GLYCINE

In Nerve Terminals

from our Neurochemistry Correspondent

By one of those strange coincidences which occasionally arise in the world of scientific research, the current issue of *Brain Research* contains reports of two studies carried out independently by T. Hökfelt and Å. Ljungdahl at the Karolinska Institute, Stockholm, and by A. I. Matus and M. E. Dennison at University College, London, who have demonstrated by autoradiography that tritiated glycine, after incubation with slices of rat spinal cord, becomes associated predominantly with nerve terminals (*Brain Res.*, **32**, 189 and 195; 1971).

Glycine, apart from its universal role as an essential component of proteins, is believed to serve an additional function in the spinal cord as a mediator of transmission at inhibitory synapses. Inhibition in the nervous system plays a crucial part in the regulation of neuronal activity; in the spinal cord, for instance, the motoneurons of the ventral horn, which give rise to axons transmitting information to skeletal muscles, are subject to a variety of inhibitory influences. Evidence implicating glycine as a spinal inhibitory transmitter (reviewed by Hebb in *Ann. Rev. Physiol.*, **32**, 165; 1970) arose from electrophysiological studies showing that iontophoretic application of glycine to certain cells in the cord causes an increase in the membrane potential of those cells similar to that occurring during natural inhibition. This hyperpolarization is blocked by the convulsant alkaloid, strychnine, which also blocks certain spinal inhibitory pathways. Furthermore, the distribution of endogenous glycine in the spinal cord suggests that it is concentrated to an extent greater than would be required

for a general "metabolic" function in areas where inhibitory neurones may be present.

If glycine is a neurotransmitter, a mechanism should also exist for its rapid removal from extracellular sites after it has exerted its physiological effects. Transmitter inactivation may be achieved by enzymatic destruction, by uptake into adjacent cells or nerve endings, or simply by diffusion from the site of action. It has been demonstrated that slices of rat spinal cord can accumulate exogenous radioactively-labelled glycine from an incubation medium by a high-affinity active transport process, but until recently there was little evidence as to the precise cellular sites responsible for this uptake. In the cerebral cortex, where γ -aminobutyric acid (GABA) is believed to be the principal inhibitory transmitter, there is an analogous uptake system and subcellular fractionation studies have shown that a proportion of the labelled amino-acid taken up into slices may be recovered in a fraction containing nerve endings. Moreover, Bloom and Iversen (*Nature*, **229**, 628; 1970) were recently able to demonstrate by electron microscope autoradiography of cortex slices or homogenates after incubation with ^3H -GABA that the label becomes localized over certain nerve terminals and preterminal axons. The present studies, by Hökfelt and Ljungdahl and Matus and Dennison, were an attempt to localize similarly the sites of uptake of ^3H -glycine in slices of spinal cord using autoradiography at both the light and electron microscope levels.

The results from both groups are strikingly similar. Light autoradiograms showed a higher concentration of grains over grey than white matter, and, at the ultrastructural level, heavy accumulations of grains were seen over

certain terminals, whereas others showed no activity. Matus and Dennison suggest that those terminals which were heavily labelled are those containing "flat" as opposed to round vesicles (see figure), although this possibility is not discussed by Hökfelt and Ljungdahl. This suggestion is, however, of considerable interest in view of the hypothesis of Uchizono (*Nature*, **207**, 642; 1965) that the shape of vesicles present in terminals may be correlated with the physiological role of those terminals—excitatory endings containing round vesicles and inhibitory endings with flattened ones.

Previous studies have shown that of the labelled glycine taken up by spinal cord slices, only 2 per cent is incorporated into protein, the remainder being recoverable as free glycine. It has also proved possible to demonstrate the release of labelled glycine from previously loaded tissue slices by electrical stimulation (J. M. Hopkin and M. J. Neal, *Brit. J. Pharmacol.*, **40**, 136; 1970). This suggests that exogenous glycine may enter the same sites as are occupied by the endogenous transmitter, and the present results may thus be interpreted as evidence that glycine is present in certain inhibitory nerve terminals of the spinal cord, thus adding considerable weight to the hypothesis that glycine is a spinal inhibitory transmitter.

TROPICAL ECOLOGY

Man-made Changes

from a Correspondent

THREE areas of concern were highlighted at the meeting of the Tropical Ecology Group of the British Ecological Society at University College, London, on October 4: first, the deterioration in the resources for cattle ranging following successful animal health control measures in Africa; second, the replacement of polyspecific forest and grassland by forest monocultures; and, third, the effects of tourism on tropical islands. The medical implications of large-scale irrigation for rice development in Kenya were also considered.

Contributions on cattle ranching in tsetse-fly infested savanna in Tanzania, by Mr J. Ford (University of Oxford), and on the effects of animal health control measures against rinderpest, by Mr A. Blair Rains (Land Resources Division, Overseas Development Administration), both illustrated very clearly, and with dramatic photographs, that increases in cattle numbers are followed by encroachment of shrubs, such as *Acacia* species, into grassland areas. Mr Ford's examples came from a large-scale attempt to ranch cattle, using drug prophylaxis against trypanosomiasis, started in eastern Tanzania in 1954; meat production increased for about ten

Electron microscope autoradiograph of a selected area from the ventral horn of rat spinal cord, after incubation in tritiated glycine, showing heavy accumulation of grains over a "flat" vesicle synapse on the right as compared with one containing round vesicles on the left. $\times 27,200$. (From *Brain Res.*, **32**, 195; 1971.)