One size does not fit all: A new look at therapies

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Statins, a commonly prescribed class of drugs used by millions worldwide to effectively lower blood cholesterol levels, may actually have a negative impact in Multiple Sclerosis (MS) patients treated with high daily dosages.

A new study by researchers at the Montreal Neurological Institute (MNI), McGill University, demonstrates that statin therapy in mice inhibits myelin repair or remyelination in the central nervous system. The findings, published in The American Journal of Pathology, highlight the crucial need to monitor the effects of central nervous system-accessible immune therapies on the myelin repair processes in patients with MS and other progressive demyelinating diseases.

Canadians have one of the highest rates of MS in the world. An estimated 50, 000 Canadians have MS, with approximately 1,000 new cases diagnosed each year. MS is an autoimmune disease of the central nervous system (CNS), in which immune cells attack the myelin sheath (the protective insulation of nerve fibres), and the myelin-producing cells of the CNS (oligodendrocytes), causing demyelination. This causes damage which disrupts the nerve cell's ability to transmit signals throughout the nervous system.

In the early stages of MS, following an immune system attack on myelin, oligodendrocyte progenitor cells or stem cells in the CNS are recruited to the lesion. These cells mature and produce new myelin to repair the damage.

"Statins, which are known to modify the immune system response and have a wide array of effects on other cellular processes, were propelled into clinical trials based on studies in an animal model of MS indicating a reduction in clinical disease severity," says Dr. Veronique Miron, post-doctoral fellow in Dr. Jack Antel's lab at the MNI, and lead investigator in the study. "The mechanism of statin action in these studies was not determined. That is, does statin directly effect myelin and/or the oligodendrocytes or is disease severity reduced indirectly due to the dampening of the immune response. This issue required further investigation, particularly due to the ability of statins to cross the blood-brain barrier and access the CNS, and the enrichment of cholesterol in the myelin sheath."

The objective of the MNI study was to determine the direct impact of simvastatin, a statin in clinical trials, on the integrity of myelin in the brain and on the remyelination process. The study uses a model of myelin damage that has relatively little inflammation and mimics the demyelinating aspect of MS, allowing MNI researchers to determine the direct effect of long-term statin therapy on remyelination, independent of its indirect effects mediated via immune modulation.

"The results of our study indicate that simvastatin has in fact, a slightly deleterious effect on myelin under non-pathological conditions," adds Dr. Miron. "During remyelination, there is a decrease not only in myelin production but also in oligodendrocyte number as a result of simvastatin treatment. The findings also suggest that simvastatin inhibits CNS remyelination by blocking oligodendrocyte progenitor cell differentiation or maturation into myelinating oligodendrocytes."

This study underscores the necessity of monitoring the long-terms effects of CNS accessible immune therapies, particularly those that can impact cell types that are postulated to be targeted in neurological disease processes and that are implicated in any brain tissue repair

processes. Understanding the underlying mechanisms of these therapies will lead to improved and enhanced treatment strategies and ultimately improved quality of life for people who suffer from a variety of neurological diseases.

Source: McGill University (news : web)