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Acknowledgments

The National Multiple Sclerosis Society and the Multiple Sclerosis Society of Canada wish to acknowledge the generous support of Bayer Healthcare Pharmaceuticals, Inc. for the 2008 North American Education Program—*Hold that Thought! Cognition and MS*.

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Preface

Welcome to the 2008 North American Education Program. This program continues the successful collaboration between the National MS Society in the United States and the MS Society of Canada to provide the latest information about research and disease management in multiple sclerosis to thousands of people on our continent and around the world.

Historically, the North American Education Program has alternated annually between a research topic and a symptom management topic. This year, thanks to our generous sponsor Bayer Healthcare Pharmaceuticals, Inc. we are able to present both topics. This program is about the management of cognitive symptoms. The research topic will be about nervous system protection and repair and will be debuted in March 2008.

On behalf of our organizations and the program sponsors, we wish to express our appreciation to our program experts, John DeLuca, PhD, Lauren Caruso, PhD, Rosalind Kalb, PhD, and Nicholas LaRocca, PhD. In addition, we want to thank the staff and volunteers of the National MS Society chapters and the MS Society of Canada for helping us bring this program to you.

We are delighted that you have chosen to participate in our program and hope that you find it interesting and exciting. Together we will be learning about the many ways in which multiple sclerosis affects mobility and providing answers and tools to help you stay more active and help you maintain a healthy lifestyle.

We look forward to sharing this program with you.

Nancy Law
Executive Vice-President
Program and Services Department
National MS Society

Jon Temme
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Program Overview

Welcome to the 2008 North American Education Program, *Hold that Thought! Cognition and MS*. The National MS Society began offering national education programs in 1988. The first national teleconference reached 700 participants in 60 sites. Since that time, we have utilized a range of technologies to expand our audience throughout North America. By archiving our programs on the National MS Society web site (www.nationalmssociety.org), we have made it possible for people around the world to share the information as well.

In an effort to reach the broadest possible audience, and maintain the flexibility of our programming, we are again offering this year's program as a videotaped conference, thus enabling the chapters of the National MS Society and the MS Society of Canada the opportunity to offer the program to audiences at their convenience over the course of the year. Near the end of the year the program will also be available on the National MS Society web site for anyone who is unable to participate in a program or would like to view the program more than once.

In the video program, recognized experts in the field of cognition and MS will discuss the ways in which multiple sclerosis affects mobility and how you can help yourself manage cognitive symptoms.

The program book provides current information about cognitive problems in MS, cognitive rehabilitation and current research.

Program Presenters

Lauren Caruso, PhD
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John DeLuca, PhD, ABPP
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Rosalind C. Kalb, PhD
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Presenter Biographies

Lauren Caruso, PhD

Dr. Lauren Caruso is a neuropsychologist that has specialized in MS for over 19 years. After conducting clinical research in cognition and sleep disorders/fatigue in persons with MS for various funding agencies including the Federal government and the National Multiple Sclerosis Society for approximately 10 years, Dr. Caruso now primarily works in clinical settings to provide individualized cognitive assessments and rehabilitation programs to persons with MS. She also maintains a continued interest in the impact of sleep disorders and fatigue on cognition, which she incorporates into her rehabilitation protocols.

Dr. Caruso is currently the director of the Cognitive Division of the International Multiple Sclerosis Management Practice in New York City and also maintains private practice offices in both New York City and White Plains, NY. In addition, she is a Clinical Assistant Professor of Neurology and Psychiatry at New York Medical College in Westchester County and a Clinical Research Scientist at the Multiple Sclerosis Research Center of New York in New York City. Dr. Caruso serves as a grant reviewer for various agencies, including the National Institutes of Health and the National Multiple Sclerosis Society, as well as an expert consultant for new research grant applications. She also sits on various committees that serve the MS population, such as the Clinical Advisory Committee for the New York City and Southern New York Chapters of the National MS Society. Dr. Caruso continues to participate in numerous publications addressing cognition as well as sleep disorders in MS, and is an invited guest speaker across the country for both professional and lay audiences. Her primary work objectives remain to disseminate information on cognitive difficulties in MS, as well as advocate and provide individualized treatment for persons with MS.

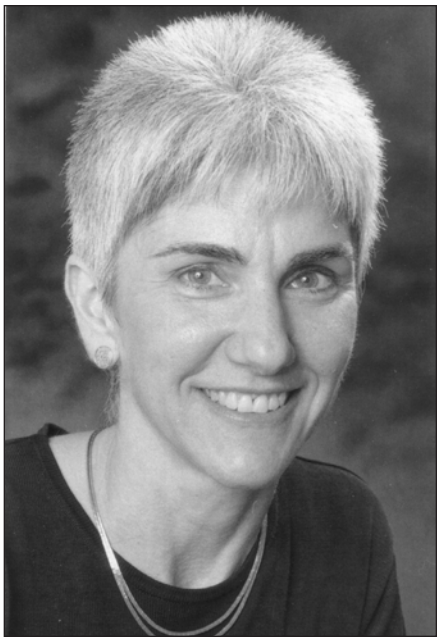
John DeLuca, PhD, ABPP

John DeLuca, PhD, is the Director of Neuroscience Research and the Vice president for Research Training at the Kessler Medical Rehabilitation Research and Education Center (KMRREC), and a Professor in the Departments of Physical Medicine & Rehabilitation (PM&R), and Neurosciences at University of Medicine and Dentistry of New Jersey—New Jersey Medical School (UMDNJ-NJMS). He is a licensed Psychologist in the states of New Jersey and New York. Dr. DeLuca directs the Neuropsychology and Neuroscience Laboratory at KMRREC, and is director of the post-doctoral fellows program in Neuropsychology. He is currently studying disorders of memory and information processing in a variety of clinical populations, and has published over 200 articles, abstracts and chapters in these areas. He is the editor of "Fatigue as a Window to the Brain" published by MIT Press. Dr. DeLuca is the recipient of early career awards for his research from both the American Psychological Association and the National Academy of Neuropsychology. He recently received the Distinguished Researcher Award from The New Jersey Psychological Association. Dr. DeLuca is Board Certified by the American Board of Professional Psychology in Rehabilitation Psychology. He is also a Fellow of the American Psychological Association and the National Academy of Neuropsychology.

Nicholas G. LaRocca, PhD

Dr. LaRocca is a clinical psychologist who has been working with people who have MS since 1979. Before coming to work for the National Multiple Sclerosis Society, he was the Director of Research at the Research and Training Center for MS at St. Agnes Hospital, White Plains, New York and Associate Professor of Neurology and Medicine at New York Medical College. In January 1997, Dr. LaRocca became Director of Health Care Delivery and Policy Research at the National Multiple Sclerosis Society in New York City. Dr. LaRocca has led support groups for persons with MS and their spouses and has given innumerable workshops and presentations for both lay and professional audiences. His research interests include assessment methods, psychological issues, cognitive rehabilitation, and quality of life. He is the author of a number of scientific papers and book chapters and serves on the editorial boards of *The Journal of Rehabilitation Research & Development, and Real Living with MS*. In 2006 Dr. LaRocca and Dr. Rosalind Kalb published a new book for people with MS entitled: *Multiple Sclerosis: Understanding the Cognitive Challenges.*

Rosalind C. Kalb, PhD



Rosalind Kalb, PhD, is Associate Vice President of the Professional Resource Center at the National Multiple Sclerosis Society in New York City, providing educational materials and consultation services for healthcare professionals. She began her career at the MS Care Center at the Albert Einstein College of Medicine in 1980, and has been providing individual, group, and family therapy for people living with MS since that time. Dr. Kalb has authored or edited a number of National MS Society publications—the *Knowledge Is Power* series for newly-diagnosed patients, as well as *Talking with Your MS Patients about Difficult Topics* and the Cavallo Professional Education series for health professionals. She has edited two books—*Multiple Sclerosis: The Questions You Have, The Answers You Need*—now in its fourth edition—and *Multiple Sclerosis: A Guide for Families,* now in its third edition. She is the senior author of *Multiple Sclerosis for Dummies,* which came out this year, and co-author of *Multiple Sclerosis: Understanding the Cognitive Challenges.*

Cognition and MS

It is fairly common to hear people with multiple sclerosis (MS) complain of problems remembering things, finding the right words, concentrating on a task or something they are reading, or following a conversation. These are all *cognitive* symptoms of the disease.

Only a few decades ago, *cognitive impairment* was considered rare in MS. We now know that 50–65 percent of people with MS have some cognitive problems. While most symptoms are mild to moderate, they can have a significant impact on a person's ability to function comfortably.

As with the physical symptoms of MS, the best way to deal with cognitive issues is to learn how to deal with the challenges they cause in your work and personal life. To do this, you need to understand:

- what cognition is;
- when and how cognitive changes may occur;
- the ways in which these changes can affect you emotionally, socially, and economically;
- the assessment tools that are used to diagnose and measure these changes;
- available treatment options; and
- management strategies that will help you deal with these symptoms every day.

Although it may be easier and less frightening to put off thinking about MS-related cognitive changes, becoming informed about them as early as possible has important benefits:

- Being knowledgeable about the ways that MS can affect cognitive abilities will help you to recognize any problems you may be experiencing. It will also help to clear up uncertainty and confusion concerning what's happening to you.

- Having a better understanding of your cognitive challenges will enable you to explain them more clearly to important people in your life, and will help your friends and family to understand what is happening and why.
- Recognizing problems when they first begin makes it easier to identify and implement treatments and management strategies that will help lessen their impact.
- Taking steps to address your problems as soon as possible, including assessment and treatment, will establish an accurate baseline against which to compare any future changes.

What Is Cognition?

The dictionary broadly defines *cognition* as "the act or process of knowing." Cognitive functions can be compared to a computer's operations of input, storage, processing, and output, and can be divided into four general areas:

- *Receptive* functions include integrating input from your five senses, paying attention, rapidly processing incoming information from the environment, and selecting and classifying that incoming information;
- *Learning and memory* includes acquiring new information, storing that information, and retrieving it when you need it.
- *Thinking* is the mental organization and manipulation of information.
- *Executive* and *expressive* functions include acting upon available information and communicating that information to others.

What Cognitive Symptoms Are Associated with MS?

The overall cognitive problem in MS can be described as a reduction in mental "sharpness." The major areas of cognition that can be impaired in MS include what are termed *complex attention* and *executive functions.* Complex attention involves such functions as multitasking; the speed with which information can be processed; learning and memory; perceptual skills. *Executive functions* include problem solving, organizational skills, and the ability to plan; and word finding.

Just as the nature, frequency, and severity of MS-related physical problems can vary widely, not all people with MS will display all of these cognitive problems, and no two people will experience exactly the same types or severity of problems.

Learning and Memory

Problems with memory are the most frequent complaint among people with MS. Approximately 40% have either no memory impairments or very mild ones, 30% have moderate impairment, and 30% have severe difficulty. Although they are often discussed as if they were a single function, learning and memory are actually quite different, and each involves multiple levels and processes that interact in a complex way.

Memory changes are probably among the easiest cognitive symptoms of MS to recognize because so much of everyday life involves learning, retaining, and recalling information. Ways in which memory changes may intrude on everyday activities include:

- Difficulty learning and/or recalling new information
- Problems remembering the plot or characters in books
- Forgetting what was said in conversations, TV shows, or movies
- Forgetting why you entered a room
- Losing or misplacing items such as glasses, keys, or the TV remote
- Forgetting people's names, appointments, or phone numbers
- Forgetting items on shopping trips
- Forgetting to do a task that you had planned

Until recently it was believed that the retrieval of stored memories was the primary memory problem in MS. However, recent research has shown that people with MS actually have more difficulty with the learning or acquisition of information than they do in retrieving it. This suggests that any problems that decrease your ability to adequately learn new information—such as difficulties with attention and concentration or information processing—may significantly affect the ability to remember it later. These findings have important implications for rehabilitation and treatment, suggesting that they should target ways to improve learning.

Information Processing

Decreased speed of information processing is another of the cognitive changes most frequently noticed in MS, especially by people with secondary-progressive disease. Many people say that they can still do everything they used to be able to do, but not as quickly or efficiently.

Some examples of typical problems include:

- Productivity within a given period of time is reduced, even though the quality of the work is unchanged.
- It is difficult to respond quickly when a lot of information is involved.
- Tasks that have a time element are more challenging; this might include card or word games or various types of work-related tasks,
- Processing information coming from several different sources at once becomes slower and more difficult.
- Planning and executing tasks becomes more difficult due to the additional time needed to complete them.

Attention and Concentration

The simple ability to "pay attention" and "concentrate" is not usually affected in MS. However, some of the more complex forms of attention and concentration may be affected, causing problems such as:

- difficulty screening out distractions, including noises, thoughts, competing activities;
- difficulty with "divided attention," such as listening to what a family member is saying at the same time that you are doing something else;
- running out of steam while reading or engaging in similar tasks that require intense concentration and focus (this can also involve fatigue);
- an inability to stick to one task for any length of time without getting distracted;
- poor recall due to a lack of attention when learning new information;
- difficulties with attention that decrease your ability to organize information in a way that will allow it to be recalled later.

The Ability to Shift between Tasks

Life would be much easier if you could always finish one task before the next one required your attention. However, we often need to shift back and forth between tasks. The mental flexibility that allows us to do this switching with relative ease may be affected in MS, and may be made worse by slow information processing and difficulty with attention and concentration.

Examples of problems with shifting might include:

- difficulty resuming a task after an interruption—for example, finding it hard to remember what you were doing before being interrupted by a telephone call; problems shifting back and forth between tasks—for example, talking with your spouse while balancing the checkbook, then finding it difficult to remember where you are in the checkbook or what your spouse was saying;
- difficulty "shifting gears" when an unexpected event demands a quick but time-limited response—for example, finding it hard to turn your attention to a child's question when you are preparing dinner; this has been described by some people as "feeling sticky."

Conceptual Reasoning and Problem Solving

Changes in conceptual reasoning and problem solving are harder to recognize than changes in memory, because reasoning is more subtle and complex than simply remembering where you left your keys. However, these types of changes can be a problem, particularly if your job or other activities involve intellectually challenging tasks. Examples might include:

- difficulty following complex arguments or explanations;
- missing subtleties and nuances, particularly in complex social situations;
- trouble solving puzzles or riddles that used to be easy for you;
- slowness in understanding analogies, symbols, or metaphors
- difficulty analyzing complex situations that formerly were easy for you
- being too "literal" or "concrete" in your interpretation of words—such as not "getting" jokes.

Executive Functions

Executive functions include planning, organization, initiating specific tasks, problem solving, reasoning, concept formation, and self-awareness. Many types of problems with executive functions can occur in MS. However, the common thread among them is difficulty in solving complex problems, which may be due to a change in your ability to plan, organize, and/or reason and conceptualize.

Common examples of this type of problem include:

- trouble organizing and following through with complicated tasks, such as filing income tax returns, planning a vacation, or buying a new car;

- difficulty in setting priorities, organizing time, and meeting deadlines;
- jumping from one task to another with no apparent logic;
- feeling bewildered and overwhelmed by a pending task and not knowing how or where to begin.

Visual Perceptual Functions and Spatial Orientation

Because we interact and learn from our world in large part through vision, how we perceive our environment greatly affects our mental development, fund of knowledge, and everyday interactions. Visual perceptual functions include everything from simple object recognition (ranging from simple shape and surface detail to object naming), to matching visual input with mental images already stored in the brain, to what is termed *semantic categorization* (matching a visual image to its meaning).

Examples of this type of problem include:

- getting lost while driving, even in familiar territory (this problem may also involve changes in memory);
- becoming confused over right and left directions;
- having trouble assembling things—such as toys or furniture—from a diagram or written instructions;
- finding it difficult to understand how machines work—such as programming a cell phone, microwave oven, or VCR;
- having difficulty visualizing an object from a verbal description of it;
- having trouble judging distances between objects, as when parking a car.

Language Functions

Word-finding difficulties are common with MS; this is referred to as the "tip-of-the-tongue" phenomenon. Another common, and probably related, difficulty is word fluency, as in listing all the words one can think of that start with the letter "c" for example. It is likely that both word finding and word fluency are related to reduced speed of processing or the speed of retrieving information from long-term storage.

What Cognitive Functions Are Not Affected by MS?

Cognitive skills that are generally not affected in people with MS include general intelligence; basic forms of attention; and essential verbal skills such as comprehension, the ability to express yourself, name objects, and repeat back what is said to you.

Although some studies have shown a decrease in IQ test scores in people with MS, this appears to be primarily due to factors such as a sensory-motor impairment that slow a person's ability to manipulate objects, or slower processing speed, which affects some aspects of IQ testing more than others. Little if any drop in IQ is observed for those components of IQ tests that are less sensitive to sensory-motor problems, such as verbal intelligence.

What Are the Emotional and Social Effects of Cognitive Changes?

Realizing that cognitive problems are symptoms of MS can be extremely difficult to accept and live with. Problems with thinking and memory can have a negative effect on your self-image and self-esteem, as well as on your relationships with others. Cognitive dysfunction can significantly disrupt daily activities, lifestyle, employment status, social functioning, and overall quality of life. Adapting to cognitive changes and finding ways to discuss them with other people can be a significant challenge. Recognizing the stresses and strains that these symptoms can cause is the first step in learning how to cope with and manage them.

Strategies for Rebuilding Confidence and Self-Esteem

- *Healthy Grieving:* As with any other change or loss caused by MS, healthy grieving sets the stage for adaptive coping and problem-solving by allowing you to let go of "the way things used to be" and preparing you to think about ways to do things differently.
- *Education:* Becoming educated about MS-related cognitive problems will enable you to understand what is happening and why. Understanding them will make the changes more comprehensible and less frightening. It can help to reduce feelings of inadequacy, self-blame, and guilt; and will also help prepare you to explain the changes to others.
- *Cognitive Assessment:* A cognitive evaluation by a trained professional will help you to pinpoint the changes that have occurred, develop a clearer understanding of how they affect everyday activities, and highlight your areas of strength and weakness. This information will be critical as you look for ways to manage your cognitive challenges.

- *Cognitive Remediation:* Working with a trained professional on a regular basis to identify tools and strategies to compensate for cognitive changes is a further step toward rebuilding your confidence.
- *Emotional Support:* As with any other aspects of living with MS, you may find that you need the support and encouragement of others—particularly people who are experiencing similar kinds of challenges.
- *Education of Others:* With or without the help of a professional counselor, it will be important to share information about your cognitive challenges—and the strategies you are using to manage them—with those closest to you. This will help dispel any misunderstandings that may have developed around your symptoms and ensure that the lines of communication are open. Once family members and friends understand what is occurring and why, they can become allies in your efforts to deal with cognitive symptoms.

Cognitive Changes and Your Relationships

Changes in cognitive abilities can affect long-standing relationships and disrupt family life, as well as your performance at work or school. Remember that less visible symptoms are hard for other people to see and understand.

Your Family Members

- By explaining to family members what you are experiencing and how they can be of help, you will be taking a major step toward managing your symptoms, relieving everyone's anxiety, and getting your family system back on track. Engaging family members in brainstorming about problem-solving strategies will increase their understanding of the challenges you face and go a long way toward helping them help you.
- Be sure you involve family members in any compensatory strategies that your cognitive rehabilitation specialist recommends. These strategies will only be effective if you have buy-in from those around you. For example, if you are trying to minimize environmental distractions during conversations so that you can process and remember what people are saying, it won't work if others don't do their part—for example, by turning off the TV or radio.
- Family members sometimes become aware of MS-related cognitive changes before you are able to recognize or acknowledge them. If they begin to express concerns about your memory, or your organizational or driving abilities, for example, your first reaction may be to deny, argue, or simply get angry. Keep in mind, however, that those closest to you are the

people who are most concerned about your well-being. If you don't feel ready to hear or discuss what they have to say, try telling them that you appreciate their concern and will give it some thought. Simply brushing them off is only likely to make them push harder.

On the Job or at School

- Cognitive symptoms can interfere with work- or school-related activities just as much as physical impairments can. As with family members and friends, less visible changes may also be more difficult for employers, colleagues, teachers, and fellow students to understand and accept. Cognitive changes that affect performance can easily be misunderstood by employers and colleagues as incompetence, lack of interest, inattention, emotional problems, or drug or alcohol abuse.
- Problems with information processing and memory can affect your ability to work. Many factors affect employment status in people with MS, including the presence of a working spouse, age, duration and course of disease, severity of physical symptoms, fatigue, and visual impairment. However, the unemployment rate among people with MS who have cognitive problems is much higher than among those without them.
- It is important to think carefully about how much to tell your employer and colleagues about any cognitive difficulties you are having; once this information has been given, there is no way to take it back. Keep in mind that an employer is far more likely to retain confidence in an employee who recognizes and addresses a challenge before it becomes a problem than one who waits until the problems have already had a negative impact on the office or company.
- The same kinds of cognitive symptoms can affect academic performance. Fortunately, most colleges and universities offer accommodations for students with special needs. Equipped with a note from your physician explaining that you have a disability, and a list of the accommodations you need (preferably provided by a cognitive remediation specialist) to succeed in the school environment, you will usually be able to get the accommodations you need.

How Do Cognitive Symptoms Relate to Other Aspects of MS?

Many misconceptions and misunderstandings exist about how cognitive problems are or are not related to other MS symptoms and issues.

- *Relationship to Physical Disability and the Course of the Disease.* Cognitive impairment can be present at any time in the course of MS—or not at all. Some newly diagnosed individuals have cognitive changes among their earliest symptoms, while others who have lived with

MS for decades have none. However, there is a trend for cognitive impairment to be less severe in people with early relapsing-remitting disease than in those who have had the disease for a longer time and whose disease may have developed a progressive course.

- *Fatigue.* Fatigue is the most common symptom of MS, usually experienced as extreme lassitude and tiredness. Research has shown that this physical fatigue of MS has less impact on cognitive performance than people think it does. However, a phenomenon known as *cognitive fatigue* can make it very difficult for people to focus and concentrate for any extended period of time. For example, you may suddenly feel unable to think or concentrate while working on an extended task—such as balancing your checkbook or reading something for work. A brief break—similar to resting your legs during a long walk—will make it possible to resume the task after a few minutes. With these kinds of periodic breaks, most people can function cognitively quite well throughout the workday.
- *Depression.* The relationship between depression and cognitive impairment in people with MS is not clear, but it does appear that depression may increase the impact of cognitive problems, particularly in situations that require significant concentration and effort.
- *Stress.* The relationship between stress and MS is complex and not well understood. However, it is commonly thought that stress may affect cognitive processes, in people with the disease as well as others.
- *The Interactions among Stress, Depression, and Cognitive Function are Complex.* Although issues such as stress, depression, and cognitive impairment are often studied in isolation, they actually interact with each other and with other factors in a complex way. Thus, it would be appropriate to ask how stress affects depression, which itself may influence cognitive processing and everyday life. For example, does the way a person copes with stress influence whether he or she becomes depressed? Does that, in turn, influence cognitive functioning?

How Are Cognitive Changes Evaluated?

Cognitive changes can often be recognized by the person with MS or an observant friend or family member. However, self-reports and family reports of cognitive changes are often inaccurate, and there is no substitute for a professional assessment. A professional evaluation can pinpoint exactly what cognitive functions are affected and to what degree, while also identifying those functions that have not been affected.

How Do You Begin?

Your first step should probably be to share your concerns with your neurologist, and to discuss the possibility of getting a professional assessment. When talking to your physician about cognitive changes, it is best to be as specific as possible. Don't simply say, "My memory seems to be shot." Instead, be prepared to provide a number of specific examples of how your memory or other functions are not working correctly. Emphasize that these difficulties are a definite change from your previous level of functioning, and don't be sidetracked by any attempt to explain away your cognitive changes as the result of depression or stress.

Anyone with MS has experienced a neurologic examination in which the physician assesses functions such as strength, coordination, reflexes, vision, and sensation. A full neurologic examination may include a brief "mental status" examination or a more extensive "Mini Mental State" test. Although these techniques may be useful for picking up severe cognitive problems, they are insensitive to the often very subtle difficulties that are the hallmark of MS cognitive changes. An adequate assessment of cognitive changes in MS requires something more. Ideally, these changes should be addressed through a formal neuropsychological evaluation.

The Cognitive Evaluation

A cognitive evaluation is a series of tests, each of which is designed to assess one or more specific cognitive changes, and to identify strengths as well as weaknesses. These evaluations can be short (a half hour or less) or long (6 to 8 hours of face-to-face contact plus additional time for scoring, interpretation, and preparation of a report). The pattern of cognitive changes in MS varies widely from person to person, and people's goals also vary. For these reasons, the evaluation must be comprehensive enough to cover a wide variety of functions, and must be sensitive to the variations between individuals.

The most comprehensive evaluations are generally performed by a neuropsychologist—a psychologist who has specialized training in the diagnosis and assessment of cognitive problems. Speech/language pathologists and occupational therapists may also assess cognitive changes, although the assessment tools they use may differ somewhat from those used by neuropsychologists. The National MS Society can often help you to find the right person to do a cognitive evaluation.

A thorough assessment can make it possible to:

- establish a baseline for future comparison, or evaluate the effects of a treatment that you are starting;

- assess your cognitive strengths and weaknesses, especially before beginning cognitive and/or vocational rehabilitation;
- identify one or more treatable conditions (e.g., depression) that may be obscured by cognitive symptoms;
- address any questions that may arise concerning your performance on the job or at school, as well as the accommodations needed to deal with them.

What Should I Expect?

The neuropsychological evaluation and its follow-up will gather information about your complaints—physical, emotional, social, cognitive, and so on—as well as details about your education, employment history, family, and other information that will help to place the results of testing in context. It will also allow the neuropsychologist to estimate what your level of cognitive functioning was before it was affected by MS, and to get a general picture of your cognitive strengths and weaknesses pre- and post-diagnosis. An important part of this interview involves looking for other factors that may have affected your cognitive functions.

The testing may continue for several hours. It will include a variety of tests, depending in part on the nature of the problems that you have reported. Some will take just a few minutes; others will take longer. Some parts will probably be very easy, others quite difficult.

Once the neuropsychologist has completed the scoring and interpretation of the tests, she should arrange for a feedback session with you, and with one or more family members if you wish. During the feedback session, the neuropsychologist will review what the testing showed in terms of your strengths and weaknesses in various cognitive functions. He or she will help you to understand what the results mean and to consider their implications for your life at home and at work. In general, this should be done before the report is released to the referring doctor.

The neuropsychologist usually will write a detailed report of the test results and forward it to your doctor. Your doctor may also want to discuss the results with you, and may refer you to another professional for follow-up. For example, the doctor might prescribe a new medication or change one that you are already taking. He or she might refer you to a neuropsychologist, speech/language pathologist, or occupational therapist for cognitive rehabilitation; a psychiatrist for further assessment and treatment of emotional changes; or a psychotherapist for counseling.

The results of an evaluation may also be used to support a request for on-the-job accommodations, by helping you to identify specific accommodations that would make it

possible for you to do your job more productively and effectively, and they may outline a course of action for you to follow.

Neuropsychological evaluations are sometimes performed to support an application for disability benefits. If this is the case, a copy of the report may be sent to the agency or group responsible for disability determination—such as a government agency or private insurer, and the neuropsychologist may help to provide the disability determination office with the information it needs to make its decision.

Treatment

There is evidence that some disease-modifying agents, some symptomatic treatments, and some approaches to rehabilitation can help to improve MS-related cognitive changes.

Disease-Modifying Agents

Disease-modifying agents (DMAs) are treatments designed to alter the course of MS. All of the approved DMAs have been shown to reduce the number of exacerbations as well as the development of new lesions on the MRI. Because studies have found that cognitive changes are associated with the total amount of lesion area or scarring in the brain, it is logical to assume that any treatment that reduces the numbers of new MS lesions in the brain would either slow or halt the progression of cognitive changes. In practice, however, confirming this assumption has been difficult, because most studies of DMAs have not looked at their effects on cognitive symptoms.

Symptomatic Treatments

Symptomatic treatments are those that relieve symptoms of MS but do not alter the course of the disease. To date, the most promising medications for treating cognitive problems have included anti-fatigue agents and the anticholinesterase inhibitors, but additional studies are needed to determine their true usefulness.

Anti-fatigue Agents

The possible effect of anti-fatigue agents on cognitive changes has been of interest because people who feel more alert and less fatigued may perform better on cognitive tasks.

- Amantadine (Symmetrel®) is commonly used to treat MS fatigue, and it has shown some promise for reducing cognitive symptoms.
- Modafinil (Provigil®), approved by the FDA for the treatment of narcolepsy, a sleep disorder unrelated to MS, is also effective against MS-related fatigue. In one study of patients taking interferon beta-1a (Avonex®) who had attention impairments, those also given Provigil® demonstrated better performance on tests of complex attention, speed of visuomotor construction, and memory. They also showed improvement on emotional well-being and mental health.

Anticholinesterase Inhibitors

Acetylcholine is a *neurotransmitter* (a chemical that allows nerve transmissions between cells) that is thought to play an important role in memory. The enzyme anticholinesterase breaks down acetylcholine, thereby reducing its brain levels. It has been theorized that memory deficits occur when supplies of acetylcholine are reduced, and that anticholinesterase inhibitors can limit the breakdown of acetylcholine and thereby improve memory. Such drugs have been used with some success for several years to treat the memory deficits in Alzheimer disease and other conditions.

Aricept®, which is approved for the treatment of memory disorders in people with Alzheimer disease, has been shown to improve verbal and visual memory, and verbal fluency in people with MS.

Potassium Channel Blockers

Potassium channel blockers may prove useful in MS because they speed up the conduction of nerve impulses in partially demyelinated nerve fibers. Several studies have examined their safety and effectiveness in MS for treating symptoms such as weakness, visual deficits, and cognitive changes. None have shown statistically significant effects on cognition, but at least one study, of 4-aminopyridine (4-AP), showed a trend in favor of its increasing processing speed and improving verbal memory.

Rehabilitation

The third approach to treatment is *cognitive rehabilitation,* also called *cognitive remediation.* Cognitive rehabilitation can be divided into two approaches: restorative and compensatory.

The *restorative approach* attempts to improve impaired abilities such as memory or attention by using various types of exercises or practice drills. For example, memory deficits might be addressed through a program of computer-mediated practice in memorizing word lists of

increasing length and complexity. The limitation of this approach is that it tends to retrain very narrowly focused skills, such as the memorization of word lists, which may have limited usefulness in actual everyday activities.

In contrast, the *compensatory approach* does not attempt to improve impaired abilities, but rather to improve everyday functions by using strategies that "work around" the impaired abilities. It primarily involves *substitution,* in which a new way of approaching a function is substituted for the old way that no longer works. For example, while the restorative approach to memory deficits might involve practice in memorizing lists of words, the compensatory approach might involve teaching the individual to use a notebook to keep track of items that are likely to be forgotten.

The compensatory approach assumes that it is not necessary to improve an ability that is impaired in order to improve a *function* that is based on that ability. This same compensatory approach is used for impaired physical functions: it is possible to compensate for an inability to walk by using a motorized scooter. The key, of course, is *substitution.*

In clinical practice, it is common to combine the restorative and compensatory approaches. For example, someone working with memory exercises may learn to memorize increasingly challenging word lists by repeating them numerous times, but also by using some internal compensatory strategy such as grouping them into logical categories, or creating a story around them. Cognitive rehabilitation generally involves both restorative and compensatory approaches, although the compensatory type has generated the greatest interest and seems to have been the most useful.

Research on cognitive rehabilitation in MS involves a bewildering array of study designs, treatment approaches, outcome measures, and conclusions. It has been difficult to draw firm conclusions from these studies because they have generally included small numbers of people and little or no post-treatment follow-up. Progress in this area has been slow, and better studies with more participants and more consistency in outcome measures across studies need to be developed.

An interesting observation is the frequency with which mood is improved by comprehensive cognitive rehabilitation. This suggests that mood, especially depression, may be the symptom that benefits most from this type of treatment. It is also possible that improvements in mood may have positive effects on cognitive functioning. It is important to keep in mind that cognitive changes do not happen in a vacuum and cannot be addressed without considering a person's emotions and home and work environments.

Strategies for Managing Cognitive Changes

To help you develop effective, individualized tools for dealing with MS-related cognitive changes, it is important to understand that each person's needs differ, and that common sense strategies applied in a consistent fashion can make a big difference. Instead of prepackaged tools, the goal is to develop your own strategies that will fit your style, abilities, and situation. You need to think about what works for *you* and design a strategy to suits *your* unique needs. This will provide you with a measure of independence in coping with cognitive changes.

When we talk about "strategies" or "tools," we are not referring to things that will reverse memory loss or speed up information processing. Instead, we are looking to "compensate" or "substitute" in some way for a function that is not working as well as it should. For example, if you cannot keep all your social and work-related appointments in your head (and who can?), you could use an appointment book or personal digital assistant (PDA) to keep track of them. This compensatory strategy substitutes a written or electronic record of appointments for those that might otherwise fade from memory. This type of strategy won't actually help you to "remember" an appointment, but it *will* make it more likely that you will appear at the right time and in the right place.

Key Elements to Build and Maintain Your Strategies

Several key elements are needed to develop and use strategies that will help you deal with cognitive changes:

- Determine what kinds of problems you are experiencing. You can do this through your own personal insight as well as objective testing. For example, if you are experiencing a memory problem, does it involve forgetting appointments, forgetting where you have left things, not remembering names, or some combination of these?
- Try to sort out your strong and weak points. For example, are you well organized, but absent-minded?
- Convince yourself that it's OK to do things differently than you did in the past. Maybe you never used to need a shopping list, but now you can't remember even a few items when you go to the store. Be willing to shift gears and use a more effective strategy—this will work far better than clinging to old ways of doing things that no longer work.
- Think about your personal "style" of doing things: how do you operate in everyday life and which types of approaches tend to work best for you. For example, are you comfortable using high-tech gadgets or do you find that good old paper and pencil works best for you?

- Design a strategy to deal with the problem. It may take a bit of trial and error and brainstorming to come up with a plan that will satisfy you and solve the problem.
- Keep it simple. Try to design your strategy so that it is as simple as possible while still addressing the problem at hand. Break complex tasks into "bite-sized" pieces that will be more manageable.
- Tweak. Like new software or a design for a new airplane, cognitive strategies may need to be revised based on actual experience. Try out your strategy, determine which parts work well and which don't, revise your strategy based on experience, and go on from there.
- Adapt your strategy based on changing conditions. Be on the lookout for changes in your life or your MS that may require you to revise your strategy.
- *Use* your strategy. How many times have you heard someone say: "I had the appointment written down, but I forgot to look at my calendar?" The strategies that you develop will only make a difference if you apply them consistently.
- Evaluate your strategies periodically. On a regular basis, ask yourself, "How am I doing?" A periodic check-up can help to identify glitches such as a strategy that no longer works as well as it used to, or whether you are no longer using your strategy consistently. You might find that you have some new ideas to make a good strategy even better. The bottom line is: Does the strategy actually make a difference in my everyday life?
- Don't ignore your emotions. How you feel and the stresses in your life can affect how well you are able to use your cognitive abilities. Dealing effectively with cognitive changes may therefore require attention to what else going on in your life.
- Do not go it alone. Although it is possible to do everything on your own, it helps to work with someone—a professional, if possible—or a peer if not. Whether it's an exercise program, a diet, or cognitive strategies, having the encouragement and support of another person can go a long way toward keeping you on track. Moreover, professional help can speed the process and open up opportunities that might be hard to recognize on your own.

Ongoing Research Efforts in Cognition and MS

Current or Recently Completed National MS Society-Funded Research Related to Cognition

Dennis Bourdette, MD

Department of Neurology
The School of Medicine
Oregon Health & Science University
Portland, OR

NMSS Chapter: Oregon
Pilot Research Award: $44,000, 5/1/03–4/30/05

Ginkgo biloba as symptomatic therapy for cognitive dysfunction in MS • Conducting a clinical trial to assess a method of treating cognitive problems in MS.

About half of those with MS experience some cognitive dysfunction, most commonly problems with learning, memory and the speed of information processing. Dennis Bourdette, MD, is attempting to treat this troublesome symptom with ginkgo biloba, an extract made from leaves of the ginkgo tree.

Ginkgo biloba has been shown to protect nerve cells from injury. In a recent study in people with Alzheimer's disease, certain measures of cognitive function improved significantly with ginkgo biloba treatment. Dr. Bourdette is administering ginkgo biloba to 30 individuals with MS and cognitive impairment, and inactive placebo to another 30 patients. A battery of neuropsychological tests will be conducted before and after the study, to determine any changes in cognitive function.

This small study may provide preliminary data to support the design of a larger study of the effects of ginkgo biloba on cognitive function in MS.

Bonnie Chakravorty, PhD

Department of Health Administration
School of Health Sciences
Tennessee State University
Nashville, TN

NMSS Chapter Area: Mid-South
Pilot Research Award: $44,000; 4/1/07–3/31/08

Psychosocial aspects of multiple sclerosis among African Americans • Exploring the mental health needs of African Americans with MS.

Multiple sclerosis occurs less frequently in African Americans than in Caucasians, and research has shown that they are diagnosed earlier and may have more severe disease. Little research, however, has focused on the psychosocial needs of this population.

Bonnie Chakravorty, PhD, is undertaking a study to analyze the physical and mental health, MS symptoms, use of health services, perceptions of MS-related stigmatization, and health-related quality of life of African Americans. She is taking two approaches to this effort: analyzing enrollment data from the patient registry of the North American Research Committee on Multiple Sclerosis (NARCOMS), and also conducting a survey of 200 African Americans with MS.

This study should yield important information on the specific needs of one population with MS.

Nancy Chiaravalloti, PhD

Neuropsychology and Neuroscience Laboratory
Kessler Medical Rehabilitation Research & Education Corp
Kessler Institute for Rehabilitation
West Orange, NJ

NMSS Chapter: Greater North Jersey
Pilot Research Award: $44,000, 4/1/03–3/31/06

Modafinil for improving new learning and memory in multiple sclerosis • Evaluating a drug used to treat fatigue in MS for its potential for improving learning and memory.

About half of those with MS experience some cognitive dysfunction, most commonly problems with learning, memory and the speed of information processing. Nancy Chiaravalloti, PhD, believes that a drug used to combat fatigue in MS—modafinil—may help to improve learning and memory as well.

Previous studies have shown that modafinil increases the activity of brain messenger chemicals, called neurotransmitters, that may be important in new learning and memory formation, and inhibits neurotransmitters that induce forgetfulness. Dr. Chiaravalloti is enrolling 20 subjects with MS and cognitive impairments in this small study. Her team is comparing treatment with modafinil with an inactive placebo. They are measuring the results using the "Selective Reminding Test," which involves learning and then recalling a list of 12 words. In addition, all participants will keep a precise journal, recording any apparent changes in cognition.

If successful, this study may lead to further testing of modafinil for treating the cognitive problems experienced by people with MS.

Christopher Christodoulou, PhD

Department of Neurology
SUNY at Stony Brook
Health Sciences Center
Stony Brook, NY

NMSS Chapter: Long Island
Pilot Research Award: $44,000; 05/01/06–4/30/07

Impact of donepezil on cerebral activation and cognition in MS • Using novel imaging technology to determine whether a treatment under study for improving memory can affect patterns of brain activation.

About half of people with multiple sclerosis may experience some degree of cognitive dysfunction, affecting the ability to think, reason, concentrate or remember. An ongoing study is examining whether Aricept® (donepezil HCI), a treatment approved to treat Alzheimer's disease, can improve memory and cognition in people with MS.

Christopher Christodoulou, PhD, is adding a novel dimension to this ongoing study, with funding from this pilot research award. His team is evaluating brain activation patterns using functional magnetic resonance imaging (fMRI), an imaging technology that measures the amount of oxygen used by different areas of the brain. By examining 20 people during the

performance of tasks involving memory, the team is attempting to determine patterns in brain activation before treatment, and how these patterns may change following treatment.

This study will help to evaluate the usefulness of Aricept as a method of improving cognitive function in people with MS.

Jill Conway, MD

University of Pennsylvania
Philadelphia, PA

NMSS Area: Greater Delaware Valley Chapter
Award: Postdoctoral Fellowship
Mentor: Laura J. Balcer, M.D.
Term/Amount: 8/1/06–7/31/08; $110,428

Relation of novel outcomes of vision and axonal loss to cognitive impairment in MS • Investigating the relationship between cognitive dysfunction and nerve fiber loss in people with MS.

More than half of the people diagnosed with MS experience some form of cognitive impairment, mainly difficulties with memory, concentration, and complex problem-solving. These problems can significantly impact quality of life.

During this clinical research fellowship, Jill Conway, MD, is investigating the relationship between cognitive dysfunction and the extent of nerve fiber loss in the nerves that extend from the retina (at the back of the eye) and transmit images to the brain. She will assess people with MS and controls without MS for cognitive dysfunction using a standard battery of tests that focuses on areas of cognition typically impaired in MS. All subjects will also undergo visual function testing, including a new visual function test that measures the ability to recognize faces. These results will be compared with the subjects' retinal nerve thickness as measured by a new imaging scan called optical coherence tomography (OCT). OCT provides rapid, non-invasive measurement of nerve fiber loss in the retina. These results will be compared to determine whether nerve fiber loss in OCT correlates with cognitive dysfunction.

This research will provide insights into the relationship between nerve fiber injury, visual function, and cognition in patients with MS. If nerve fiber loss measured by OCT predicts cognitive deficits, OCT may allow rapid identification of those most at risk for cognitive dysfunction who would benefit from cognitive testing and intervention.

John DeLuca, PhD, ABPP

Neurophysiology & Neuroscience Laboratory
Kessler Medical Rehabilitation Research & Education Corporation
West Orange, NJ

NMSS Chapter: Greater North Jersey
Pilot Research Award: $44,000; 9/30/06–9/30/07

Actual reality: Advancing functional assessment for individuals with MS • Testing a novel method of assessing the ability of people with MS to perform activities of everyday life.

Multiple sclerosis can have dramatic effects on the quality of everyday life activity. People with MS tend to engage in fewer social and vocational activities than people without the disease, and may have greater difficulties in carrying out routine household tasks. Instruments are needed to effectively measure these capabilities for quality of life studies; self-report measures are not always accurate and others often measure only very basic tasks such as washing hands or making a sandwich.

John Deluca, PhD, ABPP, is testing a new method of assessing the performance of everyday life activities called "Actual Reality." This method involves measuring the ability of people with MS to use the internet to perform a routine task. He is evaluating this technique in 20 people with MS and 20 people without MS, who are accessing the internet to purchase airline tickets for a trip.

This study should yield information on a new technique for observing how MS affects daily life, which could measure the success of interventions designed to improve these effects.

George Demakis, PhD

Department of Psychology
School of Arts and Sciences
University of North Carolina at Charlotte
Charlotte, NC

NMSS Chapter: Mid-Atlantic
Pilot Research Award: 7/1/05–6/30/07; $44,000

Cognitive impairment in nursing home residents with MS • Determining the factors associated with cognitive problems in MS using a database of extensive information on nursing home residents.

Cognitive problems are common in MS and can include difficulties with learning, memory, or attention. These deficits can affect social, vocational, and rehabilitation activities, so understanding what contributes to them and how they change over time is critical for clinicians who treat people with MS.

George Demakis, PhD, is using a unique resource to study cognitive problems in people with MS. The Minimum Data Set (MDS) is a database that contains information on residents in all Medicaid- and Medicare-certified nursing homes in the United States. The MDS includes demographic information, as well as data on diseases, treatments, and cognitive function. Dr. Demakis is studying nursing home residents with MS across a one-year period, to determine changes in cognitive function, and to assess other factors (e.g., disease activity) that may correlate with the development of cognitive problems.

This study may provide valuable information on cognitive issues experienced by people with MS in nursing homes, and possibly, how to predict them.

Yael Goverover, PhD

New York University
New York, NY

NMSS Area: New York City Chapter
Award: Postdoctoral Fellowship
Mentor: John DeLuca, PhD
Term/Amount: 9/1/04–8/31/07; $109,979

Improving learning and memory for functional activities in multiple sclerosis • Testing techniques to optimize the learning of tasks in persons with MS who have cognitive impairment.

Memory impairment is a fairly common symptom of MS. Some studies suggest that memory problems in MS may be related to difficulty in learning new information.

Yael Goverover, MD, is testing two learning techniques to determine if they can improve performance of everyday tasks in individuals with MS. One experiment compares the "generation effect," a strategy in which items such as words are self-generated, versus learning items that are merely read or heard, by having participants learn a cooking and financial management task.

Another experiment compares the "spacing effect," in which items are presented over a period of time, versus presenting items consecutively or all at once, by having participants complete three tasks—learning a paragraph, taking directions, and learning a route.

These studies should provide useful information about applying learning strategies to real-life tasks and may ultimately help people with MS to maintain their current lifestyles at home, at work, and in the community.

Lauren B. Krupp, MD

State University of New York at Stony Brook
Stony Brook, NY

Region: Long Island Chapter
Term: 4/1/02–3/31/07
Funding Required: $784,201

A longitudinal study of mild cognitive impairment in multiple sclerosis • Following a group of individuals with MS who have mild cognitive problems to evaluate whether this symptom becomes worse over time.

Cognitive problems in MS occur fairly frequently, mainly difficulties with memory, concentration, and complex problem-solving. They can interfere with family functions, job performance and social obligations. But there has been little research into whether and how these problems may worsen over time.

Lauren B. Krupp, MD, is studying three large groups of individuals to explore this question. One group has MS and mild cognitive impairment, a second group has MS and no cognitive impairment, and a comparison group has neither MS nor cognitive impairment. To track cognitive function over three years, each participant is being given initial and annual verbal learning and memory tests, and is also being given annual brain MRI scans.

The results of this unique study should provide individuals with MS a better idea of how mild cognitive impairment may change over time, enabling them to prepare for such changes. It will also lay the necessary groundwork for future studies of therapies aimed at stopping the progression of cognitive problems.

Murali Ramanathan, PhD

State University of New York at Buffalo
Buffalo, NY

NMSS Area: W. New York/N.W. Penn. Chapter
Award: Research Grant
Term/Amount: 10/1/05–9/30/08; $646,755

Brain-derived neurotrophic factor in multiple sclerosis • The possible role of a protein in susceptibility to cognitive deficits in persons with MS.

Many individuals with MS will experience some form of cognitive impairment, mainly difficulties with memory, concentration, and complex problem-solving, at some point in their lives. However, the degree of impairment varies widely among individuals. Murali Ramanathan, PhD, is investigating whether a genetic variation that affects the function of a brain protein called BDNF (brain derived neurotrophic factor) contributes to the severity of cognitive dysfunction in people with MS, thus accounting for variations in cognitive ability associated with the disease.

BDNF is produced in the brain and also by immune cells, and it appears capable of influencing the survival and function of nerve cells and regulating the production of myelin, the nerve fiber insulation attacked by immune cells in MS. BDNF also plays important roles in the biological processes underlying learning and memory. Individuals with MS carrying a particular form of the BDNF genetic variation appear to make more of the protein from immune cells and also appear to have less severe cognitive impairments than those with another form of genetic variation. To test these assumptions, Dr. Ramanathan is comparing the extent of cognitive deficits, severity of disease activity, and levels of BDNF in individuals with MS with different forms of the genetic variation.

Establishing the role of BDNF and its genetic variations in MS will lead to a better understanding of the factors causing cognitive deficits in MS and enable evaluation of therapeutic approaches to reduce or prevent such deficits.

Nancy L. Sicotte, MD

University of California, Los Angeles
Los Angeles, CA

NMSS Area: Southern California Chapter
Award: Research Grant
Term/Amount: 4/1/07–3/31/09; $277,640

Hippocampal volume loss in MS: clinical consequences • Exploring how brain tissue loss in specific regions relates to memory functions in MS.

Many people with multiple sclerosis experience cognitive problems, which can dramatically affect quality of life. Little is known about the underlying cause for such problems in MS and available treatments do not target these impairments directly.

Nancy L. Sicotte, MD, is focusing on the hippocampus, a region of the brain that is known to be important in memory processes, but has not been studied extensively in MS. Her team is using high-resolution MRI (magnetic resonance imaging) to study the structure of the hippocampus to determine if there are detectible changes in people with MS as compared to controls. Sophisticated imaging approaches are being used to look at subregions of the hippocampus that are known to have specific functions such as the learning of new material or the recall of learned material, in order to determine if brain tissue loss is occurring in these regions, and if this occurrence is related to memory performance.

These studies will further our understanding of cognitive dysfunction in MS, and help to target future therapies to address cognitive symptoms specifically.

Jeffery Wilken, PhD

Department of Neuropsychology Services
Neuropsychology Associates of Fairfax
Fairfax, VA

NMSS Chapter: National Capital
Pilot Research Award: $44,000; 10/01/06–09/30/07

A comparison of stimulant medications for MS-related fatigue and cognitive problems • Comparing treatments for improving fatigue in people with MS, and determining the effect of these therapies on cognitive function as well.

Fatigue and cognitive dysfunction are two common, troublesome symptoms of multiple sclerosis. Two wakefulness-promoting agents—Concerta® (methylphenidate HCl) and Provigil® (modafinil)—are sometimes prescribed for MS-related fatigue. Jeffery Wilken, PhD, is comparing the effectiveness of these medications, and is seeking to determine if they can improve cognitive symptoms as well.

For this small pilot study, Dr. Wilkens is enrolling 15 people with MS. Participants are undergoing fatigue and cognitive assessments before beginning treatment. During three five-week

treatment periods, participants are being randomly assigned to receive Concerta, Provigil, or inactive placebo. Fatigue and cognitive assessments are being repeated after each treatment period.

Data from this study can help to design a larger clinical trial of these medications for treating fatigue and cognitive problems in MS.

Glenn Wylie, PhD

Neuropsychology and Neuroscience Library
Kessler Medical Rehabilitation Research and Education Corporation
West Orange, NJ

NMSS Chapter Area: Greater North Jersey
Pilot Research Award: $44,000; 4/1/07–3/31/08

The neuropsychology of executive control: An fMRI and DTI study • Determining the effects of MS on certain aspects of cognitive function.

Cognitive problems, such as memory loss and decision-making, occur in as many as one half of people with MS. Glenn Wylie, PhD, is examining whether MS affects the cognitive abilities involved in one aspect of decision-making—switching from one task to the other.

Switching tasks has been found to involve a specific network of brain areas. Dr. Wylie's team is using advanced imaging techniques to examine this network of brain areas in 20 people with MS and in 20 controls without MS who are actively engaged in switching tasks.

This study may add to the growing body of research on cognitive issues that affect people with MS, and help to improve cognitive function and quality of life.

Feng Zhou, PhD

Johns Hopkins University
Baltimore, MD

NMSS Area: Maryland Chapter
Award: Postdoctoral Fellowship
Mentor: Susan M. Courtney, Ph.D.
Term/Amount: 7/1/07–6/30/09; $98,747

Neural basis of short-term memory and cognitive control dysfunction in multiple sc lerosis • Understanding tissue damage that accompanies cognitive dysfunction in MS for clues to rehabilitating or preventing them.

Problems with memory and other cognitive symptoms affect many people with multiple sclerosis. Feng Zhou, PhD, is studying the tissue damage that might signify cognitive problems in 20 people with MS and 20 controls without MS.

Dr. Zhou's team is examining these participants using imaging technology called functional MRI (fMRI) to find the brain areas that might be impacted by the disease. fMRI allows researchers to take active images of the brain while it is performing working memory tasks that require either maintaining or manipulating information. They also are using newly developed diffusion tensor imaging and magnetization transfer ratio imaging techniques to visualize nerve fibers that connect the brain areas identified by fMRI, and to quantify the damage to these never fibers.

Understanding the specific damage that accompanies cognitive dysfunction in MS will help to rehabilitate or prevent these problems in people with MS.

Rehabilitation

John DeLuca, PhD, ABPP

Kessler Medical Rehabilitation Res. & Educ. Corp.
West Orange, NJ

NMSS Area: Greater North Jersey Chapter
Award: Mentor-Based Rehabilitation Fellowship
Term/Amount: 7/1/07–6/30/12; $365,133

MS fellowship in neuropsychological rehabilitation • Training in ways to help people cope with cognitive problems associated with MS.

The goal of the National MS Society's mentor-based postdoctoral fellowship program in multiple sclerosis rehabilitation research is to recruit and train talented clinician-scientists in rehabilitation research specific to MS. The ultimate goal is to get more hands and minds working on the best ways to help people with MS maximize their abilities.

Kessler Medical Rehabilitation Research and Education Center (KMRREC) has designed a fellowship program with the aim of supporting the training of post-doctoral fellows in neuropsychology, cognitive rehabilitation and cognitive/translational neuroscience. The

training program is based on a highly individualized research training plan designed by the trainee in close collaboration with his/her mentors. John DeLuca, Ph.D., is the primary mentor for the MS fellows in this program, and assistive mentors are assigned based on the needs of each fellow. Fellows are guided through the entire process of research starting from an idea, design, and submitting a proposal, to data collection, analysis, data presentation and publication of a research manuscript.

The goal of KMRREC's program is to nurture fellows' enthusiasm for rehabilitation research by providing them with dedicated and experienced mentors who not only teach the necessary skills and methodology in science, but also serve as role models for success in emphasizing the importance of contributing to the field of MS rehabilitation.

Research/Clinical Update

Positive Results Published on Testosterone for Men with MS

Researchers from the University of California, Los Angeles have published results from a small study, funded by the National MS Society and others, suggesting that one year of treatment with a gel containing the sex hormone testosterone (applied to the skin) in 10 men with relapsing-remitting multiple sclerosis resulted in significant improvements in cognitive function and in slowing brain tissue loss. Nancy Sicotte, MD, Rhonda Voskuhl, MD, and colleagues report these positive findings in the May 2007 issue of *Archives of Neurology* (2007;64:683–688).

Further research involving larger numbers of patients and controls would help to confirm and expand these early results, and to ensure the safety and effectiveness of testosterone treatment in MS.

Background: Sex hormones may contribute to MS susceptibility by influencing the immune attack on brain and spinal cord tissues. Laboratory studies have shown that the severity of EAE, an MS-like disease, is decreased when testosterone, a male sex hormone, is administered to male and female mice. Dr. Voskuhl was awarded funding from the National MS Society's targeted research initiative on Gender Differences in MS to undertake a small study of testosterone gel in men with MS. Preliminary results of this study were originally presented at the 58th Annual Meeting of the American Academy of Neurology in April 2006.

Study: Ten men with relapsing-remitting MS, ranging from 29 to 61 years of age, were studied. Relapsing-remitting MS is the most common form of the disease, involving clearly defined flare-ups followed by partial or complete recovery periods. After a six-month observation period, they were treated with testosterone gel applied to the skin (10 grams daily, containing 100 mgs of testosterone) for one year. None of the men were taking disease-modifying therapies. Clinical assessments including blood tests, as well as clinical measures of disease activity and cognitive function were completed every three months. Magnetic resonance imaging scans were taken before treatment and monthly to measure evidence of disease activity. The extent of brain tissue loss (atrophy) was assessed by determining normalized brain volumes using automated computer software.

Since all 10 of the men received treatment and none received inactive placebo, the investigators compared measures taken before treatment versus after treatment. Testosterone levels were in the lower range of normal before treatment, and although they increased with treatment, remained in the normal range.

After 12 months of testosterone treatment, measures of clinical disease activity remained stable, blood tests were normal, and no adverse events related to treatment were reported. The men showed significant improvements in performance on a test of cognitive function called the Paced Auditory Serial Addition Task (a test of processing speed and memory) compared to the pre-treatment period. The authors report that the improvement could not be accounted for by well-known "practice effects," which had stabilized during the pre-treatment period.

MRI scans showed no increases in disease activity or tissue damage during treatment, although the authors note that the patients began the study with relatively low levels of disease activity on MRI.

Significantly, the rates of brain atrophy, measured by normalized brain volume, slowed by 67 percent during the last nine months of treatment. Muscle mass increased significantly during the study; testosterone is sometimes used for this purpose in other chronic diseases.

This small study shows that testosterone treatment may have therapeutic benefit in men with relapsing-remitting MS. Further study involving larger numbers of patients and control groups is necessary to confirm these early results, and to ensure the safety and effectiveness of testosterone treatment for MS.

"We're gratified that these early, promising results stemmed from the National MS Society's targeting of gender differences as an important area of research in MS," said Dr. John R. Richert, the Society's executive vice president of research. "It also demonstrates how basic laboratory findings can quickly translate into possible new therapeutic strategies."

Dr. Voskuhl and colleagues are already proceeding with a similar effort involving the sex hormone estriol: Based on a small, early-phase trial that showed decreases in disease activity in 12 women with MS, she is now launching a multicenter, controlled clinical trial of oral estriol (added to the approved MS therapy glatiramer acetate) in 130 women with relapsing-remitting MS.

APPENDIX A

Resources

National Multiple Sclerosis Society
Call toll-free in the United States: 1-800-344-4867
Web site: www.nationalmssociety.org

Brochures from the National MS Society

Information for Employers
For people to give to their employers if they decide to disclose their MS

A Place in the Workforce
On employment strategies and options

A Cup of Ambition
Could you work if you had training? Transportation? Special equipment? You may have overlooked a major resource: Vocational Rehabilitation!

The Map Store—"Our Map to Independence"
The author's success included facing what MS had done.

Pop Quiz: Should You Tell Your Boss?

The Self-Employment Option
When it works, it works. Read this first!

Pop Quiz: Should You Think About a Different Job?

Disclosure or NOT?
To tell or not to tell—when is it in your best interest?

Maximize Your Options
Basic points from the Society's employment expert.

Should I Work? Information for Employees
General overview of the employment issues that might concern people newly diagnosed

The Win-Win Approach to Reasonable Accommodations: Enhancing Productivity on Your Job
A practical guide to obtaining workplace accommodations. By Richard T. Roessler, PhD, and Phillip Rumrill, PhD

Web Resources

Solving Cognitive Problems (brochure)
http://www.nationalmssociety.org/site/PageServer?pagename=HOM_LIB_brochures_cogproblems1

6-part Brochure: MS and the Mind
http://www.nationalmssociety.org/site/PageServer?pagename=HOM_LIB_brochures_msmindcontents

Cognitive Function (Sourcebook)
http://www.nationalmssociety.org/site/PageServer?pagename=HOM_LIB_sourcebook_cognitive

You Can . . . Remember
http://www.nationalmssociety.org/site/PageServer?pagename=HOM_LIVE_youcan_remember

On the Job with Fatigue and Cognitive Issues
http://www.nationalmssociety.org/site/PageServer?pagename=HOM_LIB_imsfeb06_fatiguecognitiveissues

Loosening the knots of cognitive changes
http://www.nationalmssociety.org/site/PageServer?pagename=HOM_LIB_imsapr07_looseningcognitive

APPENDIX B

Information from the MS Society of Canada

Multiple Sclerosis Society of Canada
Call toll-free in Canada: 1-800-268-7582
Email: info@mssociety.ca
Web site: www.mssociety.ca

The mission of the Multiple Sclerosis Society of Canada is: To be a leader in finding a cure for multiple sclerosis and enabling people affected by MS to enhance their quality of life.

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Multiple Sclerosis Society of Canada's Publications Listing

MS Society of Canada publications are available online at (www.mssociety.ca) or in print format by calling 1-800-268-7582.

About multiple sclerosis—general information

Multiple Sclerosis and How We Can Help

Key Facts for Those Affected by Multiple Sclerosis

MS: Its effects on you and those you love

Living with Progressive MS

Talking with Your Patients About Difficult Topics

- Diagnosis of Multiple Sclerosis
- Progressive Disease
- Elimination Problems
- Sexual Dysfunction
- Depression and other Emotional Change
- Cognitive Dysfunction

Red Flags, Green Lights: Accessing reliable health information

Managing MS Symptoms

Living Well with MS: Managing fatigue

Living Well with MS: Mind matters

Sexuality and MS

Living For Today: Managing MS pain

New: Fall 2007—Urinary Dysfunction and MS

Understanding Bowel Dysfunction

New: Fall 2007—Cognitive Change and MS

Health and Wellness

Healthy Eating

Multiple Sclerosis and Your Emotions

Everybody Stretch

Taming Stress in MS

Living Well with MS: Ten tips for people living with MS

Multiple Sclerosis and Family

How to Talk about MS with Your Children

My Mommy Has MS

Keep your Balance!

Keep S'myelin: An Activity Book about MS for Kids

Managing Practical Issues

A Guide to Employment and Income Support

Insuring Your Future: Your guide to life insurance and multiple sclerosis

MS and Caregivers

New: Fall 2007—Guide for Caregivers

Young Persons with MS

Mighty Special Kids

Kids Get MS Too: A guide for parents whose child or teen has MS

Becoming a Member of the MS Society of Canada

Since our founding in 1948, the core support of the MS Society has been from tens of thousands of dedicated individuals, companies and foundations in communities across Canada. The Society receives almost no funding from government.

The MS Society of Canada has a membership of 28,000. It is the only national voluntary organization in Canada that supports both MS research and services for people with MS and their families.

Eighty-two percent of MS Society net revenue is devoted to program areas: MS research, services for people with MS and their families, MS clinics, social action, public education and chapter development. Management and fund raising costs are just 18 percent.

Membership has numerous benefits. As a member of the MS Society, you will:

- Have a say in the future of the MS Society
- Allow us to speak on behalf of Canadians with MS with a more powerful voice
- Receive your division newsletter
- Receive your local chapter newsletter
- Receive MS Canada, the national newsletter, four times per year

To become a member please visit our website: www.mssociety.ca/en/involved/member.htm or call 1-800-268-7582.

MS Clinics

The MS Society of Canada is proud to work with a network of specialized MS clinics across the country. Clinic services vary, but most offer a wide range of services, delivered by a multi-disciplinary health care team. Visit the MS Society of Canada website (www.mssociety.ca) for a list of MS clinics across Canada, or call the MS Society of Canada for more information: 1-800-268-7582.