



National Multiple Sclerosis Society
733 Third Avenue
New York, New York 10017-3288
Tel +1 212.986.3240
Fax +1 212.986.7981
E-mail nat@nmss.org
Nationalmssociety.org

RESEARCH/CLINICAL UPDATE

cc: Chapter President, Programs, Development

June 3, 2011

Researchers Pinpoint Novel Gene-Environment Interaction in Cells from People with MS

Studying human cells isolated in the laboratory, researchers reveal a novel interaction between two genes that influence susceptibility to developing MS, certain environmental factors, and a chemical process (called N-glycosylation) that modifies the structure of molecules, which together may contribute to our understanding of how complex interactions lead to the development of MS. Michael Demetriou, MD, PhD (University of California, Irvine) and colleagues have published these findings in *Nature Communications* (May 31, 2011, Volume 2, Article #334, <http://www.nature.com/ncomms/journal/v2/n5/full/ncomms1333.html>). The team was funded in part by the National MS Society.

Background: The cause of MS is still not known, but scientists believe that a combination of several factors may be involved to trigger the immune attack that is launched on the brain and spinal cord. While MS is not directly inherited, genes are known to make people susceptible to developing the disease. Researchers also are working to understand how MS gene variations may interact with some environmental triggers that have been linked to MS, such as viral infection, cigarette smoking and low levels of vitamin D/sunlight to increase the risk of MS.

Michael Demetriou, MD, PhD, has previously shown that changes in the addition of specific sugars to proteins involved in the MS attack (N-glycosylation) trigger a spontaneous MS-like disease in mice, which could be suppressed by interfering with the process with a dietary supplement. . The current study aimed at translating this finding to the development of human disease.

The Study: In this study, Dr. Demetriou's team examined DNA samples from about 13,000 people with MS or controls with autoimmune diseases such as rheumatoid arthritis or diabetes. They looked at how four previously reported susceptibility genes that are involved in immune

system activities (interleukin-7 receptor-alpha, interleukin-2 receptor-alpha, MGAT1 and CTLA-4) affect N-glycosylation. Then they examined how a particular environmental factor such as vitamin D affected this interaction.

The results suggest that these genes do alter N-glycosylation in cells isolated in the laboratory, but that both vitamin D and a dietary supplement called N-acetylglucosamine (GlcNAc) was able to suppress this process in cells and in mouse models of MS.

Comment: This study provides new evidence for a link between genes and the environment in the development of MS. However, additional research is needed before it is possible to generalize these findings to all cases of MS, since this study focused on just a few of the many genetic susceptibility factors linked to MS. More research is also needed to determine whether administering vitamin D and GlcNAc will be helpful in MS. A new clinical trial getting underway with support from the National MS Society will test the ability of vitamin D supplements to alter MS disease activity.

[Read more](#) about vitamin D research funded by the National MS Society.

Watch a webcast on the range of ongoing efforts to find the cause and cure for MS, “Who? Why? How? - Searching for the Cause of Multiple Sclerosis,”

<http://www.nationalmssociety.org/multimedia-library/ms-learn-online/ms-learn-online-research/index.aspx#FeaturePresentations>.



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May 31, 2011

Study: No Link Found Between Stress and Development of Multiple Sclerosis

A new study finds that stress does not appear to increase a person's risk of developing MS. The study, published in the May 31, 2011 issue (<http://www.neurology.org/content/76/22/1866.abstract>) of *Neurology*, focused on two large groups of women involved in the Nurses' Health Study, involving hundreds of thousands of female nurses followed over time. The nurses were asked to report on general stress at home and at work, as well as recall physical and sexual abuse in childhood and as teenagers. The investigators, led by Trond Riise, PhD (University of Bergen, Norway), concluded that their results do not support a major role of stress in the development of MS, but that more research is needed to definitely exclude stress as a potential risk factor for developing MS.

Background: Some studies have suggested that stress may be linked to MS exacerbations, or attacks, but there is still no conclusive evidence that links the two (<http://www.nationalmssociety.org/living-with-multiple-sclerosis/healthy-living/stress/index.aspx>). There have been a few previous studies linking stressful events with the onset of MS, but there has not been definite evidence that stress could cause MS. This is the question posed in this study.

Details: With funding from the National Institutes of Health, Dr. Riise and collaborators focused on two Nurses' Health Study groups, involving female nurses in the U.S. followed over time: the NHS1 included 121,700 nurses between the ages of 30-55 who have been followed from 1976. NHS2 included 116,671 nurses between the ages of 25-42 who have been followed from 1989. The participants had responded to past questionnaires about their history of stressful events. Later, a small proportion of the nurses developed MS, and the investigators were able to compare the answers about stressors between those who developed MS and those who did not.

The investigators found that those who later developed MS did not respond significantly different than those who did not develop MS in terms of their histories of general levels of stress or physical or sexual abuse. They accounted for other variables, such as smoking, that have been linked to increasing the risk of developing MS. The authors conclude that this study does not support a major role for stress in the development of MS, but suggest that further research is needed to definitely exclude stress as a risk factor for MS.

Read more about stress and MS: <http://www.nationalmssociety.org/living-with-multiple-sclerosis/healthy-living/stress/index.aspx>

Read more about what causes MS: <http://www.nationalmssociety.org/about-multiple-sclerosis/what-we-know-about-ms/what-causes-ms/index.aspx>