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Some behavioural and anticonvulsant actions in mice of ethanolamine O-sulphate, an inhibitor of 4-aminobutyrate aminotransferase

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Ethanolamine O-sulphate (EOS) is a specific active-site-directed irreversible inhibitor of 4-aminobutyrate aminotransferase (GABA-T) (Fowler & John, 1972a and b), the major catabolic enzyme for GABA in mammalian brain (Balazs, Machiyama, Hammond, Julian & Richter, 1970).

We have given EOS intracerebroventricularly to mice (method of Brittain & Handley, 1967), in order to re-investigate the possible relationship between elevated brain GABA concentrations and the response to maximum electroshock. Previous studies with non-specific inhibitors of GABA-T failed to establish a correlation (Kuriyama, Roberts & Rubenstein, 1966; Maynert, 1969).

Injection of 80–320 μg of EOS caused decreased locomotor activity, hunched posture, ptosis and hypothermia and these effects more closely resembled those of reserpine than of chlorpromazine. Such doses of EOS also protected against the hind limb extension induced by electroshock, the effect at 48 h being greater than at earler times. Whole brain concentrations of GABA were significantly increased 6 to 48 h after 160 μg EOS whereas 5-HT concentrations were only increased from 24 h.

The anticonvulsant studies revealed only weak protection against maximum electroshock during the first 36 h although GABA concentrations were greatly increased. The anticonvulsant activity of EOS over the first 36 h may be related to the increased 5-HT concentrations and it may be relevant that the action of anticonvulsant drugs has been associated with increased 5-HT concentrations (Bonnycastle, Giarman & Paasonen, 1957). However, the marked increase in anticonvulsant effect between 36 and 48 h was not paralleled by a corresponding elevation of brain 5-HT. The changes in 5-HT concentrations throughout the period of elevated GABA concentrations support the suggestion of Yessaian, Armenian & Buniatian (1969) that there may be an interrelationship between the GABA and 5-HT systems in brain.

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