Clear Thoughts

on Cognitive Problems in Multiple Sclerosis

What is Multiple Sclerosis?

Multiple sclerosis (MS) is a disease of the ***central nervous system*** (CNS) that affects 2.5 million people worldwide. The cause of MS is unknown, but it may be triggered by an environmental factor such as a virus. The virus may cause the body's immune system to attack parts of the brain and spinal cord. A genetic component may also be involved. It is unknown how these factors work together to cause an immune attack.

The cause of MS is unknown, but environmental and genetic factors are probably involved.

Three times as many women as men develop MS. MS is also more common in regions that are farthest north or south from the equator. Typically, the initial diagnosis of MS is made in people between 20 and 40 years of age.

People with MS have inflammatory ***lesions*** that develop around small blood vessels in the brain or spinal cord. Over time, these inflammatory lesions

destroy the ***myelin*** covering that protects the nerves. The exposed nerve fibers become damaged, and nerve signals cannot travel as well between the brain or spinal cord and muscles or organs. The continued loss of myelin results in breakdown of the nerve ***axon***, which permanently blocks nerve signals. Repeated episodes of inflammation may cause the loss of brain tissue over time, resulting in brain ***atrophy***.

MS is still active during periods of apparent disease remission, so continuous treatment is critical.

The course of MS is unpredictable. Some people with MS may have mild disease, but over 80% of people experience a worsening of MS over time. The majority of people with MS experience periods of ***exacerbations*** or ***relapses*** (increased symptoms or "attacks") followed by periods of ***remission*** (improve-ment in symptoms). During periods of remission, it is very important to remember that MS may still be active. People with MS are known to have episodes of inflammation that don't produce symptoms, but lead to further neurological damage over time. Therefore, early and continuous treatment is critical in slowing the progression of MS.

Symptoms of Multiple Sclerosis

In some individuals, the onset of MS is characterized by the sudden appearance of neurologic symptoms that may resolve completely or nearly completely over days or weeks. These symptoms may include difficulty walking, abnormal sensations such as numbness or "pins and needles," and visual disturbances. People with MS also may experience dizziness, weakness, problems with bladder and bowel functions, and ***cognitive impairment***. Less common symptoms include tremor, slurred speech, and the sudden onset of paralysis.

The symptoms of MS may be either visible or invisible to others.

The symptoms of MS may be categorized as "visible" or "invisible." Examples of "invisible" symptoms include fatigue, pain, cognitive problems, numbness, tingling, burning, dizziness, and light-headedness. Friends and family members may doubt the existence of "invisible" symptoms. Therefore, it is important to find someone to talk with who is understanding and supportive. Tracking these

Cognitive impairment affects many aspects of everyday life.

symptoms in a journal or diary may also help. If you are experiencing any of the "invisible" symptoms of MS, inform your health care provider. These symptoms may not be initially apparent to the health care provider; however, many are treatable. One of the "invisible" symptoms, cognitive impairment, is increasingly being recognized as an important symptom because it affects social functioning, employment, household responsibilities, and quality of life.

Symptoms of Cognitive Impairment in People with Multiple Sclerosis

Most people think of MS as a physically disabling disease. However, people with MS may also suffer from cognitive impairment. Cognitive impairment is an alteration of the thinking processes, such as attention, problem solving, memory, reasoning, and use of language to express ourselves. It is estimated that up to 65% of all people with MS have some degree of cognitive impairment. Of those, only 20% have obvious signs of cognitive impairment.

Up to 65% of people with MS experience some type of cognitive impairment.

Cognitive impairment is not related to the amount of physical impairment that is present. People with severe physical symptoms may not experience any cognitive symptoms, while people with no signs of physical disability may experience significant cognitive dysfunction. Some people experience cognitive problems from the day their MS was diagnosed, but others never experience it. Surprisingly, MS may be diagnosed based on the presence of cognitive symptoms alone.

Symptoms of cognitive impairment may be worsened by heat, stress, or fatigue.

It is important to recognize the signs and symptoms of cognitive impairment because even mild problems can interfere with daily life in people with MS. The initial symptoms of MS-related cognitive impairment might be subtle. For example, people with MS may occasionally forget to do something, such as turn off the stove. Problem solving may take more time. It may be difficult to solve more than one problem at a time. Symptoms may come and go depending on heat, stress, worsening of disease, pain, infections, and level of fatigue. While some people may notice that they have developed the symptoms of cognitive impairment, others do

not realize it until family members have called it to their attention. The most common problems to look out for include the following, which are illustrated by examples from people with MS:

Recent memories become difficult to recall.

- *"It took me 2 years to remember to ask my doctor about the difficulties I was experiencing with my memory!"*
- *"I was supposed to meet my spouse at a restaurant for dinner the other night, but I forgot and went home instead."*
- *"Someone asked me what I had for breakfast this morning, and I couldn't even remember!"*
- *"I wanted to retrieve my voicemail messages while driving to the grocery store, but I couldn't recall my phone number."*
- *"After years of knowing it, I find myself unable to state my own social security number."*

Language fluency is diminished.

- *"The word is on the tip of my tongue, but I just can't seem to recall it."*
- *"I keep struggling to find the right words."*
- *"I know what I want to say, but I have trouble translating that into words."*

Information processing is slowed.

- *"I'm finding it more and more difficult to balance my checkbook."*
- *"I can't read the newspaper while the television is on."*

- *"Preparing a bowl of cereal has become complicated — I have to remember that the milk is in the refrigerator, the cereal is in the pantry, and the bowl is in the cabinet."*
- *"Cooking was one of my favorite pastimes. I don't like to admit that I can't remember how to make many of my favorite dishes."*

Judgment and problem solving are slower or less reliable.

- *"I locked my keys in the car and became totally overwhelmed. Although an incident like that would have never upset me before, I just can't deal with it now."*
- *"A simple task such as getting dressed became more complicated."*

Emotional instability.

- *"My friend told me that one of her plants died, and I started crying!"*
- *"I can go from being very happy to extremely angry in a matter of seconds."*

Tables 1 and 2 provide tips for people with MS and their care partners/families to help them cope with cognitive impairment. For example, there are many memory aids available to help patients overcome problems. Such aids include sticky notes, calendars, date books, and day planners. An electronic organizer or hand-held tape recorder may be useful in people without significant physical disability.

Table 1. Tips for People With MS

- Keep your mind stimulated
  - Do crossword puzzles
  - Read newspapers and books
  - Play card games
  - Listen to books on tape
  - Watch game shows
  - Don't watch too many TV shows that aren't stimulating
- Rely on emotional support
  - Join support groups
  - Make phone calls to friends and family
- Use organizational aids
  - Pill boxes for medications
  - Day planners/date books/calendars
  - Electronic organizers/tape recorders
  - "To do" lists; write everything down
- Use a kitchen timer or wristwatch with alarm for reminders
- Leave messages on your answering machine when you are away from home
- Keep maps and important phone numbers in your car
- Pace yourself and keep calm
- Concentrate on one task at a time
- Avoid high temperatures
- Don't do challenging tasks when you are fatigued or hot
- Rest when you are tired
- Plan for your medical appointments
  - List your top three concerns
  - Bring medications with you (prescription and nonprescription)

Table 2.
Advice for Care Partners and Families

- Accompany the person with MS to medical visits whenever possible
- Share your concerns with the health care provider
- Remind the person with MS to bring medications to medical visits
- Organize medications to assist the person with MS
- Offer to help with medication administration
- Recognize and allow successes
- Give praise in recognition of accomplishments
- Encourage independent activity
- Avoid unrealistic expectations
- Do not overwhelm the person with MS
- Plan attainable goals
- Utilize support groups and counseling resources
- Provide a stimulating environment for the person with MS
- Understand that people with MS may be more irritable at times when they don't feel well
- Understand that people with MS may have trouble controlling their emotions
- Recognize that cognitive impairment is not the fault of the person with MS

Is Cognitive Impairment in People With MS Similar to Alzheimer's Disease or Depression?

Alzheimer's disease is sometimes confused with MS-related cognitive dysfunction. However, several important features distinguish the two disease states. MS-related cognitive impairment is less severe and less progressive than Alzheimer's disease. Most people with MS-related cognitive impairment do not experience worsening symptoms.

Symptoms of cognitive impairment may mimic some symptoms of depression.

Furthermore, memory and language functions are affected differently in MS-related cognitive impairment and Alzheimer's. People with Alzheimer's are not able to store new information from moment to moment and can experience severe problems using language to communicate. By contrast, people with MS rarely have language or communication problems, and they are capable of learning and storing new information. However, more time is required to learn new information. Furthermore, people with MS-related cognitive impairment have less accurate recollections. Memory aids such as a day planner

or an electronic organizer are not useful in people with Alzheimer's because they won't remember why they have them.

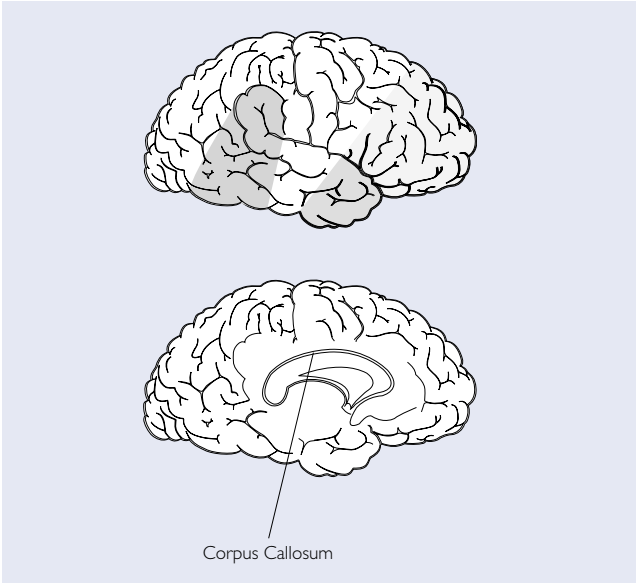
Depression and cognitive impairment do not go hand in hand. In fact, the frequency of cognitive impairment is similar between MS patients who are depressed and those who are not depressed. Similarities between depression and cognitive impairment include deficits in memory and attention, loss of interest in social activities, sexual dysfunction, and inability to maintain employment. These symptoms are typically abrupt in onset when caused by depression and occur more gradually when caused by MS.

Why Does Cognitive Impairment Develop in People with MS?

Cognitive impairment develops when lesions arise in certain "thinking" parts of the brain called ***cerebral hemispheres*** (Figure 1). These lesions affect the manner in which electrical signals travel across nerve cells. Another cause of cognitive dysfunction in people with MS is brain atrophy.

Cognitive impairment can result from atrophy of the brain.

Figure 1. Cerebral Hemispheres



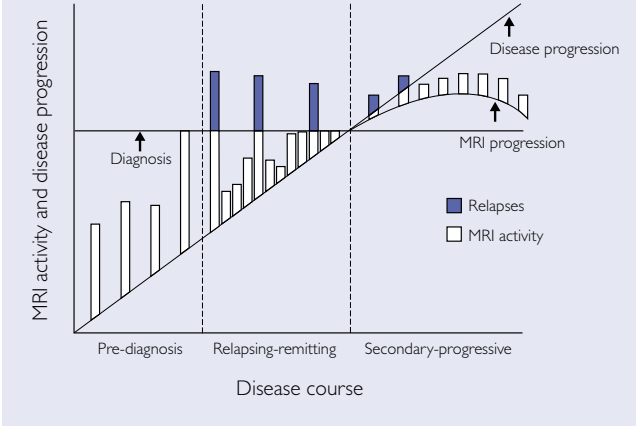
Brain atrophy may be marked by shrinking of the ***corpus callosum***, an overall decrease in brain volume, or increased size of the third ventricle. Ventricles are filled with fluid. As the brain shrinks, fluid fills an increased amount of space.

Injuries to various parts of the brain may be associated with distinct problems. For example, lesions in the corpus callosum are linked to decreased information processing, poor short-term memory, and difficulty finding words. Mental processing speed, nonverbal memory, and ***executive function*** are linked to total ***white matter*** volume. Increased ventricular size causes defects in reasoning and ***concept formation***.

How is Cognitive Impairment Diagnosed in Multiple Sclerosis?

Cognitive impairment is diagnosed using a series of neuropsychological tests that measure abnormalities in attention, memory span, and problem solving. The results of these tests are compared with the test results of healthy individuals who are the same age as the person with MS. Another marker of cognitive impairment is the development of brain lesions. Brain lesions may be identified through an imaging technique called magnetic resonance imaging (MRI). MRI may be used to identify the *risk* for developing cognitive problems, as people who have numerous lesions on MRI are at a much higher risk for developing cognitive problems. However, MRI does not diagnose cognitive impairment because the presence of lesions does not necessarily mean that symptoms are present. Some areas of the brain are not affected by the presence of lesions. Furthermore, repetitive episodes of inflammation may be necessary before symptoms show up. Lesions may be identified on MRI even before symptoms become apparent. Lesion activity eventually decreases as MS progresses because there is less inflammation and more atrophy present in the brain (Figure 2).

Figure 2. MRI activity as MS progresses



The Importance of Early Treatment

People with MS can lead productive, vibrant lives. Effective treatment is available through the use of ***immunomodulatory agents***. These agents include interferon beta-1a (Avonex), interferon beta-1b (Betaseron), glatiramer acetate (Copaxone), and interferon beta-1a (Rebif). These medications cannot reverse damage that is already present, but they can prevent further relapses and delay the onset of further disability. These medications should be taken even in times of apparent disease remission because MS is still *active*.

Medications should be taken even in times of disease remission because MS is still active.

Studies (CHAMPS and ETOMS) of people who experienced the initial symptoms of MS show that early treatment with interferon beta-1a delays the definite diagnosis of MS and results in fewer relapses and fewer new lesions. Researchers also found that interferon beta-1a (Avonex) delays the progression of cognitive impairment associated with MS. Compared with people who did not receive treatment, treated people were much less likely to experience continued decreases in cognitive function. The differences in cognitive function between those who did and did not receive treatment were between 40% and 47%, depending on the type of neuropsychological test that was used.

The beneficial effects of interferon beta-1a are thought to work over the short-term by inhibiting inflammatory substances that are produced by the body and over the long-term by preventing injury to the brain and spinal cord. In year 2 of treatment with interferon beta-1a (Avonex), one study showed that people had a 55% reduction in the rate of brain atrophy compared with people who received no treatment. This finding is encouraging since brain atrophy has been linked to cognitive decline. Other medications are currently under investigation for the treatment of cognitive dysfunction in MS.

Hope for the Future

Fortunately, the course of MS can be altered, and early treatment is shown to slow the progression of MS. Nonpharmacologic treatments are also available that can be tailored to the person's needs. For example, people with severe cognitive problems may enroll in cognitive retraining programs, which are available at some medical centers. Rehabilitation programs that use retraining techniques are offered by clinical neuropsychologists, speech pathologists, and occupational therapists. One technique that may be employed involves a computer-based program that uses a repetitive sequence of illustrated exercises to jog the memory. If a person is in need of retraining a specific skill needed in the work-place, treatment interventions will be prioritized accordingly. There are a number of ways to cope with and improve cognitive impairment in persons with MS. The future of people with MS is continuously improving.

Glossary

Atrophy: Shrinking or loss of tissue.

Axon: A nerve fiber that transmits messages between different points in the nervous system.

Central nervous system: The brain and the spinal cord.

Cerebral cortex: The outer layer of nerve cells that covers the entire surface of the two halves of the brain; thinking and other complex activities occur here.

Cerebral hemispheres: The two halves of the cerebrum, the largest part of the brain.

Cognitive impairment: Impairment of thinking processes, including problem solving, memory, reasoning, and the ability to use language to express oneself.

Concept formation: Ability to categorize concepts, such as ideas, objects, symbols, or events, that share common characteristics or critical attributes.

Corpus callosum: A thick band of more than 200 million myelinated nerve fibers that is the principal connection between the cerebral hemispheres.

Exacerbations: Episodes of acute worsening of neurologic function. Also called relapses.

Executive function: The regulation of the thinking processes involved in problem solving, including identifying tasks, predicting outcomes, evaluating progress, and behavior modification. Also, determination of order that steps should be performed to complete tasks and decisions regarding allocation of resources.

Immunomodulatory agents: Medications that change the body's immune response.

Lesion: An area of inflammation, demyelination, or tissue loss (T1 black hole) that produces abnormal signals on the MRI scan.

Myelin: A fatty substance that covers and insulates axons of nerves to facilitate the high-speed transmission of electrical signals between the central nervous system and the rest of the body.

Relapses: Episodes of acute worsening of neurologic function. Also called exacerbations.

Remission: Partial or complete recovery periods during which people with MS are free of symptoms.

White matter: Material in the brain and spinal cord that contains the axons and myelin sheaths of nerve cells. Because myelin is fatty tissue, it appears white to the naked eye.

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MS Organizations and their Web Sites

National Multiple Sclerosis Society
733 Third Avenue
New York, NY 10017
www.nmss.org

Consortium of Multiple Sclerosis Centers
c/o Bernard W. Gimbel MS Center
718 Teaneck Road
Teaneck, NJ 07666
201-837-0727
www.mscare.org

International Organization of Muliple Sclerosis Nurses
P.O. Box 450
Teaneck, NJ 07666
201-384-2752
www.iomsn.org

Multiple Sclerosis Association of America
706 Haddonfield Road
Cherry Hill, NJ 08002
1-800-532-7667
www.msaa.com

Multiple Sclerosis Society of Canada
250 Bloor Street East, Suite 1000
Toronto, Ontario M4W 3P9
416-922-6065
www.mssociety.ca

International MS Support Foundation
9420 E. Golf Links Road, #291
Tucson, AZ 85720-1340
www.msnews.org

MS Crossroads
www.mscrossroads.org

Multiple Sclerosis International Federation
www.msif.org

International MS Support Foundation
www.msnews.org

MS Awareness Foundation
www.msawareness.org

MSWorld, Inc.
www.msworld.org

The Heuga Center
www.heuga.org

Web Sites Sponsored by Pharmaceutical Companies

www.understandingms.com
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The ultimate goal of the IOMSN is to improve the lives of all those persons affected by multiple sclerosis through the provision of appropriate health care services.

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