Neuromyelitis Optica (NMO), or Devic’s Syndrome, is an inflammatory autoimmune disease that causes damage to the cells of the central nervous system. NMO is a relapsing-remitting disease, characterized by recurrent and severe episodes of optic neuritis and transverse myelitis. Damage to the optic nerve leads to vision loss and eye pain, while damage to the spinal cord leads to weakness and paralysis of limbs, loss of sensation, and issues with bladder and bowel function. Until recently, NMO was classified as an acute form of multiple sclerosis. However, in 2003, data from the Mayo Clinic confirmed the presence of a disease-causing antibody, NMO-IgG. Various studies have shown that NMO-IgG binds to aquaporin-4 (AQP4) found in high concentrations on the foot processes of astrocytes in the central nervous system. This binding causes astroglia to produce classical and alternative complement factors with a convergence at C3, which is hypothesized to recruit other cells to complete the lytic cascade.

To understand the role of C3 in NMO pathology, we elucidated the relationship between C3 and other immune cells present, with particular focus on neutrophil activation and recruitment.

**DIAGNOSTIC CRITERIA**

I. Patient must present core clinical symptoms
   i. Optic neuritis
   ii. Acute transverse myelitis
   iii. Area Postrema syndrome (hiccups, nausea and vomiting)
   iv. Brain lesions or spinal cord lesions (visible on MRI scan)
II. Positive test for NMO-IgG antibodies
III. Exclusion of alternative diagnoses

**MECHANISM OF DISEASE (cont.)**

In the disease model, autoimmune B-cells produce NMO-IgG, an antibody selectively binds to AQP4 channels expressed on the foot processes of astrocytes in the CNS. Reactive astroglia produce classical and alternative complement factors, resulting in a high concentration of C3. The rapid, proinflammatory response by astroglia which demyelinates particular regions of the spinal cord and optic nerve. Lesions also form in these areas, causing optic neuritis and transverse myelitis in affected patients. While AQP4 is concentrated within the CNS, this protein is also present in other regions in the body, particularly in the kidneys. These proteins are also affected by this disease, leading to bladder and bowel problems as well.

**PROJECT DATA**

The presence of early, non-lytic complement products provide possible therapeutic targets. C3 appears to be activating neutrophils, however, they do not appear to be involved in trafficking neutrophils into the central nervous system. Future experiments are needed to discover the driving mechanism for recruitment of neutrophils.

When C3 is cleaved, it produces C3a and C3b. However, C3a was not discovered. This chemokine may be interacting with other immune cells. Further investigation may provide insight into its role in the NMO model.

**REFERENCES**


Neuromyelitis optica (NMO) - Medline Plus

**RESOURCES**

**CONCLUSIONS**

- Astroglia and pure astrocytes produce large amounts of functional complement molecules in vivo when stimulated with NMO-IgG.
- The classical and alternative complement pathways are shown to be upregulated, with convergence at C3.
- Quantitation of C3 shows an increase with sustained stimulation by NMO-IgG.
- C3 produced by astroglia is shown to activate neutrophils, but C3 is likely not driving trafficking of neutrophils.