J Neurol (2007) 254 [Suppl 2]: II/43–II/48
DOI 10.1007/s00415-007-2011-8

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Brain atrophy and cognitive impairment in multiple sclerosis: a review

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Abstract Multiple sclerosis (MS) is a common neurological disease in the Western hemisphere that leads to neurological dysfunctions and frequently from its onset to cognitive impairment, which together predict quality of life. Recent pathological and imaging studies have focused on brain atrophy representing axonal injury and loss as being crucial for developing disability and neuropsychological impairment. Brain atrophy has therefore been proposed to be a tool for monitoring disease progress. Here, we review the possible origins of brain atrophy and its correlation with cognitive impairment in MS.

Key words multiple sclerosis · cognitive impairment · cognitive training · brain atrophy · magnetic resonance imaging

Multiple sclerosis and brain atrophy

Despite the fact that axonal pathology has been recognised for many years, MS was traditionally considered to be a T-cell mediated autoimmune inflammatory process of the central nervous system (CNS) affecting myelin and oligodendrocytes in the white matter, which induces neurological deficits. However, recent data provide evidence that generalised ongoing subclinical axonal degeneration in lesional and non-lesional white matter as well as in grey matter is equally important in understanding disease progression, and at least some authors state that "inflammatory demyelination is not central to the pathogenesis of multiple sclerosis" [9]. Active demyelinising inflammatory lesions responding focal plaques, the hallmarks of MS, are associated with a loss of trophic myelin support and axons may be directly attacked in presence of CD8 + T-cells and macrophages [3]. This may lead to an axonal transection followed by secondary Wallerian degeneration in the plaques [13]. The correlation between clinical impairment and conventional MRI lesion load as well as the correlation between atrophy and lesion load is weak and, moreover, atrophy is already present in patients with clinically isolated syndromes (CIS) converting to MS [23]. Axonal degeneration seems to develop independently from the total brain lesion load, also in normal appearing white matter [24], and focal demyelination does not seem to be the only cause for diffuse axonal tissue damage. Recent data showed diffuse white matter injury, which may contribute to permanent neurological deficits at a stage of disease (PPMS, SPMS), where focal white matter plaques are either only slowly expansive or even absent. White matter injury therefore may be partly independent of demyelination [19]. It has been argued that axonal transection within lesions can cause remote neuroaxonal damage due to a loss of pre- and postsynaptic signals [22]. The third pathway for diffuse atrophy in MS is cortical demyelination, which can be extensive especially in the forebrain, and which correlates with clinical impairment and with diffuse white matter injury [19].

Brain atrophy therefore occurs in all stages of MS. It expresses irreversible damage of the neurones, is partly