Diabetic mice provide a surprising breakthrough for multiple sclerosis research

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(Medical Xpress) -- In humans, active periods of the debilitating disease Multiple Sclerosis (MS) can last for mere minutes or extend to weeks at a time. They're caused by lesions in the brain that develop, partly heal, and then recur. Research into a cure has been difficult, because to date scientists have not been able to replicate these brain recurring symptoms in laboratory mice. That's frustrating because these lab animals, known as animal "models," are the primary tool for research into the mechanisms and potential treatments for MS.

But now, by using a mouse model for diabetes instead, Dr. Dan Frenkel of Tel Aviv University's Department of Neurobiology, working

alongside Prof. Yaniv Assaf and Ph.D. student Hilit Levy, may provide a surprising breakthrough for research into a cure for MS. The team has discovered that when mice with Type 1 Diabetes are injected with myelin protein — the insulating material that coats neurons — they experience the periods of relapsing and remitting disability associated with brain lesions in humans. And for the first time, they've been able to monitor this brain lesion process using magnetic resonance imaging.

Dr. Frenkel believes his finding will lead to the development of more effective treatments for MS. This research has been published in *Experimental Neurology*.

Tracking lesions in the brain

MS, an autoimmune disease in which the immune system attacks in the brain and inhibits the transfer of signals between neurons, often leads to devastating disabilities such as blindness and paralysis. From its onset, the disease attacks in peaks which become increasingly more severe until patients are permanently disabled.

Traditionally, mouse model populations for MS research have been created by injecting mice with myelin protein emulsified in bacteria. With the addition of bacteria, the immune system mobilizes against the myelin, creating an MS-like autoimmune response. However, the disease does not present in this model as it does in human sufferers — most mouse models experience a single inflammatory peak which leaves them with permanent symptoms such paralysis of the legs. The damage can be detected in the spinal cord, but not in the brain.

"We discovered that when we gave them the same myelin protein injection, a mouse model that develops Type 1 Diabetes will instead exhibit peaks of inflammatory responses similar to those of chronic progressive MS, which relapses and remits," Dr. Frenkel says. The mice

also suffer from brain lesions in addition to spinal cord damage, making them a more viable model for studying and developing treatment for MS in humans.

Using a special MRI machine for imaging small animals, the researchers followed each mouse model over the course of several months, noting the activity of the brain and the development of lesions corresponding to peaks of inflammation. The lesions and the inflammation in the brain can be followed in the same way within these animals as in a human with MS, says Dr. Frenkel. "Now, we can follow the different stages that occur after the autoimmune response is already triggered, and look for different targets that will not only help to enhance recovery, but prevent further damage as well."

Turning temporary recovery into permanent repair

Currently, all FDA approved drugs on the market to treat MS were developed using traditional mouse models. Their focus is to delay the clinical signs of the disease caused by autoimmunity, lengthening the time between attacks. So far, this method has led to a temporary fix, but not a cure. With his alternative mouse model, Dr. Frenkel says, researchers can gather more information on how the brain heals after an attack, and start to develop treatment options that mimic this natural recovery process — turning temporary recovery into permanent repair.

"With the use of magnetic resonance imaging, we can follow the brain lesions within the mouse model, and characterize the process of relapsing," Dr. Frenkel says. They have already begun to develop treatments with initial success. “We are looking at ways to encourage the glia cells — cells in the brain that support the neurons — to promote brain repair," he says.

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