Amino acid receptors on frog spinal motoneurones

R.H. EVANS & J.C. WATKINS*

Department of Pharmacology, The Medical School, Bristol BS8 1TD

The isolated hemisected amphibian spinal cord is a convenient preparation for demonstrating the action of neuro-active amino acids (Curtis, Phillis & Watkins, 1961). However, changes in motoneurone activity, as recorded from the ventral roots, reflect not only the direct action of applied substances but also the action of substances on neurones which synapse with motoneurones. Thus, the precise site of action of the applied substances is unknown. To overcome this difficulty, we have blocked regenerative activity with procaine, so allowing the recording of electrotonic propagation in the ventral root to be used as a direct measure of the action of the substances on the motoneurone membrane. With this system L-glutamate and L-aspartate depolarized motoneurones, while γ-aminobutyric acid (GABA) and taurine caused hyperpolarization. The action of GABA was blocked by picrotoxin and bicuculline, but not by strychnine. The action of taurine was blocked by strychnine but not by picrotoxin. Glycine caused a weak depolarization, and neither strychnine nor picrotoxin antagonized this action.

No specific blocking agents are yet available to enable a comparison to be made of the receptors for excitatory amino acids on frog motoneurones with those present on neurones in the mammalian central nervous system. However, a series of excitants covering a wide range of potencies might be expected to show the same order of activity on frog motoneurones as on mammalian spinal neurones if the receptors were similar. Eight such substances (including three new excitants, marked with an asterisk, which have not been previously studied) were tested and the order of excitatory potency was found to be: kainate > N-methyl-D-aspartate ≃ DL-2-amino-4-thiosulphonylbutyrate (thiohomocysteic acid)* ≃ DL-homocysteate > L-glutamate ≃ L-aspartate ≃ 6-hydroxy-2-pyridylalanine (6-H-2PA)* > L-2-amino-3-thiosulphonylpropionate (thiocysteic acid)*. The same order of potency was found for rat spinal interneurones when the substances were administered by microelectrophoresis (Biscoe, Headley, Martin & Watkins, unpublished observations). Moreover, in the frog cord experiments, all the compounds gave a log dose-response plot parallel to that for L-glutamate.

The close similarity between the excitatory amino acid receptors on frog and rat spinal neurones which is apparent from these studies contrasts with the results of structure-activity studies for glutamate agonists on invertebrate preparations, where, for example, kainate and DL-homocysteate have been found to have only weak excitatory actions (Clements & May, 1974). It seems likely that results of further investigations using this amphibian system, including a search for glutamate antagonists, will be relevant to the mammalian central nervous system.

References

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Sodium and the response of rat descending colon and rat uterus to angiotensin II

ANN D. CROCKER & K.A. WILSON*
(introduced by C.B. FERRY)

Pharmacological Laboratories, Department of Pharmacy, University of Aston, Birmingham B4 7ET, England

Angiotensin produces a contraction of most isolated smooth muscle preparations (Gross, 1971) and in lower concentrations stimulates transepithelial sodium transport (Crocker, 1971). It has been reported that the contractile action of angiotensin on guinea-pig ileum is dependent upon the extracellular sodium concentration (Blair-West, Harding & McKenzie, 1967). In the present study the role of Na^+ has been investigated on the contractile response of rat colon and uterus to angiotensin by altering the Na^+ concentration of the Tyrode solution and by the use of inhibitors of Na^+ movement.

Muscle preparations, from Wistar rats, were suspended in Tyrode solution and gassed with air. Contractions were measured at the maximum sustained deviation from resting tension using