magnetic activity was low (*Kp* <20) (see the table). In the first interval, protons (H$^+$) are the dominant ion; the ionosphere is clearly an important source as indicated by the low He^{2+}/H$^+$ ratio of ~ 0.01 compared with usual values of ~ 0.05 in the solar wind. In November 1979 the absolute H$^+$ and He^{2+} average densities were little altered, while the densities of the heavier ionospheric ions, O$^+$, He$^+$ and O^{2+}, had each increased by at least an order of magnitude, so that the average number densities of H$^+$ and O$^+$ became comparable. Thus during solar maxima heavy ionospheric ions, notably O$^+$, are important not only during magnetically disturbed periods, but also during quiet conditions. An O$^+$-dominated magnetosphere therefore occurs at these times.

Turning to correlations with magnetic disturbance, the GEOS 2 solar maximum data used for this study show relatively small (~ 60 per cent) increases in both H$^+$ and He^{2+} from quiet to active conditions (typical H$^+$ values being ~ 0.4 cm^{-3}), while O$^+$ increases markedly from ~ 0.1 to ~ 0.6 cm^{-3}. These results reflect a moderately greater injection of solar wind ions into the inner ring current during active conditions, together with increased ion outflow, particularly of O$^+$, from the ionosphere. The marked increase in O$^+$ probably results from localized increases in ionospheric ionization and heating in the auroral zone which occur during magnetic disturbance, as discussed by Young *et al.*, as well as perhaps to an expansion in the area of the ionosphere where accelerated outflows occur. In view of the latter it is perhaps surprising that Young *et al.* find no *Kp* response at all in the He$^+$ and O^{2+} densities which remain constant at ~ 10^{-2} cm^{-3} levels.

Finally, no evidence has been found for the presence of heavy molecular ions from the lower ionosphere (for example N$_2^+$, NO$^+$ and O$_2^+$) in the ring current plasma, at levels ⩾0.3 per cent of the total ion density, indicating that the usual ionospheric heating rates are insufficient to raise appreciable numbers of these ions into the ionospheric accelerator region. During major storm periods, however, large fluxes of these ions have been observed above ~ 1,000 km altitudes, so that as Young *et al.* point out, it may then be profitable to search for their presence in the ring current. In fact two intense storm periods in July and September 1982 may already have provided such an opportunity, and the outcome of investigations during these intervals are awaited with interest. □

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1. Shelley, E.G., Johnson, R.G. & Sharp, R.D. *J. geophys. Res.* **77**, 6104 (1972).
2. Balsiger, H., Eberhardt, P., Geiss, J. & Young, D.T. *J. geophys. Res.* **85**, 1645 (1980).
3. Horwitz, J.L. *Rev. Geophys. Space Phys.* **20**, 929 (1982).
4. Young, D.T., Balsiger, H. & Geiss, J. *J. geophys. Res.* **87**, 9077 (1982).

Obituary

Ulf von Euler 1905-1983

from Sir William Paton

THE death of Ulf von Euler on 9 March, at the age of 78, breaks a link with a classical period of physiological pharmacology in the 1930s when the foundations of the theory of chemical transmission were laid, along with the development of sensitive bioassay and of drug receptor theory. His own major discoveries were Substance P, with J.H. Gaddum in 1931, prostaglandins (now a large family of substances) in seminal fluid in 1934, and noradrenaline as the final neurotransmitter of the sympathetic nervous system in 1936, for which he was awarded the Nobel Prize in 1970. His papers were always distinguished, compact and crisply focused, but one can think it probable that they all stem in part from the time he spent in 1930–31 working with Gaddum on the pharmacological activity of tissue extracts in Dale's Hampstead laboratory — remembered affectionately as 'F4' by those who worked there. Had Gaddum been alive, one would expect him, too, to have shared the award.

There is little need to develop the significance of the pharmacologically active substances today, although their full physiological and pathological role in the body is still to be revealed. But it is worth considering the methods by which they were discovered, and whether they still have lessons for us.

Although extracts of tissues or body fluids had been long and profitably studied (yielding, for instance, thyroid extract, sex hormones and adrenaline), it was only with the unequivocal isolation of histamine as a constituent of mammalian tissue, and with Loewi's experiments on the release by nerve stimulation of active substances in the heart, that intensive work on such activity was seen to be really worthwhile. And how primitive the available technology now seems! String, plasticine and the smoked drum; no specific antagonists beyond atropine and ergotoxine; no chromatography; impure enzymes; and chemical characterization only possible when enough of the pure substance could be obtained in crystalline form for elemental analysis. Sensitivity to temperature, acid, alkali and proteases, and different solubility in organic solvents were the primary chemical tools. Sometimes skilful use of pharmacological desensitization helped. The other main weapon was careful choice of biological test object; and no doubt a Senator Proxmire of the day could have made due capital out of tests with a tissue mush on the dorsal muscle of a leech or on the rectal caecum of a hen. It was fiddly work, unimpressive to watch, with its own tricky logic, and it needed both a faith in pharmacological specificity and an experimental mastery of dose-response relationships. Yet it allowed the first recognition of most of the neurotransmitters and active substances worked on today.

One may ask how this was possible. The answer is surely that on the side of the pioneers was what one can now see as almost a biological truism: that if there is some diffusible chemical substance in the tissues that exerts physiologically important effects, then such issues must also contain recognition sites coupled to effector systems mediating those effects. Even if the substance is present in an amount too small by a factor of 10^3 or more for chemical detection, yet if it is biologically effective, the recognition site should have a comparable sensitivity. It is this that led to the rise of the bioassay in the 1930s and maintains it as an experimental technique today.

It is interesting that the capacity for biological detection still commonly runs ahead of chemical detection, although mass fragmentography and (where specific antibody can be raised) immunoassay are rapidly closing or reversing the gap. One must still expect bioassay to be needed for the discovery of many other unknown substances; clumsy it may be, but its great strength remains, that the assay itself incorporates something of the functional significance of the substance, and even if the assay is not perfect, the functional importance remains.

It is, therefore, perhaps timely to let von Euler's work remind us of the importance of the biological response, as the pendulum swings towards chemical techniques. *Mutatis mutandis*, Dale's words in 1933 in his third Dohme lecture are also worth recalling:

"The discovery, in artificial extract from an organ or tissue, of a substance which on artificial injection produces a pharmacodynamic effect provides only a first item of presumptive evidence in support of a theory that the action of this substance plays a part in normal physiology. Much more evidence is required before we can attribute clearly defined functions to such a substance, as we can now do in the cases of histamine and acetylcholine. But even when this is already possible, we have still no evidence to justify the assumption that the substance comes naturally into action in the body in the free condition in which we isolate and identify it in the laboratory after various unnatural chemical procedures."

Few have done more than von Euler to satisfy the demands of Dale's programme. □

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