Mouse model of progressive multiple sclerosis (Ramot)

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Multiple sclerosis (MS) is an autoimmune disease of the central nervous system characterized by damage to the neuronal myelin sheath, which results in different levels of muscle paralysis that can lead to neuronal death. In most MS mouse models, the neurologic damage mostly affects the spinal cord with limited damage to the brain, which cannot be monitored by magnetic resonance imaging (MRI) as used for humans.

We show that immunization of non-obese diabetic (NOD) mice with myelin oligodendrocyte glycoprotein peptide 35–55 leads to the development of relapsing–remitting stages, evident from days 20 to 70, which then develops into a chronic progressive stage. This cycle is similar to MS stages found in humans. Brain MRI gadolinium-enhanced T1-weighted image analysis showed an increased blood–brain barrier permeability in brain gray and white matter specific to the corpus callosum, fimbria, and internal capsule as found in humans. MRI fractional anisotropy analysis showed demyelination and axonal damage in identical regions. Immunohistologic analysis supported the MRI data. No evidence of brain lesions was found in a common model of MS using C57BL/6 mice.

We suggest that an increase in astrocyte toxicity in experimental autoimmune encephalomyelitis-induced NOD mice may be linked to brain lesion development.

We suggest using NOD mice as a suitable model for studying MS using MRI methods toward future diagnostic and drug development.

By characterizing a chronic stage following the formation of brain lesions, the NOD model of MS could contribute to the understanding of pathologic processes in the MS brain and the development of new therapeutic approaches that would address the chronic progressive stage, demyelination processes, and axonal injury in the brain, which can be monitored by MRI as done in humans.

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