Central uptake and cardiovascular effects of δ-aminolaevulinic acid

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A characteristic feature of acute intermittent porphyria is the increased biosynthesis of the porphyrins and their precursors δ-amino-laevulinic acid (ALA) and porphobilinogen. Although the purified porphyrins and porphobilinogen are pharmacologically inactive, ALA has recently been shown to inhibit both membrane sodium transport (Isaacson, Douglas & Eales, 1971) and brain ATPase activity (Becker, Viljoen & Kramers, 1971) *in vitro*. It is possible that some such action of ALA could be a contributory factor in the pathogenesis of acute porphyria.

There have been conflicting reports on the ability of ALA to pass the blood-brain barrier in the rat. It was found that at plasma concentrations known to occur in acute porphyria, (1–24 μg/ml), ALA could pass the blood-brain barrier. ALA was found also to cause a short lasting hypotensive response in the anaesthetized and pithed rats. This response could be elicited by a dose of 1 mg/kg but usually a dose of 2–4 mg/kg was employed. The response to these larger doses was normally an immediate fall of 10–30 mmHg gradually returning to normal over 30 s to 5 min. It is unlikely that this action is centrally mediated as the hypotensive response was still evident in the pithed rat when the blood pressure was raised by vasopressin. It is more likely that ALA causes vasodilatation either directly, or by the release of histamine. The ALA response is qualitatively similar to that of histamine, and shows many of the characteristics of a typical 'histamine releaser' response.

Further elucidation of the pharmacological actions of ALA, particularly in the C.N.S., may considerably increase our understanding of the mechanisms and course of acute porphyria.

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The relationship between ethyl oleate/Krebs solution partition coefficient and depression of myocardial contractile force in a number of pharmacologically active compounds (T)

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The prediction of drug activity (T)

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DEMONSTRATIONS

Use of dansyl chloride to detect amino acids and 5-hydroxytryptamine in small quantities of tissue

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It is generally accepted that certain amino acids and 5-hydroxytryptamine (5-HT) are involved in synaptic transmission in the invertebrate and vertebrate central nervous system. A sensitive microbiochemical method has therefore been developed by Neuhoff