

Section Editors

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Multiple sclerosis and stress

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WHAT WAS THE STUDY ABOUT? Multiple sclerosis (MS) is a chronic disease of the CNS. The exact cause of MS is not known. However, this is a very active area of research. In MS, the immune system attacks the brain and spinal cord, causing areas of tissue damage, or lesions. Typically, the lesions are seen on MRI. In some instances, the lesions are “silent,” meaning that the person was not aware that there was a problem. Other times, a lesion may cause a neurologic deficit like weakness or numbness.

Just as scientists do not understand the cause of MS, they also do not fully understand what causes the MS lesion. Are there triggers for developing new lesions? Prior studies suggested that MS lesions occur more often after a stressful life event. Other studies showed that people with MS had fewer attacks (also called exacerbations) when they coped well with their stress.

HOW WAS THE STUDY DONE? In the article “A randomized trial of stress management for the prevention of new brain lesions in MS,”¹ the authors looked at how stress may make MS worse. This study was a randomized controlled trial. In other words, the authors separated the people with MS into 2 groups. One group was assigned to no stress management. In the other group, the participants used specific stress management therapies. The authors used repeated MRIs of the brain, looking carefully for any changes due to MS. The goal of this study was to look at the role of emotional stress on the development of lesions in MS.

The study took place in several medical centers. In total, there were 121 participants. All the patients had active MS. This means that that even though each person was being treated for their MS, they still had a new lesion that appeared on their MRI in the year before they enrolled in the study.

As mentioned, the patients were divided into 2 groups. One group would receive stress management therapy. The other group did not. The 2 groups were selected randomly. The doctors and nurses who were caring for and evaluating the patients were purposefully kept unaware of the randomization results.

In other words, they did not know (on purpose) if the person was receiving the stress therapy or not. This seems strange, but it is an important part of a

randomized clinical trial. If the doctors knew that the person was receiving treatment, their observations might be biased by this knowledge. They might score the person getting treatment better. That is not to say that they are lying, which suggests that they are consciously trying to alter the results. The influence is subconscious, but can still affect the results (the bias). Not knowing if the person is getting treatment eliminates this possible bias.

In the therapy group, each person had 16 therapy sessions over 20–24 weeks. In these sessions, they learned techniques of stress management specifically tailored for patients with MS. The therapy was based on a cognitive behavioral model and also focused on managing MS-specific symptoms.

The patients in both groups had repeated MRI scans. One was done at baseline (the start of the study). This was followed by MRIs at 8, 16, 24, 40, and 48 weeks. The MRI scans were evaluated for the presence of new brain lesions by comparing them to the baseline. The investigators analyzed the data to determine if the patients in the treatment group had fewer new brain lesions on MRI in the 24-week period during the therapy and in the 24-week period after the therapy was completed as compared to the group that did not receive therapy.

In addition, the patients in both groups answered several questionnaires during the course of the study. In the no treatment group, this was needed in order to follow the person’s “stress levels” throughout the study. In the treatment group, the questions allowed the authors to assess each person’s stress levels at baseline, after therapy, and again after the therapy had ended.

WHAT WERE THE RESULTS? There were 121 people in the study. Sixty patients were assigned to the therapy (treatment) group and 61 patients were assigned to the waitlist (control or no therapy) group. In the group that received the therapy, fewer patients developed new MS lesions when compared to those in the waitlisted group. In the therapy group, 76.8%/69.5% remained free of new lesions, compared to 54.7%/42.7% of the waitlist group. In the 24 weeks after treatment (therapy), the difference was not as robust, with 60.6% remaining free of new lesions vs 43% (in the no treatment group).

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About multiple sclerosis

WHAT IS MULTIPLE SCLEROSIS? MS is an inflammatory disease. In MS, the person's immune system "attacks" the CNS (the brain and spinal cord). It affects women about twice as often as men. It usually starts at age 30.

The cause of MS is unknown. However, there are several clues about how MS begins. For instance, MS occurs more often in people who live in northern latitudes. Some have proposed that northerners are exposed to an infection in childhood. As it is designed to do, the immune system forms antibodies to the infection (it could be a bacteria or virus).

Later in life, for reasons that are unclear, the antibodies attach to a protein on the surface of the nerve cell's coating. This coating is called myelin. Myelin covers the long, thread-like part of the nerve cell called the axon. The axon conveys the electrical signals of the nerve cell. Axons are covered with myelin. The myelin acts as insulation, allowing the nerve cell to send signals very rapidly. This works just like an electrical wire. When an electrical wire is coated with an insulator (like plastic), it conducts electricity very fast. When the insulation is removed, the wire "short-circuits."

In MS, the immune system becomes "confused." The immune system sees antibodies that are attached to the myelin coating on the nerve cells. Thinking it is part of a virus or bacterium, the immune system thinks that the myelin needs to be destroyed. It "attacks" the much-needed myelin just like it would any type of invader. In MS, when the myelin is damaged, the nerve cell signals travel much more slowly. The slower signals cause neurologic problems like weakness, numbness, or problems with balance (to name a few symptoms).

In addition to the exposure to viruses in the environment, there may be something in our genes that is responsible for MS. For a long time, scientists have known that MS occurs more often in first-degree relatives (mother, father, brother, or sister) as compared to distant relatives or unrelated individuals. For instance, 25% of identical twins, who have identical genetic makeup, develop MS. In comparison, only 2% of fraternal twins, whose genetic makeup is like a brother or sister, develop MS.

The genetic research in MS focuses on how our bodies are able to recognize foreign substances. One example of this is in organ transplantation. In some people, the immune system recognizes that the transplanted organ is "foreign" and "rejects" it. Research into the genetics of MS may show how some people's bodies become "confused." This would help us to identify who is more likely to develop illnesses like MS, where the body attacks its own myelin.

Most people think MS is an illness that mostly affects white matter. Studies show that MS affects gray matter as well. When MS affects gray matter, the nerve cells die (see below). Nerve cell death causes a decrease in the volume of the gray matter. A reduction in volume is called atrophy. Years ago, before MRI, an autopsy might show atrophy. Today, MRI can identify atrophy in the living brain. Newer MRIs are able to detect subtle changes even more easily.

If MS primarily affects the white matter, why do nerve cells die? Some scientists believe that an attack on myelin also affects the axon. Some nerve cells cannot live without their axons. Others have proposed that MS affects the nerve cell body directly. In other words, the nerve cell body is destroyed first. Which is correct? Is it the axon first, or is an attack on the cell body the beginning of what we call MS? The answer to this question could lead to a cure of this illness.

WHAT ARE "GRAY MATTER" AND "WHITE MATTER"? Brain cells are called neurons. Neurons are made up of a cell body. In the brain (and spinal cord), the cell bodies are grouped together in highly organized ways. When looking at the brain with the naked eye, these groups of cell bodies have a grayish color, and are therefore called gray matter.

The outer layer of the brain is one area where cell bodies are grouped together; this region of gray matter is called the cerebral cortex. Deeper within the brain are other specialized groups of cell bodies. These are also called gray matter. However, they are separate from the cerebral cortex, and are referred to as nuclei. The 2 areas of gray matter are connected together in many ways. The rich connections between these areas allow for highly complex tasks to occur such as language and thinking.

Nerve cells communicate with each other using electrical signals. These signals must be sent very rapidly. In order for this to occur, cells must be connected by “wires.” These “wires” are long projections from the nerve cell body called axons. Some axons are short, and travel from one region of brain to another. Others are very long, and travel from the brain to the spinal cord. In other words, some nerve cells are several meters long.

Electrical signals travel much faster through wires which are coated or insulated. This prevents them from “short-circuiting.” Axons are coated with a substance called myelin which allows for very rapid transmission of signals from one area of the brain to another, or from one region of the body to another. Like gray matter, axons are also grouped together.

Because myelin appears white to the naked eye, portions of the brain or spinal cord that are made up of axons are called white matter.

FOR MORE INFORMATION

AAN Patients and Caregivers site

<http://patients.aan.com/golhome>

Multiple Sclerosis Association of America

<http://www.msassociation.org>

Multiple Sclerosis Foundation

<http://www.msfocus.org>

National Multiple Sclerosis Society

<http://www.nationalmssociety.org>

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1. Mohr DC, Lovera J, Brown T, et al. A randomized trial of stress management for the prevention of new brain lesions in MS. *Neurology* 2012;79:412–419.

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