Pinpointing pain

New research into MS-specific pain management points to a brighter future.

by Donna Shryer

Pain, whether chronic or acute, can affect every aspect of life, including mood, thoughts and behavior—a reality that affects nearly two-thirds of people diagnosed with multiple sclerosis. While no medications have been approved specifically for pain that occurs as a result of MS lesions, a variety of medications and other strategies are used to manage the kinds of pain that MS can cause.

The good news is that a number of new studies focus on why and how pain occurs as a part of MS, and they may provide insight into how to treat it.

The pain process

MS-related pain can be associated with faulty nerve signals in the brain and spinal cord. To better understand MS pain, Heather Wishart, PhD, associate professor of psychiatry and neurology in the Neuropsychology Program and Brain Imaging Lab at Geisel School of Medicine at Dartmouth Medical School, is investigating why and how these faulty signals affect the way people with MS process pain.

The National MS Society-funded study uses functional magnetic resonance imaging (fMRI)—an MRI that shows areas of specific activity in the brain—to monitor 40 people with relapsing-remitting or secondary-progressive MS, and a control group of 20 people without MS. “If we can identify changes in the brain that contribute to MS pain, then we may be closer to targeted treatments,” Dr. Wishart explains. Currently, the team is focused on how

people with MS reduce their response to pain over time.

This study sprang from previous research investigating changes in the thalamus and other subcortical structures (the region of the brain below the outer layer of the brain called the cortex) in people with MS, and also from studies that looked at pain processing in the brain. These studies comprehensively show promise of improving our scientific understanding of the basis of pain in MS, and guiding development of future pain management strategies for people with MS.

Understanding the emotions behind pain

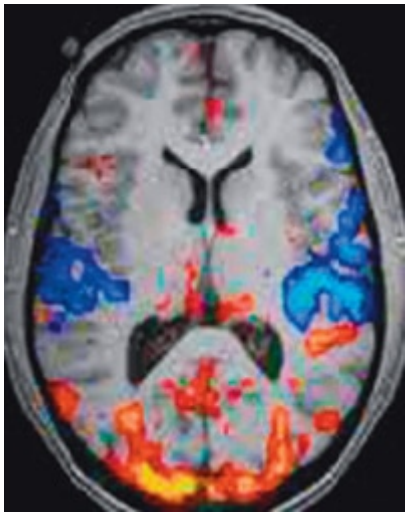
Pain in MS is complex, and emotions such as fear and worry seem to heighten it. That begs the question: Can thoughts and feelings affect how people experience pain? And if yes, which methods are the most effective in modifying people's response to pain? Several Society-funded studies at the University of Washington (UW) have set out to answer these questions.

In a small 2012 study, 15 people with MS were divided into four groups. Each group was introduced to a different pain treatment method:

- self-hypnosis (for deep relaxation);
- cognitive-behavioral therapy (reframing thoughts, reactions and feelings associated with pain);
- education about pain; and
- self-hypnosis combined with cognitive-behavioral therapy.

All four treatments had some effect on pain perception, although only self-hypnosis and combined self-hypnosis/cognitive therapy showed statistically significant decreases in pain severity from pre- to post-treatment. The combined treatment was statistically superior to all other treatments in reducing pain severity, negative side effects of pain, and unhelpful, stressful thoughts about pain. These results triggered a larger clinical trial funded by the National Institutes of Health, which is currently recruiting participants. The new study hopes to ascertain how and why these treatments are effective.

Another UW study is testing cognitive therapy versus mindfulness therapy (which teaches people to focus on the present) in 30 people with MS. "The next phase is to tease apart why certain people respond to cognitive versus mindfulness therapy," explains Dawn M. Ehde, PhD, professor at UW Medicine and the study's principal investigator. "Then, we'll be able to build treatments better suited to different individuals."



“If we can identify changes in the brain that contribute to pain, then we may be closer to targeted treatments,” says Dr. Heather Wishart.

This team also is testing whether self-hypnosis can help people achieve a deeper level of relaxation to control chronic pain. This study, involving 20 people with MS, is investigating whether using neurofeedback can heighten the pain-reducing benefits of self-hypnosis. Neurofeedback involves placing electrodes on a person’s scalp to view the brain’s electrical activity. The person then learns how to self-regulate undesirable brainwaves associated with pain. “My hope is that neurofeedback will enhance the efficacy of self-hypnosis and allow people to more easily respond to self-hypnotic suggestions,” says Mark P. Jensen, PhD, professor and vice chair for research at the UW Department of Rehabilitation Medicine and the study’s principal investigator.

Evolving therapies to manage MS pain

Investigators are hoping to harness interleukin-10 (IL-10), a natural anti-inflammatory protein, in combating MS-related pain. Ordinarily, certain cells in the spine (called glial cells) regulate the transmission of pain signals, but in MS, these cells can become agitated and cause chronic pain in the spinal cord. Researchers hope that when the non-viral gene therapy that encodes IL-10 is delivered to the spinal fluid, cells in the area will produce the body’s own IL-10 and dampen pain signals.

Linda Watkins, PhD, chief scientific officer for Xalud Therapeutics and neuroscience professor at the University of Colorado, induced experimental autoimmune encephalomyelitis (EAE), an animal disease that mimics MS, in rats. “A non-viral gene therapy that produced IL-10 completely prevented central neuropathic pain, but what shocked everyone was that it reversed paralysis,” Dr. Watkins reports. “The rats had absolutely no motor impairments at

the end of study and they didn’t relapse.”

But EAE progresses quickly in rats, leaving no time for long-term evaluations. Now, with Society funding, the project has expanded to mice, in which EAE progresses slowly. “We want to know if IL-10 injections only work after the first sign of pain, or if we can get results if the drug is administered much later,” Dr. Watkins says.

A compound known as C-21191 shows promise in a study funded by the Society, in collaboration with Concert Pharmaceuticals Inc. The hope is that C-21191 will reduce muscle spasms, stiffness (spasticity) and pain but without the sedation and coordination problems typically associated with current treatments, which often involve benzodiazepines, such as Ativan® (lorazepam) or Xanax® (alprazolam). The company is currently completing preclinical toxicology and pharmacology studies.

The future of pain treatment

Worldwide, 2.3 million people are living with MS and many must deal with pain. New discoveries and evolving studies are moving us closer to improved MS pain management—and a better quality of life.

Donna Shryer is a Chicago-based freelance writer.

Download “Pain: The Basic Facts” to learn about what you can do to manage the several sources of pain in MS.