Myelin is a highly specific membrane formed by oligodendrocytes in the central nervous system. Its accurately regulated localization around axons permits fast saltatory nerve conduction and trophic support. In pathological conditions, however, these vital functions can be abrogated. Multiple sclerosis (MS) is such a disease, switching over the own immune system in order to attack endogenous myelin. In patients, this results in typical hallmarks such as immune cell infiltration, demyelination and axonal damage. It is believed that loss of myelin leads to deprivation of axon-supporting factors and consequently axonal damage and death. At the same time, the inflammatory environment provides cytokines and reactive oxygen / nitrogen species that might directly harm axons. Lack of evidence therefore calls for a better understanding of the myelin-axon interplay and the influence of the inflammatory milieu. For this purpose, we used a mouse model overexpressing the proteolipid protein (PLP). These PLPtg mice develop thinner myelin with age and are known to show markers of astrogliosis and microgliosis. We use experimental autoimmune encephalomyelitis (EAE) as a model to reflect the immune component of MS. To cover different disease phases, we analyse animals at disease peak (4 days post onset of symptoms) and after 40 days. We show that PLPtg mice become sick faster than control mice but recover almost completely. In accordance with the clinical scoring, they show less and smaller, but morphologically similar lesions and more axonal damage in the spinal cord. PLPtg mice show comparable, but slightly increased numbers of macrophages / microglia, astrocytes and T cells. This demonstrates that in this mouse mutant, general inflammation cannot be equated with clinical symptoms. After 40 days, PLPtg show an ongoing astrocytes and increased numbers of unmyelinated axons.

This study gives first indications that pre-inflammation within the spinal cord might have a beneficial effect on the course of an MS-like disease. Further experiments need to be performed in order to proof this hypothesis. It can also not be excluded that the thickness of myelin might have a direct influence. However, data suggest a possible role of a primed immune system and would have a direct impact on therapeutic strategies, as most drugs aim for a general suppression of the immune system.