Influence of folic acid on noradrenaline stimulation of rat brain synaptosomes

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Many antiepileptic drugs may produce a megaloblastic anaemia in man. These drugs impair the absorption of folic acid, but administration of folic acid, which corrects the anaemia, may aggravate the epilepsy. It is thus possible that folic acid increases neuronal excitability and that the antiepileptic drugs may antagonize this.

In these experiments rat brain synaptosomes were exposed to a range of concentrations of formyl tetrahydrofolic acid (f-THF) (0·0016–0·635 mM) and of noradrenaline (NA) (0·015–0·15 mM). The rate of oxygen consumption in a glucose medium was measured in an oxygen electrode. Neither f-THF nor NA affected respiration rate, but when both substances were present the rate of oxygen consumption was increased. Adrenaline with f-THF also stimulated respiration, but isoprenaline, pteroyl glutamic acid, acetylcholine, histamine and dopamine did not affect oxygen uptake in this system.

The NA plus f-THF stimulation was blocked by concentrations of phenobarbitone which did not affect the control respiration rate. The effect was also inhibited by administration of 5-fluorouracil (100 mg/kg) *in vivo* for 3 days before the *in vitro* experiment.

This experiment suggests that, in the presence of extraneuronal NA, f-THF but not pteroyl glutamic acid can stimulate brain function. This provides a possible explanation of the antiepileptic properties of drugs which block folate reductase.

Distribution of octopamine in nervous tissues of *Octopus vulgaris*

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Octopamine (*p*-hydroxyphenylethanolamine) was first discovered in the posterior salivary glands of *Octopus vulgaris* (Erspamer & Boretti, 1951). A sensitive enzymatic assay (Molinoff, Landsberg & Axelrod, 1969) for octopamine has been developed and used to show that octopamine occurs normally in the sympathetic nerves of rat organs (Molinoff & Axelrod, 1969). The high concentration of octopamine in *Octopus* salivary glands suggested the possibility that it might also be present in neural tissues of octopods.

Tissues, dissected out as previously described (Juorio, 1971), were weighed and then quickly frozen on dry ice. After heat denaturation of the proteins the concentration of octopamine was estimated. Significant amounts of octopamine were found throughout the *Octopus* nervous system (Table 1).

The concentration of octopamine in most neural tissues is similar to the concentrations of catecholamines and of 5-hydroxytryptamine (Juorio, 1971). The concentration of octopamine in the posterior salivary gland was more than 1 mg/g. The administration of reserpine (4 mg/kg, i.m.) led to a fall in the octopamine concentration in most neural tissues but did not affect the concentration in the posterior salivary gland.