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The effect of Δ^8-tetrahydrocannabinol (Δ^8-THC) on dopamine metabolism in the rat corpus striatum: the influence of environment

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Many workers have tried to relate behavioural actions of THC and brain monoamines with varying success. In some of its actions (e.g., catalepsy, hypothermia) THC closely resembles the neuroleptics which appear to block dopamine (DA) receptors as well as altering central noradrenaline (NA) metabolism (see Andén, Corrodi & Fuxe, 1972). It is therefore of interest to examine the effects of THC on central monoamine, and particularly dopamine, metabolism. In these experiments, depletion of rat brain catecholamines 2 h after administration of α-methyl p-tyrosine methyl ester (α-MT) (400 mg/kg i.p.) was used as an index of catecholamine turnover. Pooled (4) hypothalami or corpora striata, dissected as described by Glowinski and Iversen (1966), were analysed fluorimetrically for monoamines (NA, DA + 5HT). Male, Wistar rats (120-150 g) were kept in groups of six at 21°C and fed and watered freely before each experiment.

Δ^8-THC (10 mg/kg i.p.) administration under the above environmental conditions produced no change in regional brain monoamine concentrations, and did not alter the depletion of catecholamines when administered simultaneously with α-MT. Similarly, Δ^8-THC administration caused no change in monoamine concentrations in brains of rats subjected to isolation (24 h), food deprivation (24 h), or acute cold stress (2 h at 4°C). Under these conditions, however, the α-MT-induced depletion of DA in the corpus striatum was reduced by simultaneous administration of THC, whereas NA depletion in corpus striatum and hypothalamus was unaffected. The vehicle for THC (Tween 80, 4% in saline) did not affect catecholamine concentrations or the depletion produced by α-MT. Thus, it appears that striatal DA depletion after inhibition of tyrosine hydroxylase is inhibited by THC in animals subjected to isolation plus food deprivation, and isolation plus acute cold stress. Our results suggest that food deprivation is the most effective environmental factor studied in revealing this effect of THC.

These experiments suggest that, under certain environmental conditions, Δ^8-THC reduces striatal DA turnover without affecting other monoamines. It is not clear why we obtained these changes only under these environmental conditions. Food deprivation, isolation and cold stress may all change DA metabolism *per se* which may be relevant, but possible effects on drug absorption, distribution and metabolism cannot be discounted.

In conclusion, we suggest that reduction in central DA turnover in the corpus striatum by THC may explain some of its actions (e.g., hypothermia and catalepsy) and an asymmetrical reduction could explain the turning behaviour described by Waters & Glick (1973). Thus, although THC shares some properties with the neuroleptics, these could be mediated by inhibition of DA release rather than by DA receptor antagonism.

K.I. MacLean acknowledges a CAPS award from the SRC and Beecham Research Laboratories, and the help and advice given by Drs M. Clarke and M. Palfreyman, who also provided the Δ^8-THC.

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