversion of dopamine to noradrenaline, DDC may also inhibit tyrosine hydroxylase as shown by the increased tyrosine levels reported here. The decrease in noradrenaline content of rat brain after treatment with DDC may therefore be attributed to the inhibition of tyrosine hydroxylase in addition to dopamine-β-hydroxylase.

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