These results are consistent with a positive correlation between the changes in tryptophan metabolism and cyclic AMP as this is known to mediate the lipolytic action of the catecholamines and aminophylline and nicotinic acid increase and decrease fat cell cyclic AMP respectively.

This suggests that the disposition of plasma tryptophan and hence brain 5-HT metabolism can be influenced by the hormonal factors (Robison, Butcher & Sutherland, 1971) controlling extracerebral cyclic AMP and fatty acid production.

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In vivo changes in the concentration of cerebral cyclic AMP, phosphorylase *a* and glycogen induced by biogenic amines

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A number of *in vitro* studies have provided evidence indicating that cyclic AMP may play a role in the functioning of the central nervous system. Thus, certain biogenic amines, which are believed to act as neurotransmitters in the central nervous system, enhance the formation of cyclic AMP when added to brain slices (Kakiuchi & Rall, 1968 ; Forn & Krishna, 1971). Parallel experiments *in vivo* have been hampered (a) by the very rapid increase in cerebral cyclic AMP content which occurs post-mortem, and (b) by the inability of most systemically administered biogenic amines to pass the blood-brain barrier. In the present study these difficulties have been overcome by the use of an apparatus which removes and freezes the brain in less than 0·5 s (Nahorski, Rogers & Slater, 1973) and by using the neonate chick which has an immature blood-brain barrier but possesses a functionally mature C.N.S. (Spooner & Winters, 1966).

Experiments were performed on four to six day old Rhode Island Red×Sussex Brown hybrid chicks. All drugs were administered by injection into the right jugular vein, and the chicks were killed using the rapid freezing apparatus. Adrenaline, isoprenaline, noradrenaline and dopamine were each administered in a dose of 60 μg/100 g. The dose of histamine was 800 μg/100 g. Drug doses are expressed as free base. Cyclic AMP was assayed by the protein binding saturation assay of Brown *et al.* (1971). The percentage changes quoted are all significantly different from control values ($P<0{\cdot}05$).

The injection of adrenaline, isoprenaline and histamine increased the concentration of forebrain cyclic AMP by 48%, 72% and 48% respectively, at two minutes. On the other hand, noradrenaline and dopamine caused reductions in the cyclic AMP concentration (noradrenaline 19%, dopamine 25%).

Although it has been well established that cyclic AMP is a mediator of the glycogenolytic effect of catecholamines in some peripheral tissues, the possible metabolic role of this nucleotide in brain remains obscure (Rall, 1972). The concentration of glycogen and phosphorylase *a* in chick forebrain was therefore measured following injection of certain of the biogenic amines. Adrenaline and histamine significantly increased the forebrain content of phosphorylase *a* by 158% and 262% respectively after 2 min, and lowered the glycogen concentration with maximal decreases of 19% and 35% between 5 and 10 min after injection. The phosphorylase *a* and glycogen levels were unchanged following the injection of noradrenaline.

The results show that some putative neurotransmitter substances can influence the concentration of cerebral cyclic AMP *in vivo*, and indicate that there may be a metabolic role for cyclic AMP in the C.N.S.

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Evidence of a role for brain monoamines in ethanol dependence

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Brain monoamines have often been implicated in the neurochemical changes leading to ethanol dependence, although few attempts have been made to relate tolerance to, and dependence on ethanol with direct measurements of central monoamine metabolism.

We have measured changes in mouse brain monoamine concentrations during the chronic administration of ethanol by inhalation. Withdrawal of ethanol after ten days is followed by a marked withdrawal syndrome which lasts for some 12 h (Griffiths, Littleton & Ortiz, 1973).

In our experiments mice were killed by immersing them in liquid nitrogen after varying periods of ethanol administration and withdrawal. Brains were dissected out and taken for fluorimetric estimation of monoamines. Noradrenaline and dopamine were estimated by the method of Brownlee & Spriggs (1965). 5-Hydroxytryptamine was estimated by the method of Curzon & Green (1970).

There was an initial significant reduction in brain monoamine concentrations during ethanol administration, but this was short-lived. Otherwise chronic administration of ethanol was associated with a slow rise in catecholamines so that after ten days they were some 50% higher than controls. Withdrawal of ethanol at this time was associated with a further transient rise in catecholamine concentrations, followed by a fall back to control levels over the next 10 h. These changes were also shown to a smaller extent by brain 5-hydroxytryptamine.

Arresting the withdrawal syndrome by the intraperitoneal injection of ethanol (2 g/kg) also arrested the changes in brain monoamine concentrations associated with withdrawal.

The administration of the tyrosine hydroxylase inhibitor, α-methyltyrosine methylester, and and dopamine β-hydroxylase inhibitor FLA-63 before ethanol withdrawal modified the withdrawal syndrome.

These experiments are thought to provide evidence for the involvement of noradrenaline, dopamine and perhaps 5-hydroxytryptamine in ethanol dependence and withdrawal.

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