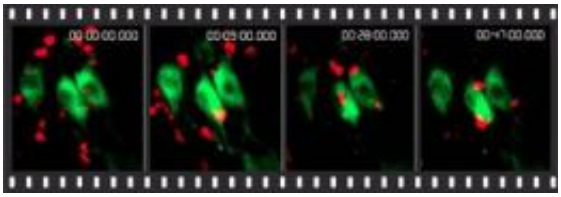
Imaging study provides new view of multiple sclerosis

September 23 2010



Researchers in Germany have gained new insight into how the immune system causes damage associated with multiple sclerosis, an incurable neuroinflammatory disorder. Using imaging tools which enable investigation of processes in living organisms, they were able to show a direct interaction between immune cells and neurons which plays a significant role in neuronal injury. However, this direct interaction may respond to therapeutic intervention. The study by Dr. Volker Siffrin and Professor Dr. Frauke Zipp has now been published in the journal *Immunity*. Credit: Dr. Volker Siffrin/Copyright: MDC

Scientists have uncovered an alternative source for some of the damage associated with multiple sclerosis (MS), an incurable neuroinflammatory disorder. The research, published online by Cell Press on September 23rd in the journal *Immunity*, reveals a direct interaction between immune cells and neurons that plays a significant role in neuronal injury and may respond to therapeutic intervention.

MS is an autoimmune disease in which a person's own immune system attacks their central nervous system. Symptoms of MS are variable depending on which nerves are affected, but often include muscle

weakness, numbness and visual disturbances. Research has shown that MS is caused by damage to the protective myelin sheath, an insulating substance that surrounds nerve processes and is critical for transmission of nerve impulses.

Research has also indicated that direct damage to neurons is prominent in early disease stages. "The contribution of direct neuronal damage to MS pathology has been debated since the first description of the disease," explains senior study author, Professor Frauke Zipp, from Johannes Gutenberg University Mainz in Germany. "Although many different theories about possible underlying mechanisms have been proposed, such as neuron damage being a secondary effect of the disrupted myelin sheath, actual events leading to neural damage are not well understood."

Dr. Zipp and colleagues studied the role of immune cells in neuronal damage in mice with experimental autoimmune encephalomyelitis (EAE, an animal model of MS) by monitoring the development of neuroinflammatory lesions with sophisticated imaging techniques. They observed direct synapse-like interactions between immune cells and neurons. Immune cells called Th17 cells, which have been linked to autoimmune inflammation, induced localized toxic changes in neuronal calcium levels. This is significant because fluctuations in neuronal intracellular calcium levels that were linked with cell injury were partially reversible when cells were exposed to compounds used to treat excitotoxicity.

These results highlight a specific interaction between the immune system and the nervous system, implicating direct neuronal damage in autoimmune-mediated inflammation. "Our use of live-imaging during disease has led to the characterization of neuronal dysfunction as early and potentially reversible, and suggests that immune-mediated disturbances of the neurons themselves contribute to multiple sclerosis,

in addition to interruptions in nerve cell transmission as a result of changes to the myelin sheath," concludes Professor Zipp. "Furthermore, immune-mediated reversible calcium increases in neurons are a viable target for future therapeutics."

Provided by Cell Press