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Neurotransmitter defect may trigger autoimmune disease

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A potentially blinding neurological disorder, often confused with multiple sclerosis (MS), has now become a little less mysterious. A new study by researchers at the Mayo Clinic in Rochester, Minnesota, may have uncovered the cause of Devic's disease. Their new study, which will appear online on October 6th in the *Journal of Experimental Medicine*, could result in new treatment options for this devastating disease.

Devic's disease, also known as neuromyelitis optica (NMO), results in MS-like demyelinating lesions along the optic nerves and spine. Affected individuals often experience rapid visual loss, paralysis, and loss of leg, bladder, and bowel sensation. Some lose their sight permanently. Unlike MS, Devic's disease can be diagnosed by the presence of a specific self-attacking immune protein—an autoantibody referred to as NMO-IgG—in the blood. Until now, however, clinicians didn't know how that protein damaged nerves and contributed to disease symptoms.

The Mayo team, lead by Dr. Vanda Lennon, now show that NMO-IgG sets off a chain of events that leads to a toxic build-up of a neurotransmitter called glutamate. NMO-IgG binds to a protein that normally sops up excess glutamate from the space between brain cells. When NMO-IgG is around, this sponge-like action is blocked, allowing glutamate to accumulate. And too much glutamate can kill the cells that produce myelin—the protein that coats and protects neurons. The authors suggest that glutamate-induced damage to nerve cells and their insulating myelin coats might account for the neurological symptoms

associated with Devic's disease.

If the groups' results—generated using nerve cell cultures—are confirmed in vivo, drug development could be very straightforward. Therapeutic trials for glutamate blockers, created to treat other neurodegenerative diseases like Lou Gehrig's disease (or ALS), are already underway.

Source: Rockefeller University Press