

in its upper frequency channels, above about 30 kHz. The duration of the bursts ranged from 0.5 to several hours, with intervening intervals of as much as 24 hours during which the signals might be undetectable. The first problem was to identify the type of wave being detected. On comparing the results from the two sets of aerials, it was found that the electric and magnetic field intensities were linearly related, with a constant of proportionality which identified the waves as ordinary electromagnetic waves. The frequency spectrum of the bursts was determined with Imp 8 and shown to be remarkably narrow, most of the

radio wave energy being contained between 60 and 300 kHz.

When Imp 8 was at a distance of about 200,000 km from the Earth, the measured electric field signals were found to be strongly spin modulated, showing that the waves originated from an approximately point source, since had their distribution been isotropic the signal would not have depended on the orientation of the spacecraft. In fact the source was shown to have an angular diameter of less than 12° and to be in the direction of the Earth. At this distance, the diameter of the Earth subtends 4°, so though the Earth was clearly the source, its precise location

on the Earth could not be determined. On the other hand, a source relatively low in the atmosphere, rather than in the magnetosphere, is suggested, a supposition which is rather strengthened by the observation that, statistically, the intensity of the bursts falls off in an inverse square law fashion with distance from the Earth, at least at considerable distances (more than 4 Earth radii).

More precise information on the location of the source, however, was obtained from the intensity variations at various points in the magnetosphere. The waves were not observed whenever the spacecraft were inside the boundary surface known as the plasmapause.

LONGO and Penhoet reported<sup>1</sup> that a rat glioma releases, among other molecules, a protein which shares some immunological, chemical and biological properties with the mouse salivary nerve growth factor (NGF). A correspondent writing in these columns<sup>2</sup> about their work raised the question of a possible new role for the glial cell. Though this question is legitimate on theoretical grounds I wish to point out other findings which would not support the hypothesis.

NGF is present in large quantities in snake venom and male mouse submaxillary glands, but these are not the only sources of NGF. This protein molecule is also released from some mouse sarcomas<sup>3</sup> and is produced by granuloma<sup>4</sup> and embryonic tissues<sup>5</sup>. Recently a sensitive immunoassay was used to show that two neoplastic cell lines, L and 3T3, derived respectively from mouse C3H subcutaneous and adipose tissues and from simian virus-40 transformed A31, likewise produce a biologically active NGF which is immunologically similar if not identical to mouse submaxillary gland NGF<sup>6</sup>. Since in the experiments by Longo and Penhoet the NGF-like protein was isolated from solid rat tumours which were obviously contaminated with fibroblasts and other host cells, one cannot decide whether the NGF was of glial or fibroblastic derivation, and one wonders why the investigators did not extract the NGF protein from a pure glial cell line rather than from transplanted tumours.

In favour of an NGF-releasing role of glial cells the correspondent also quotes some recent experiments by Swedish investigators who reported that NGF injected intracerebrally enhances regenerative processes in noradrenergic nerve cells in the CNS<sup>7</sup>. Since glial cells outnumber nerve cells in the CNS

## A new role for the glial cell?

a reply from Rita Levi-Montalcini

in the ratio of 10:1, these findings seem to the correspondent to suggest that this astronomically large cell population may provide the NGF which could not readily enter the brain from the bloodstream. It should however be remembered that the number of noradrenergic nerve cells in the CNS is of the order of a few thousand (the locus coeruleus, by far the largest noradrenergic nucleus in vertebrate brains, contains about 1,400 noradrenergic neurones<sup>8</sup>) while the whole neuronal population in the mammalian CNS is in the range 10<sup>8</sup>–10<sup>10</sup> according to the size and phylogenetic position of brains. Hence only one out of a million nerve cells in the CNS would be receptive to NGF. An NGF-releasing role of glial cells would therefore benefit only an exceedingly small nerve cell population.

The situation in the peripheral nervous system is not much better. Regeneration of damaged axons occurs in peripheral nerves, irrespective of the receptivity of their cells of origin to NGF. Somatic motor and sensory differentiated neurones do not in fact respond to NGF and yet their axons are tightly wrapped by glial cells. Furthermore sympathetic neurones show a maximal NGF response at an early stage of differentiation when only a few glial and other satellite cells are present in the ganglia and are very loosely scattered among, but not adherent to post-ganglionic axons.

The possibility that glial cells surrounding other nerve cell types might contain hitherto undiscovered nerve growth factors cannot be discarded. But before considering this

it is highly desirable to obtain much more convincing evidence for the release of NGF by cells unequivocally identified as glial cells.

The correspondent suggests using immunofluorescence histochemistry to see whether NGF can be found in glial cells which are "wrapped around" their target neurones. But glial cells are not wrapped around noradrenergic neurones in the vertebrate CNS. The locus coeruleus consists of a small population of densely packed nerve cells in reciprocal contact with each other. Glial cells are not seen around individual neurones. Only a few loosely scattered, small non-neuronal cells are found intermingled with nerve cells of this nucleus, and there is no way of deciding whether these are glial cells or other cell types. Since some fibroblastic lines release NGF (refs 4–6) a positive fluorescence reaction would still not prove that glial cells release NGF. Even if they do, the NGF is probably present in the cells that produce it in such small quantities as to be undetectable by this technique.

While therefore there is no *a priori* reason to object to an "NGF-releasing role" of glial cells in the same way as this property has already been proved for a number of other cell lines, the hypothesis submitted by the correspondent that this role would explain the intimate relationship between glial cells and neurones is considerably weakened by the above considerations.

<sup>1</sup> Longo, A. M., and Penhoet, E. E., *Proc. natn. Acad. Sci. U.S.A.*, **71**, 2347–2349 (1974).

<sup>2</sup> *Nature*, **251**, 100–101 (1974).

<sup>3</sup> Levi-Montalcini, R., and Hamburger, V., *J. exp. Zool.*, **116**, 321–362 (1951).

<sup>4</sup> Levi-Montalcini, R., and Angeletti, P. U., in *Proc. 4th Int. Neurochem. Symp.* (edit. by Kety, S. S., and Elkes, J.), 362–376 (Pergamon Press, New York).

<sup>5</sup> Becker, E. D., Schenkein, I., and Bane, J. L., *Cancer Res.*, **20**, 1220–1228 (1960).

<sup>6</sup> Oger, J., Arnason, B. G. W., Pantazis, N., Lehrich, J., and Young, M., *Proc. natn. Acad. Sci. U.S.A.*, **71**, 1554–1558 (1974).

<sup>7</sup> Björklund, A., and Stenevi, U., *Science*, **175**, 1251–1253 (1972).

<sup>8</sup> Descarries, L., and Saucier, G., *Brain Res.*, **37**, 310–316 (1972).