Neurodegeneration, neuroprotection, glial cells, and myelin in multiple sclerosis

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Axon and neuron damage in the CNS of patients with multiple sclerosis (MS) was noted in the earliest studies. Over the past 10 years, such damage has become the focus of increased interest among researchers and in the clinical neurology and neuroscience communities. The rediscovery of axon damage as a component of early inflammatory white matter lesions, the evidence of lesions in both cerebral cortex and deep gray matter nuclei, and the uncertain relation of many of these gray matter lesions to the focal inflammatory lesions in the white matter have raised fundamental questions about the pathogenesis of the different types of MS lesions and about the ultimate etiology (or etiologies) of this serious and often disabling disorder. In addition, the two-way relation (i.e., interaction) between axons/neurons and glial cells has been highlighted by recent investigations into both axonal/neuronal dysfunction and permanent damage, including the eventual failure of remyelination and other reparative processes and ultimately, cell death.

The availability of partially effective immunomodulatory treatments for the relapsing–remitting phase of MS and the observation that degeneration of axons and neurons with accompanying atrophy may occur in some individuals who appear to respond to these therapies (with a reduction in occurrence of relapses and a lack of obvious new lesions in white matter of the brain and spinal cord) raises the question of whether the processes involved in loss of neurons and axons are primary or secondary to the processes of inflammation and demyelination, or whether they are triggered by an immune/inflammatory process that has become independent of the proximate cause.

Much of the permanent disability that emerges in the long term appears to be attributable to loss of axons and neurons. Therefore, strategies are needed to assess the process of such losses and to distinguish demyelination from inflammation and edema by use of imaging and other methodologies. At the same time, treatments to inhibit degeneration and enhance natural reparative mechanisms in both experimental paradigms and in patients are of increasing importance.

The articles and discussions in this supplement are the products of a meeting held in Geneva, Switzerland on May 24, 2006, to discuss the issues of neurodegeneration, neuroprotection and repair, and the interrelated issues of glial cells and myelin in MS.

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