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Titel des Beitrags:
The intrinsic pathogenic role of autoantibodies to aquaporin 4 mediating spinal cord disease in a rat passive-transfer model.

Abstract:
Neuromyelitis optica (NMO) is causally linked to autoantibodies (ABs) against aquaporin 4 (AQP4). Here, we focused on the pathogenic effects exclusively mediated by human ABs to AQP4 in vivo. We performed cell-free intrathecal (i.th.) passive transfer experiments in Lewis rats using purified patient NMO immunoglobulin G (IgG) and various recombinant human anti-AQP4 IgG-ABs via implanted i.th. catheters. Repetitive application of patient NMO IgG fractions and of recombinant human anti-AQP4 ABs induced signs of spinal cord disease. Magnetic resonance imaging (MRI) revealed longitudinal spinal cord lesions at the site of application of anti-AQP4 IgG. Somatosensory evoked potential amplitudes were reduced in symptomatic animals corroborating the observed functional impairment. Spinal cord histology showed specific IgG deposition in the grey and white matter in the affected areas. We did not find inflammatory cell infiltration nor activation of complement in spinal cord areas of immunoglobulin deposition. Moreover, destructive lesions showing axon or myelin damage and loss of astrocytes and oligodendrocytes were all absent. Immunoreactivity to AQP4 and to the
excitatory amino acid transporter 2 (EAAT2) was markedly reduced whereas immunoreactivity to the astrocytic marker glial fibrillary acid protein (GFAP) was preserved. The expression of the NMDA-receptor NR1 subunit was downregulated in areas of IgG deposition possibly induced by sustained glutamatergic overexcitation. Disease signs and histopathology were reversible within weeks after stopping injections. We conclude that in vivo application of ABs directed at AQP 4 can induce a reversible spinal cord disease in recipient rats by inducing distinct histopathological abnormalities. These findings may be the experimental correlate of "penumbra-like" lesions recently reported in NMO patients adjacent to effector-mediated tissue damage.