Research improves diagnosis and potential treatment of neuromyelitis optica

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Mayo Clinic researchers have identified critical steps leading to myelin destruction in neuromyelitis optica (NMO), a debilitating neurological disease that is commonly misdiagnosed as multiple sclerosis (MS). The findings could lead to better care for the thousands of patients around the world with NMO. The paper was published in the journal, *Proceedings of the National Academy of Sciences*, USA.

NMO is an inflammatory autoimmune disease of the central nervous system that damages the optic nerves and spinal cord, causing vision loss, weakness, numbness and, sometimes, arm and leg paralysis and loss of bowel and bladder control. NMO was historically misdiagnosed as a severe variant of MS until 2005 when a team led by Vanda A. Lennon, M.D., Ph.D., a Mayo Clinic research immunologist, identified an antibody unique to NMO, and discovered that its unexpected target was the major water channel of the central nervous system (aquaporin-4). A blood test emerging from this discovery has revolutionized the diagnosis of NMO, allowing its distinction from multiple sclerosis and introducing more appropriate treatments.

The NMO antibody targets astrocytes, which are 10 times more numerous in the brain and spinal cord than neurons. In addition to providing nutrients to neurons and supporting the repair and scarring process, other critical functions of astrocytes include regulation of tissue water and electrical activities of neurons, and the stabilizing the protective covering of nerves (myelin). By attacking the water channels on astrocytes, the antibody disrupts all related dynamic functions of the

astrocyte and in acute attacks kills many astrocytes.

The new findings advance the understanding of the basic mechanisms of NMO, critical to the ultimate development of optimal treatment or even a cure. Key findings include:

- The antibody associated with NMO affects two forms of the aquaporin-4 water channel: M1 and M23. M1 more readily escapes from antibodies, but antibody binding to M23 causes aggregation of M23 on the astrocyte surface which amplifies cell damage.
- As a consequence of antibody interfering with the transfer of water in the brain, water accumulates in the myelin sheath, preventing rapid transmission of nerve messages) and causing breakdown of myelin, a traditional hallmark of MS, thus contributing to the diagnostic confusion.
- Traditional therapies used to treat MS may actually make NMO worse.

"These findings build on our initial research and greatly advance our understanding of disease development and progression in patients with NMO," Dr. Lennon says. "Only by learning more about NMO can we develop new therapies and new approaches to treat people with this terrible disease."

About Neuromyelitis Optica

Because NMO has only recently been identified as a syndrome distinct from MS, it is difficult to know how many people have it. To date the Mayo Clinic Neuroimmunology Laboratory has detected the antibody in three thousand patients in the United States. Thus NMO is more common than was previously thought. Disease progresses with each new attack, and there is no cure. For most patients, a combination of drug

and physical therapy is required to manage NMO, with the focus being on preventing recurrent attacks after treatment of the first attack, thus reducing disability and preventing relapses.

Provided by Mayo Clinic