

DEBATE: IS DISABILITY PROGRESSION IN MS DUE TO AN INFLAMMATORY OR NEURODEGENERATIVE PROCESS? AN INFLAMMATORY DISEASE

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Multiple sclerosis is an inflammatory demyelinating disease of the central nervous system. Inflammation in multiple sclerosis is detected in focal white matter lesions, grey matter lesions, the normal-appearing brain tissue as well as within the meninges. Neurodegeneration occurs in the same locations, the focal white matter lesions, grey matter lesions as well as the diffusely abnormal white matter. The inflammatory component of the disease is composed of cells of the adaptive as well as the innate immune system. Clinical disability progression is mainly linked to neurodegenerative processes such as axonal or neuronal loss and this neurodegeneration is clearly linked to inflammatory processes. The extent of axonal damage within white matter lesions clearly correlates with the extent of inflammation and this has been shown not only for early disease stages but has also been demonstrated in progressive MS. In addition, the diffuse axonal loss in MS spinal cord as well as cortical pathology itself is clearly linked to meningeal inflammation. This meningeal inflammation may in some cases even lead to the formation of so-called B cell follicle-like structures. Grey matter lesions themselves are also inflammatory, in early disease stages the adaptive immune system predominates here, whereas in progressive MS, innate immune cells such as microglial cells are the major inflammatory component present in these lesions. The same holds true for white matter lesions. In relapsing-remitting MS, cells of the adaptive immune system enter the lesions via the open blood brain barrier. In progressive MS, the typical plaque is the so-called slowly expanding lesion in which mainly resident microglial cells cause a further expansion of preexisting lesions. Inflammation is also present at that disease stage; however, it is trapped behind an intact blood-brain barrier. The latter observation led to the formulation of the concept of compartmentalized inflammation in progressive MS. In conclusion, multiple sclerosis is an inflammatory disease and all neurodegenerative processes occurring are closely linked to this inflammation.