## LETTER TO THE EDITOR

## Phosphonic analogues as antagonists of amino acid excitants

J. C. WATKINS, D. R. CURTIS<sup>\*</sup><sup>†</sup>, S. S. BRAND<sup>\*</sup>, Department of Pharmacology, University of Bristol, Bristol, BS8 1TD, U.K. and \*Department of Pharmacology, Australian National University, Canberra, Australia

A glutamate analogue, 2-amino-4-phosphonobutyrate, has been reported to interact with glutamate receptors of locust muscle and to antagonize, possibly competitively, the excitatory action of electrophoretically administered glutamate on this muscle (Cull-Candy, Donnellan & others, 1976). Although  $\omega$ -phosphonic (and  $\omega$ -boronic) analogues of depressant and excitant amino acids related to GABA and glutamate were mentioned as weak or inactive when tested on feline spinal neurons (Curtis & Watkins, 1965), details of this investigation were not published. Accordingly this communication concerns a study of the phosphonic analogues of aspartate and glutamate as possible antagonists of excitant amino acid action in the spinal cord of the cat.

With standard microelectrophoretic techniques, neither DL-2-amino-3-phosphonopropionate (0.2 M, pH 7.5) nor DL-2-amino-4-phosphonobutyrate (0.2 M,

† Correspondence.

pH 7.5) reduced the excitatory actions of either L-glutamate (1 M, pH 7.5), L-aspartate (1 M, pH 7.5) or DL-homocysteate (0.2 M, pH 7.5) on dorsal horn interneurons and Renshaw cells (12 neurons, 3 animals), within lumbar segments of cats anaesthetized with pentobarbitone sodium. The phosphonic analogues were generally ejected with electrophoretic currents twice those used to administer L-aspartate and Lglutamate, and weak excitation was occasionally observed. Spontaneous firing was not depressed.

Such results indicate that these analogues would be of no use as antagonists of the possible transmitter function of aspartate and glutamate in the feline spinal cord, and suggest that glutamate receptors in this tissue, and presumably also those elsewhere in the central nervous system of this and other mammals, differ from those of locust muscle.

November 19, 1976

## REFERENCES

CULL-CANDY, S. G., DONNELLAN, J. F., JAMES, R. W. & LUNT, G. G. (1976). Nature, Lond., 262, 408-409. CURTIS, D. R. & WATKINS, J. C. (1965). Pharmac. Rev., 17, 347-391.