HISTOCHEMISTRY OF NEUROGLIA AND MYELIN BREAKDOWN

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In recent years much interest had centred on the rôle of astrocytes in fluid transport in the brain, in their response to trauma, and in their rôle in repair processes. Although oligodendroglia might share some of these functions—and might possibly be one of the precursor cells of astrocytes—theyir main rôles seemed to be to support symbiotically the neuronal cell-body and to form as well as to maintain CNS myelin.

During CNS myelination, Friede (1962) had demonstrated a marked increase in the oligodendroglial population and in enzyme activity. These observations together with well-substantiated ultrastructural studies showed that the oligodendrocytes was the major cell involved in myelin formation. The question considered here was what happened to the oligodendroglia in demyelinating disease.

Lumsden (1951) reported that the oligodendroglia abruptly disappeared at the edge of plaques of multiple sclerosis. In their experience, however, this situation only applied in those plaques that they regarded as inactive (Ibrahim and Adams, 1963)—and even then a few oligodendroglia persisted in the plaques. Around those plaques that they believed to be active, the oligodendroglia proliferated, hypertrophied, and showed increased oxidative activity; such plaques appeared to be active as judged by the presence of lipid-laden microglia within them and, in occasional cases, as indicated by the clinical history.

It had been suggested that this activity at the edge of certain multiple sclerosis plaques represented a remyelinating process. However, they did not believe this interpretation was correct, because oligodendroglia proliferated and developed increased oxidative activity both in the prodromal stages of experimental cyanide encephalopathy and in very early multiple sclerosis plaques (Ibrahim and Adams, 1965).

In recent further studies of five cases of multiple sclerosis, they had found that proteolytic activity (pH 3.6 and pH 7.4) increased at the edge of active plaques. Trypsin, pepsin, and elastase digested the basic (trypanophic) protein of myelin and released myelin lipids in vitro (Tuqan and Adams, 1961; Adams and Bayliss, 1968). Moreover, they had found that extracts of degenerating peripheral nerves could induce similar changes in CNS myelin—namely, removal of trypanophic basic protein and acceleration of myelin-bud formation.

Proteolytic activity increased in the early phase of Wallerian degeneration in peripheral nerves. Thus, the initial disruption of the sheath in the primary stage of myelin breakdown—where Rossiter (Johnson, McNabb, and Rossiter, 1950) had shown that the myelin lipids remained chemically normal—could be attributed to digestion of the myelin basic-protein. In fact, trypanophilic basic protein was abruptly lost at the edge of the multiple sclerosis plaque and, moreover, substantially decreased during the first few days of Wallerian degeneration in the peripheral nerve. Conversely, chemical degradation of the lipids and the formation of Marchi-positive esterified cholesterol were delayed and proceeded in the second stage of myelin breakdown. Therefore, the myelin basic-protein seemed to be a particularly vulnerable part of the myelin sheath in that it was first attacked during myelin-breakdown.

An outstanding problem was where these proteolytic enzymes came from. It would not be unreasonable to suppose that they were derived from lysosomes, as was suggested by the early increase in acid phosphatase in Wallerian degeneration. However, myelin was compacted cell-surface membrane and itself contained leucin aminopeptidase (L-creatyl-β-naphthylamide) as well as a neutral protease. At present they were further investigating the origin of proteolytic enzymes by analysis of subcellular fractions from both normal and degenerating peripheral nerves.

REFERENCES


IMMUNOLOGICAL FACTORS IN EXPERIMENTAL ALLERGIC ENCEPHALOMYELITIS AND MULTIPLE SCLEROSIS AS REVEALED BY CULTURES OF MAMMALIAN NERVE TISSUE

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Organized cultures of mammalian central nerve tissues characteristically developed and maintained myelin and polysynaptic relationships. These cultures were used as a model system to examine the blood of animals with experimental allergic encephalomyelitis (EAEE) and patients with multiple sclerosis (MS) for the presence of immunological factors which might be involved in these disease processes. The serum of EAEE-affected animals and a majority of MS patients experiencing an active phase of their illness contained factors which produced a characteristic pattern of demyelination in the cultured CNS tissues. Their potency had been demonstrated to be complement dependent in both the human and the animal serum. Those in the animal serum had been shown to be localized in the 7-S component of the gamma globulins and to be removed by exposure to brain tissue, but not by liver, kidney, or red blood cells. Immunofluorescence examinations of exposed cultures revealed the globulins concentrated on the neuroglial cell membranes and the