Focus on fatigue



Research studies are targeting the most common MS symptom.

by Lori De Milto

Most people with multiple sclerosis experience fatigue, one of the most common—and most difficult—MS symptoms to treat. This makes fatigue an important target for research studies. Among a range of scientific projects on the topic, researchers are studying the link between higher body temperature and fatigue, ways to help people with MS exercise and whether too much iron in the brain contributes to cognitive fatigue.

Helping people with MS exercise

Exercise may help people with MS manage fatigue, but exercising can be difficult. "Many people with MS would like to exercise and can exercise, but are worried due to fear of exhaustion," says Victoria M. Leavitt, PhD.



Victoria M. Leavitt, PhD. Photo courtesy of Victoria M. Leavitt, PhD

Leavitt and Deborah Backus, PhD, are both studying ways to help people with MS exercise. Leavitt is an assistant professor of neuropsychology (in neurology) and director of the Multiple Sclerosis Cognitive Neuroscience Laboratory at Columbia University in New York City. Backus, who is a physical therapist is director of MS Research at the Shepherd Center in Atlanta.

Taking aspirin to relieve exercise-related fatigue

After learning that higher body temperatures are linked to more fatigue in people with relapsing-remitting MS, Leavitt and colleagues studied whether taking aspirin, which cools the body, before exercising could help people exercise longer without being exhausted.

The first two studies showed that people with relapsing-remitting MS (94 people) had higher body temperatures than people with secondary-progressive MS (22 people) and people who don't have MS (84 people). The National Institutes of Health and the Kessler Foundation provided partial funding for one study.

Next, Leavitt and colleagues compared taking aspirin to taking a placebo before exercising on a stationary bike. Participants were able to exercise longer after taking aspirin. The eight participants who were sensitive to heat when they exercised reduced the increase in their body temperature after exercise by 56 percent when they took aspirin first. The National Multiple Sclerosis Society provided partial support for this study.

"Aspirin works on many levels," Leavitt says.

"It reduces temperature, relieves pain and relieves inflammation." Leavitt hopes to do larger studies to confirm these results. If these new studies confirm her results, she says aspirin "would be the first symptomatic treatment for MS that's available over the counter and is not prohibitively expensive." Anyone wishing to try this approach should ask their doctors about whether there are any medical concerns for them if they were to take two aspirin before a workout — the regimen Leavitt recommends to her patients. She recommends exercise for 30 minutes three times a week. Aerobic exercise is best, but stretching and yoga are helpful, too. "Start with one day a week, and do something you enjoy," she says.

Cycling for strength, endurance and less fatigue

Supported by a grant from the Society, Backus and colleagues studied whether functional electrical stimulation (FES) cycling relieved fatigue in people with moderate to severe MS who use wheelchairs. Done on a stationary bike, FES uses low-level electrical impulses to stimulate the leg muscles. "We think FES exercise may make it easier for people with MS to use the muscles for other tasks so they experience less physical fatigue," Backus says.



Brian Thompson, diagnosed with MS in 2012, exercises on a hand cycle at Venice Beach, California. He cycles in the early morning or late evenings because his fatigue is worsened by heat intolerance. Photo by Keith Carlsen

Fourteen participants completed the study, cycling for 30 minutes three times a week for one month. An exercise specialist documented each participant's fatigue, pain and spasticity, and monitored symptoms. Overall, 86 percent of the participants improved their performance on the FES cycle, either by cycling longer or with more resistance. The impact of FES cycling on fatigue wasn't as strong as the impact on performance, but the majority of participants said they felt less tired. Researchers concluded that FES cycling may be a safe and viable option for exercise for people with MS who use wheelchairs. The study was published in the International Journal of MS Care.

Backus is now doing more research on FES in people with MS who use wheelchairs and also in people who don't. Early results suggest that both groups can build stronger muscles and

increase their endurance using FES. "I hope we demonstrate that people have more capacity for change and improvement, even if they have severe MS, and that FES might be a good tool for them. Then we can develop programs so they can get access to FES cycles," says Backus. While people can buy FES cycles, they're very expensive and are usually only available at MS centers or rehabilitation institutes.

Looking for the cause of cognitive fatigue

Iron in the brain is important, but too much iron in a part of the brain called the basal ganglia may be linked to cognitive fatigue in people with MS. Cognitive fatigue affects your ability to learn and remember information, organize, plan and solve problems, focus and other aspects of thinking.



Bing Yao, PhD. Photo Courtesy of Bing Yao, PhD

Under a grant from the Society, Bing Yao, PhD, is studying the link between iron in the brain and cognitive fatigue. Yao is senior physicist and manager of the Rocco Ortenzio Neuroimaging Center at the Kessler Foundation and an assistant professor in the Department of Physical Medicine and Rehabilitation at Rutgers University, both in New Jersey.

The study will include about 120 people: 80 with relapsing-remitting MS and 40 people who don't have MS. At one study visit, participants will complete questionnaires about and take tests related to cognitive function. They'll also have an MRI scan while doing a cognitive test. The impact of iron will be measured using an advanced MRI technology called Susceptibility Contrast Imaging.

During the cognitive test, participants will look at images on a screen on the back of the scanner and respond to what they see by pushing buttons on a box they hold. The images are in different colors and shown at different speeds. An eye-tracking system is available for participants who can't move their fingers quickly.

Yao will measure the difference in iron and the severity of cognitive fatigue between the two groups. "The findings will greatly improve our knowledge of fatigue mechanisms in MS," says Yao. "This may lead to effective treatments such as medication that reduces the concentration of iron in certain regions of the brain."

As of April 2018, the study was still enrolling participants. For more information about the study, contact the Research Recruitment Specialist at <u>researchstudies@kesslerfoundation.org</u>.

More research on MS fatigue

Study: An interactive, self-directed MS fatigue management website is being tested to let people with MS monitor, communicate about and get help managing fatigue. **Researcher:** Marcia Finlayson, PhD, is studying how well the site works. Finlayson is vice dean (Health Sciences), professor and director at the School of Rehabilitation Therapy, Queen's University in Canada.

Study: Ruth Ann Marrie, MD, PhD, and colleagues studied how having MS along with other conditions affected fatigue in 949 people with MS. Participants completed a fatigue questionnaire and reported their other conditions. Participants who were older and had more disability were more likely to report fatigue. Depression, irritable bowel syndrome, migraines and anxiety were associated with persistent fatigue over two years.

Researcher: Dr. Marrie is a professor of internal medicine (neurology) and community health sciences, and director of the Multiple Sclerosis Clinic at the University of Manitoba. Dr. Marrie published results in the International Journal of MS Care.

Study: Dawn M. Ehde, PhD, and colleagues compared self-management to symptom education in 163 people with MS. Both groups had eight weekly 45- to 60-minute telephone sessions led by a therapist plus two 15-minute follow-up calls. The self-management group learned proven cognitive-behavioral strategies for managing symptoms, while the symptom education group only received information. Both groups had meaningful improvements in fatigue, pain and mood. Half of the participants who reported severe fatigue at the start of the study had a major, lasting reduction in fatigue.

Researcher: Ehde is a clinical psychologist at the University of Washington School of Medicine Department of Rehabilitation Medicine. The study was published in Archives of Physical Medicine and Rehabilitation, 2015.

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