

Gray matter under attack in multiple sclerosis

April 30 2009

Autoimmune disease is a condition in which the immune system attacks the body's own material just as aggressively as it would attack a foreign pathogen. Multiple sclerosis, MS for short, is just one such autoimmune disease, and is one of the most common neurological diseases in the 20 to 30 years age group. The disease can have very severe consequences for those afflicted, since the body's defenses attack the central nervous system. It has long been assumed that myelin is the most important target for the misdirected immune response. This white, fat-rich protective layer of specialized cells enshrouds the long extensions of neurons. However, the central nervous systems of MS patients also exhibit damage in the gray matter, where the nerve cell bodies are located. How the patient's disability develops depends greatly on the damage of the gray matter. An international group headed by medical scientist Professor Edgar Meinl of LMU Munich has now discovered a possible connection: The protein Contactin-2 is produced both in the myelin sheathing and by neurons in the gray matter - and is attacked by misdirected immune factors. "Our results suggest that these processes also play a role in MS patients," says Meinl. "It could even be that proteins existing both in myelin and in the gray matter are in fact the critical points of attack."

Multiple sclerosis often advances in phases, where [nerve fibers](#) are successively and irreversibly destroyed by attacks from certain immune cells - so-called T-lymphocytes. The axons that make up nerve fibers are sheathed in myelin. This protective layer consists of individual cells that wrap around the long extensions of the neurons to insulate them and to

allow signals to propagate all the way along the [nerve cells](#). MS first causes in an irrecoverable loss of myelin, and then ultimately to the demise of the neurons thus exposed.

"It is the irreversible destruction of axons in particular that causes the lasting disability of patients," explains Professor Edgar Meinl of the Institute of Clinical Neuroimmunology at LMU Munich Klinikum and of the Max Planck Institute of Neurobiology. Little by little, damage spreads out in the brain and spinal cord. Different symptoms can follow, depending on where these lesions first appear and how severe they are. These could be loss of sight and speech, or tremors, numbness, impaired bladder function or impaired mobility.

It is only a recent discovery that the immune system actually attacks the gray matter in the early stages, along with the myelin sheathing. "This extensive damage is a factor in the advancement of the symptoms," says Meinl. "Until now, it has been unclear which molecules direct the immune system against the gray matter." The researchers therefore performed large-scale tests to investigate which proteins in human brain tissue the antibodies of MS patients dock onto, instead of docking onto foreign intruders as they are supposed to.

In the course of their investigations, they identified Contactin-2 as a new autoantigen - a molecular structure that belongs to the body but which provokes an immune response. This protein is found in the brain and spinal cord, and is present in both the myelin sheathing and in the neurons themselves - which means it exists in the gray matter.

"Contactin-2 triggers an immune response in which T-cells and antibodies turn against this molecule," reports Meinl. "In some ways, this immune response is similar to those that occur in pathogen-induced inflammations."

In an animal model, autoreponsive T-cells responded to TAG-1, the

animal protein analogous to human Contactin-2. The T-cells triggered an inflammation in the brain, predominantly in the gray matter.

Furthermore, these [immune cells](#) also opened the blood-brain barrier, which is a barrier that most molecules and cells can normally not get past. "Without this barrier, the antibodies were able to invade the brain in great numbers, where they caused severe damage to the [gray matter](#)," says Meinel. "What we now need to clarify is whether these mechanisms also take place in human MS patients, and what role is played by antigens that occur inside the neurons."

Source: Ludwig-Maximilians-Universität München

Citation: Gray matter under attack in multiple sclerosis (2009, April 30) retrieved 1 May 2024 from <https://medicalxpress.com/news/2009-04-gray-multiple-sclerosis.html>

<p>This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.</p>
--