

Multiple sclerosis: Damaged myelin not the trigger

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Damaged myelin in the brain and spinal cord does not cause the autoimmune disease multiple sclerosis (MS), neuroimmunologists from the University of Zurich have now demonstrated in collaboration with researchers from Berlin, Leipzig, Mainz and Munich. In the current issue of Nature Neuroscience, they therefore rule out a popular hypothesis on the origins of MS. The scientists are now primarily looking for the cause of the development of MS in the immune system instead of the central nervous system.

Millions of adults suffer from the [incurable disease](#) multiple sclerosis (MS). It is relatively certain that MS is an autoimmune disease in which the body's own defense cells attack the myelin in the brain and spinal cord. Myelin enwraps the [nerve cells](#) and is important for their function of transmitting stimuli as [electrical signals](#). There are numerous unconfirmed hypotheses on the development of MS, one of which has now been refuted by the neuroimmunologists in their current research: The death of [oligodendrocytes](#), as the cells that produce the [myelin sheath](#) are called, does not trigger MS.

Neurodegenerative hypothesis obsolete

With their research, the scientists disprove the so-called "neurodegenerative hypothesis", which was based on observations that certain patients exhibited characteristic myelin damage without a discernable [immune attack](#). In the popular hypothesis, the scientists

assume that MS-triggering myelin damage occurs without the involvement of the immune system. In this scenario, the immune response against myelin would be the result – and not the cause – of this pathogenic process.

The aim of the research project was to confirm or disprove this hypothesis based on a new mouse model. Using genetic tricks, they induced myelin defects without alerting the immune defense. "At the beginning of our study, we found myelin damage that strongly resembled the previous observations in MS patients," explains Burkhard Becher, a professor at the University of Zurich. "However, not once were we able to observe an MS-like autoimmune disease." In order to ascertain whether an active immune defense causes the disease based on a combination of an infection and myelin damage, the researchers conducted a variety of further experiments – without success. "We were unable to detect an MS-like disease – no matter how intensely we stimulated the immune system," says Ari Waisman, a professor from the University Medical Center Mainz. "We therefore consider the neurodegenerative hypothesis obsolete."

Focus on immune system

The teams involved in the study want to continue researching the cause and origins of MS. "In light of these and other new findings, research on the pathogenesis of MS is bound to concentrate less on the brain and more on the immune system in future," says Professor Thorsten Buch from the Technischen Universität München.

More information: Giuseppe Locatelli, Simone Wörtge, Thorsten Buch, Barbara Ingold, Friederike Frommer, Bettina Sobottka, Martin Krueger, Khalad Karram, Claudia Bühlmann, Ingo Bechmann, Frank L. Heppner, Ari Waisman and Burkhard Becher. Primary oligodendrocyte death does not elicit anti-CNS immunity. *Nature Neuroscience*. February

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