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What researchers are doing for people with MS now

by Sara Bernstein

Imagine if something in the medicine cabinet could reliably alleviate MS fatigue, without keeping you awake all night. Or that speaking a few words could improve how you think. These dreams are shared by researchers who—working in parallel with those who are seeking the cause and cure—are trying to help people with this disease **now**, with interventions to improve the great variety of symptoms that can interfere with quality of life. Here is a small sample of ongoing research on just a few symptoms.

Fighting fatigue

Fatigue occurs in as many as 80% of people with MS, disturbing people's ability to function at home and work. It may be the most prominent symptom in people who might otherwise have minimal limitations.

Dean Wingerchuk, MD, FRCPC (Mayo Clinic, Scottsdale, AZ), and colleagues noticed that some people with MS reported less fatigue when using aspirin for other reasons. So they decided to study aspirin formally, giving

1,300 mg or an inactive placebo to 30 people with MS and fatigue.

The primary goal of the study was to determine if aspirin treatment would improve scores on the Modified Fatigue Impact Scale—a measuring tool in which patients report on how fatigue affects their physical, cognitive, and psychosocial functioning.



MFIS scores improved significantly in those taking aspirin. There were no serious adverse effects. (*Neurology* 2005 Apr 12;64[7]:1267–9)

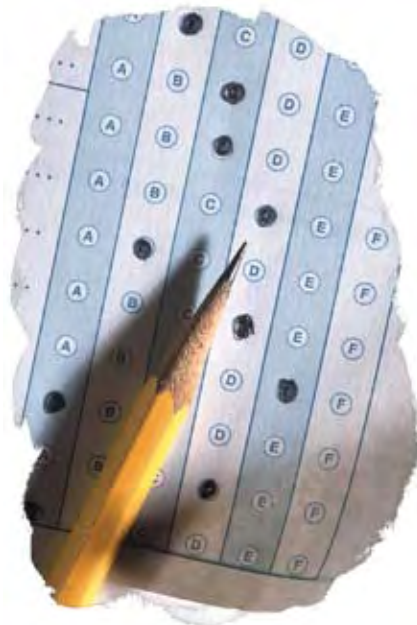
Based on these results, the National MS Society is now funding Dr. Wingerchuk to conduct a larger study at three sites, which is necessary to determine if aspirin indeed is safe and effective for MS-related fatigue. The team is giving aspirin or placebo to 135 people with MS-related fatigue.

Participants are completing questionnaires about the severity and impact of their fatigue, undergoing memory testing to assess cognitive fatigue, and are having blood taken to measure markers of inflammation. This further evaluation is necessary, particularly considering the risk of gastrointestinal bleeding that is possible with long-term aspirin use, even at low doses.

If this study is successful, it may add an important new option for treating MS-related fatigue.

Another approach to fighting MS fatigue could be “energy conservation strategies”—such as effort-saving devices, eliminating or delegating tiring tasks, and including rest periods every day. Virgil G. Mathiowetz, PhD (University of Minnesota, Minneapolis) investigated whether these strategies really help by evaluating a six-week course that teaches energy conservation. His study was funded by the National MS Society.

Dr. Mathiowetz’s team recruited 169 people to participate. Scales that measure fatigue were administered before and after the course—as well as before and after control periods during which no intervention occurred—to determine any changes. The course succeeded in significantly reducing the impact of fatigue on physical and social function, and in increasing vitality. (**Multiple Sclerosis** 2005 Oct;11[5]:592–601)



Dr. Mathiowetz followed people for one year after completing the course to see if the effects would last. Not only were the original results maintained, but they were improved upon, with the impact of fatigue on cognitive function being reduced significantly as well! (**International Journal of Rehabilitation Research** 2007 Dec;30[4]:305–13) Occupational therapists often recommend energy conservation strategies to people with MS and these results provide important evidence of how such strategies can succeed.

Minding cognitive function

Cognitive problems may be experienced by about half of all those with MS at some point in their disease, possibly affecting the ability to learn, remember, organize, plan and problem-solve—all critical parts of the activities of daily life. These prob-

lems are not related to physical function—a person with MS can have no physical limitations and yet experience significant cognitive impairment.

A drug under study for its possible ability to protect nerve tissue may also improve cognitive function in people with MS. Hannelore Ehrenreich, MD, DVM (Max Planck Institute of Experimental Medicine, Gottingen, Germany) and colleagues reported results from a small, uncontrolled study of a laboratory-produced version of erythropoietin, a naturally-occurring hormone used to treat anemia.

They administered the drug to eight people with chronic, progressive (secondary-progressive) MS and followed them for 48 weeks. Five people took a high dose of the intravenous drug, along with two control patients who had Parkinson’s disease, and three received a low dose.

Although this was primarily a safety study, with no adverse events reported, the investigators found that cognitive function improved and improvements persisted for three to six months after treatment. The low-dose and control groups did not improve. (**Brain** 2007 Oct;130[Pt 10]:2577–88)

This is not the first evidence of this capability—erythropoietin has improved cognitive function in rodent models of neurological and psychiatric disorders, and in people with schizophre-

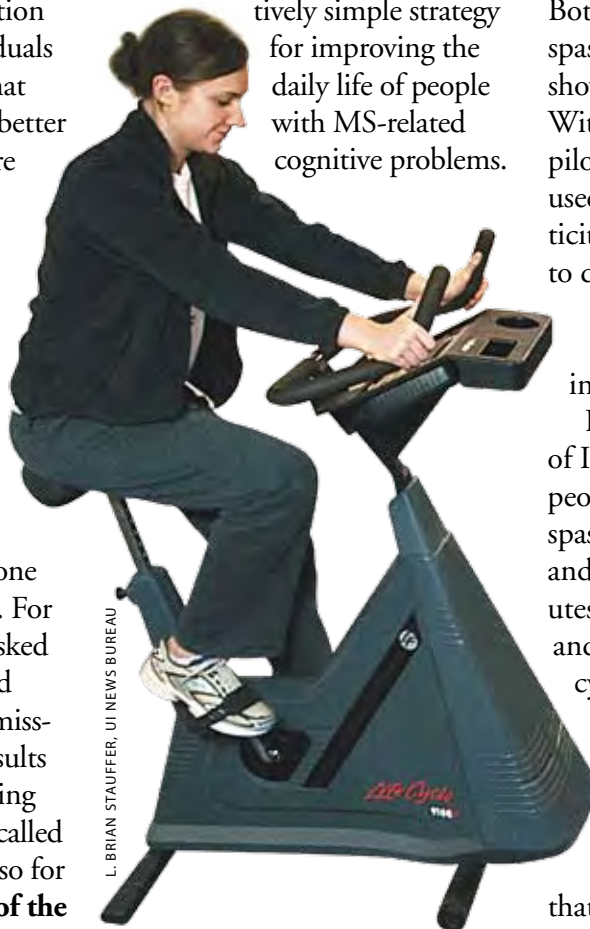
nia. (**Journal of Renal Nutrition** 2008 Jan;18[1]:146–53) Further research will determine the safety and effectiveness of this drug for protecting nervous tissue in MS as well as improving cognitive function.

Memory impairment in MS may be related to difficulty in learning new information. Yael Goverover, PhD (New York University, New York, NY), and colleagues tested a method of “self-generation” with funding from the National MS Society. The self-generation strategy suggests that individuals remember items or words that they generate or “make up” better than if the items or words are just provided to them.

Twenty people with MS and mild cognitive impairments and 18 controls without MS were asked to complete two cooking tasks and two financial management tasks. One task was carried out with all instructions provided, and in the other task, participants generated one key word in the instructions. For example, a participant was asked to “beat together _____” and would have to generate the missing item, “two eggs.” The results showed that tasks learned using self-generated words were recalled and performed better, more so for the cooking tasks. (**Journal of the International Neuropsychological Society** 2005;11[S1]:49)

Now Dr. Goverover is extending these studies with further

funding from the National MS Society. Her team is studying 78 people with MS—26 with mild cognitive impairments, 26 with moderate to severe cognitive impairments, and 26 with no cognitive impairments. Participants are completing a variety of tasks using provided and self-generated instructions, and the ability to remember these instructions will be tested 30 minutes and one week after the tasks are completed. The results may yield important information on a relatively simple strategy for improving the daily life of people with MS-related cognitive problems.



University of Illinois researchers are studying the use of cycling to alleviate spasticity. Participant Ashley Hayes.

Addressing muscle trouble

Spasticity may be as mild as the feeling of tightness of muscles or may be so severe as to produce painful, uncontrollable spasms, usually in the legs. Although there are prescription medications that can treat spasticity, they often cause unwanted side effects.

Robert Motl, PhD, found that an electrical reading from muscles, called the H-reflex, was higher in persons with MS than in others without the disease. Both intense exercise and anti-spasticity medications have been shown to reduce the H-reflex. With funding from a Society pilot research award, Dr. Motl used clinical measures of spasticity and tests of the H-reflex to determine whether sessions of exercise with a stationary bike could relieve spasticity in MS.

His team at the University of Illinois collected data in 27 people with MS and leg muscle spasticity before and 10, 30, and 60 minutes after 20 minutes of leg cycling and before and after a control exercise. The cycling resulted in prolonged reductions in H-reflex and spasticity scores. (**Neuroscience Letters** 2006 Oct 9;406(3):289–92)

The team also has found that combining cycling and anti-spastic medications in six people with MS showed positive results. (**International Journal of Neuroscience** 2007

Jul;117[7]:895–901, **Archives of Physical Medicine & Rehabilitation**, in press)

Proponents of the use of marijuana (cannabis) or its derivatives in MS have suggested that it may help reduce spasticity, although it has been difficult for researchers to obtain objective data of its effectiveness. Mark Agius, MD, and colleagues (University of California, Davis) are conducting a well-designed, placebo-controlled study to test the safety and effectiveness of inhaled cannabis and of oral tetrahydrocannabinol, a cannabis derivative, for the treatment of spasticity in 60 persons who have MS and spasticity.

The team has developed novel instruments to objectively test muscle tone and other measures of spasticity and is using them to compare these experimental therapies with inactive placebo.

In addition to funding this important study, the National MS Society is seeking to find the “bottom line” on cannabis treatments for MS symptoms such as spasticity and pain. A task force gathered by the Society recently released an expert opinion paper on the use of marijuana for MS. For more details on this effort, see page 18.

Driving away depression

Depression in its various forms is common during the course of multiple sclerosis—from feeling down for a few hours on a given day to severe clinical depression

that may last for several months. David C. Mohr, PhD (Northwestern University, Chicago, IL) is studying ways to identify depression earlier in people with MS and treat it more effectively.

Dr. Mohr recently published findings on both these goals. In one study, his team attempted to simplify the diagnosis of depression by administering this simple two-question screen to 260 people with MS: During the past two weeks, have you often been bothered by feeling down, depressed, or hopeless? During the past two weeks, have you often been bothered by having little interest or pleasure in doing things?

The results were correlated with a standard diagnostic method. This simple screen, using even just one question, correctly identified 66 of 67 people with a major depressive disorder, and correctly ascertained that 167 of 193 people did not have such a disorder. (**Multiple Sclerosis** 2007 Mar;13[2]:215–9)

As far as treating depression, Dr. Mohr has reported on a technique that could especially help people with MS and mobility issues—telephone-administered psychotherapy. In a group of 127 people with MS and depression, participants showed significant improvements in mood during 16 weeks of two types of phone therapy. Cognitive-behavioral therapy (a structured therapy that teaches skills aimed at changing thoughts and behaviors that lead

to depression) showed significantly greater improvements than a less structured therapy called supportive emotion-focused therapy (a therapy that encourages discussion of difficult feelings).

There were significant, lasting improvements in both groups even 12 months following the end of treatment, and the dropout rates were significantly lower than those reported in studies of face-to-face psychotherapies for depression. (**Archives of General Psychiatry** 2005;62:1007–1014)

Dr. Mohr’s team then showed that participants in both groups showed significant reductions in disability and fatigue (more so in the cognitive-behavioral group), which were related to the reductions in depression. So treating depression in people with MS—even via phone—may even improve their battle with the disease itself. (**Health Psychology** 2007 Sep;26[5]:554–63)

The symptoms of MS are varied and unpredictable. As the search for cause and cure continue, so does the search for interventions to help people with MS address these challenges now.

For more information about MS symptom management: **nationalmssociety.com/symptoms**

Henze, T. What is new in symptom management? **International MS Journal**. 2007 Mar;14(1):22–7.

Davis, Winston, “A More Livable Life Now” **InsideMS**. June–July 2006. Volume 25, Issue 3.