Is neurodegeneration an absolutely inflammation-related process in MS?

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Multiple Sclerosis (MS) is considered an autoimmune demyelinating disorder of the Central Nervous System (CNS) affecting mostly young people. The clinical process of the disease varies from the relapsing to almost purely progressive forms. Whatever the case might be, the patients may exhibit progression of disability at various time points after the disease initiates. The underlying pathology of the ongoing disability is neurodegeneration characterized by axonal degeneration, loss of dendrites and synapses etc. Currently available treatments aim to control disease activity by interfering with the adaptive immune reaction and concomitant demyelination in the CNS. However, the same drugs may hardly halt the ongoing disability in the long term.

Several factors, either directly or indirectly related to the immune system have been implicated in the ongoing neurodegenerative process. Among them, oxidative stress, mitochondrial injury and subsequent ion channel dysfunction secondary to chronic inflammation seem to have a constant impact on neurons and axons, leading to their demise during progressive MS. The balance between continuous inflammatory stressors and intrinsic buffering mechanisms depends partly on age, sex and genetic factors, which eventually determine the clinical course of MS. Interestingly enough, in an animal model of MS, few molecular targets with proven neuroprotective properties that are separable from their impact on inflammatory responses have been identified; these molecules include CyPD, ASIC1 and TRPM4.

Presumably, the ongoing neurodegeneration may only partly be related to the inflammatory component of the disease. This is probably the reason that treatments aiming to control adaptive immunity activation are not able to protect axons of becoming gradually degenerated.