Medical Xpress

Solving the mysteries of fibromyalgia could help patients break free

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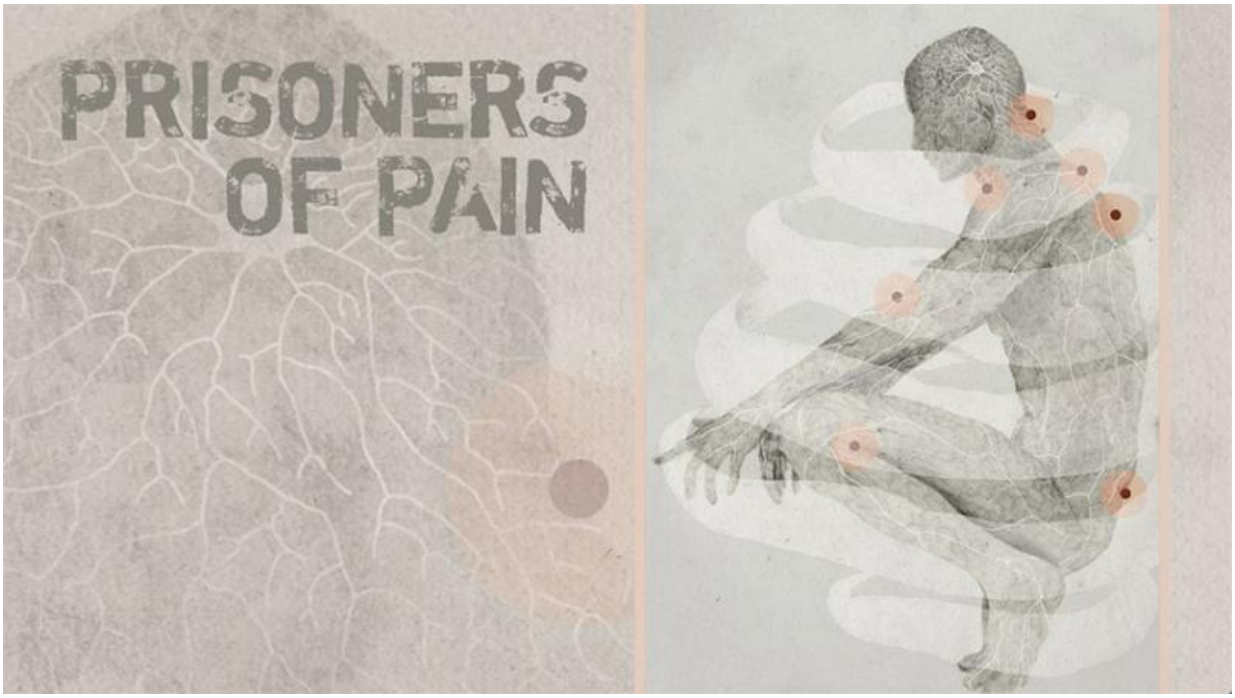

For 10 years, Gail De Sciose felt that pain controlled her activities, her schedule, her every move. She often found herself sprawled on the floor of her Birmingham home, sharp pains radiating down her neck, back, and hips. It was an abrupt change from the vibrant life she once led in New York City, where she had worked as a sales manager, traveled around the country, and volunteered at a local animal shelter.

"It felt like a hot poker being dragged across my body," De Sciose recalls. And the pain was accompanied by debilitating fatigue; De Sciose remembers falling asleep in the middle of conversations. "There were times I just couldn't function," she says. "I had to cancel theater tickets, vacations, and lunches with friends."

De Sciose is one of five million Americans and more than 200,000 Alabamians with fibromyalgia, a disorder characterized by widespread pain that has lasted at least three months and can't be attributed to any definitive cause. But a fibromyalgia diagnosis doesn't lead to a cure. For years after she had a name for her hot poker stabs, De Sciose remained in pain, and that's not unusual: The Centers for Disease Control and Prevention highlights studies showing that fibromyalgia patients rate their quality of life lower than patients with other chronic diseases, and are three-and-a-half times more likely to develop depression than those without the disorder.

Those responses could be on the verge of changing, however. At UAB, Jarred Younger, Ph.D., hopes to establish Alabama's first research and clinical care center specializing in fibromyalgia and related conditions, including chronic fatigue syndrome and Gulf War Illness. Already, research by Younger and his team in UAB's new Neuroinflammation, Pain, and Fatigue Lab has revealed possible underlying causes for the disorders and pointed to treatments that are helping to ease pain and fatigue—without side effects—in patients.

Younger's work "is really cutting-edge; it's groundbreaking," says David McLain, M.D., a Birmingham rheumatologist who treats the disease and often collaborates with UAB researchers. "He's responsible for opening up a whole new avenue of treatments, and it's fortunate he came to UAB."

A brainy solution

Younger, an associate professor recruited to the UAB College of Arts and Sciences Department of Psychology in 2014, became interested in fibromyalgia and chronic fatigue syndrome as a postdoctoral fellow at Stanford University's medical school. He had been studying pain more broadly when he realized how poorly understood these disorders were.

"Patients are wholly affected," Younger says. "Some used to be athletes, some used to be business owners, and then their lives are taken over." Often, he points out, patients visit doctor after doctor, only to be told repeatedly that they're healthy—and that the pain or fatigue is all in their heads.

Younger, along with many other researchers and clinicians, believed otherwise. "I made it my mission to figure out what is wrong with these patients and how to treat them," he says.

As a Stanford postdoctoral fellow and faculty member, Younger spearheaded studies that surveyed immune molecules in the blood. He homed in on one particular protein called leptin, released by fat tissue, which appears in greater amounts in the blood of chronic fatigue patients. In fact, Younger could even gauge the day-to-day severity of a patient's symptoms just by tracking his or her leptin levels. These initial findings spurred him to continue investigating inflammatory immune molecules—and to start looking at the brain's role in the diseases.

Leptin has the ability to cross the blood-brain barrier and affect neural cells, causing pain and fatigue. But exactly how that happens remains a mystery. Younger thinks it has something to do with microglia, a type of immune cell found in the brain that normally helps to protect neurons.

(Left to right) Graduate student Kelsey Campbell, postdoctoral student Joanne Lin, Ph.D., and Younger prepare a neuroimaging scan as part of research to develop a noninvasive tool for measuring brain temperature, which could diagnose neuroinflammation.

"Microglia defend our brain against everything," Younger explains. "When we get the flu, for instance, microglia are activated. These cells make us want to crawl into bed and do nothing—so our body can devote its resources to fighting off the flu."

In both fibromyalgia and chronic fatigue patients, Younger hypothesizes, the microglia are turned on when they're not supposed to be, causing fatigue or pain, a depressed mood, and cognitive dysfunction. At UAB, he is planning follow-up studies to help find evidence supporting this idea. He faces a crucial challenge, however: Currently, no methods are available to look directly at the activation or inflammation of microglia

in living humans. But Younger and his colleagues are working on solutions, including specialized brain scans that measure the temperature of the brain or the presence of certain chemicals.

"It's only very recently that people are starting to explore what sensitizes microglia," Younger says. "The cells can be in a quiet, helpful state, or an active, warlike state." His findings, he hopes, will help reveal the difference.

Small gains, big impact

At the same time that Younger began studying the pathways underlying inflammation, he also started investigating alternative medicine and off-label treatments that had been used by patients with chronic fatigue and fibromyalgia. In 2009, he first reported the effectiveness of low-dose naltrexone—a drug normally used to treat opioid and alcohol addiction. Women who took 4.5 milligrams per day of the drug reported less pain throughout the weeks that they received it.

Interestingly, the naltrexone linked back to Younger's other studies: The drug is known to stop activated microglia from producing inflammatory chemicals.

De Sciose—who had resisted taking fibromyalgia drugs throughout the course of her disease because of the side effects that most can cause—heard about low-dose naltrexone from a friend in 2012, shortly after Younger published the results of his second, larger study on the drug. The science behind it seemed sound, she says, and Younger's studies had revealed few side effects. So she started taking a daily dose of naltrexone prescribed by her doctor.

"I didn't have any expectations; we hear so much about miracle drugs," De Sciose says. "But within the first two or three weeks, I stopped

having that daily searing hot-poker pain. Then, a month later, different massage therapists told me that my muscles were feeling better."

Today, De Sciose wouldn't say she's cured of fibromyalgia—she still has to watch her activity levels to prevent flare-ups. But she can make plans again—lunch dates, theater tickets, and trips—without worrying that she'll end up sprawled on the floor every night. "Any small gain in pain reduction or quality of life is very important to me," she says.

Chain of Events

Younger's discoveries about leptin, microglia, and naltrexone have already begun to change the face of fibromyalgia and chronic fatigue research and treatment. But his work is just beginning, he says. "It's essential that we have a fuller understanding of what's wrong before we're able to find the best treatments," Younger says.

So while he's conducting further studies on low-dose naltrexone—as well as other compounds, including the spice curcumin, that are known to affect microglia—he's guiding the efforts of the Neuroinflammation, Pain, and Fatigue Lab toward uncovering the mechanisms behind the diseases. He would like to understand what triggers an increase in leptin production, what leptin activates, and what fires up microglia. He also wants to know how everything connects. "There's a chain of events, and we don't know where leptin falls in that chain," he says. "So we begin with one piece of the puzzle and start looking in both directions."

For patients, having any piece of the puzzle can be heartening. "These patients are not well understood," says McLain. "Their families and often their doctors think they're lazy or making up their symptoms. Being able to say, 'here's some of the science behind my illness' certainly makes them more hopeful."

Younger, too, is satisfied with the small bits of progress so far, but says that the treatment of chronic fatigue syndrome and fibromyalgia is a decade or two behind other inflammatory diseases. "Twenty years ago, rheumatoid arthritis absolutely wrecked people's bodies, and there wasn't a lot that could be done about it," he says. "Over time, researchers discovered the parts of the immune system that were involved, and that helped them develop better treatments."

If Younger's timeline holds true, then relief could be on the horizon for patients who must endure the pain, fatigue, and other symptoms every day. "I feel optimistic that I may wake up some day in the future and be able to feel even better and stronger than I do now as the result of a research finding and treatment to come," De Sciose says.

Quick facts about fibromyalgia and related diseases

- Affect mainly women, though they can impact men and children.
- Symptoms may include pain; fatigue; cognitive/memory problems; sleep disturbances; numbness and tingling; and sensitivity to temperature, noises, and light; among others.
- There is no simple, specific test to diagnose these disorders. Physicians often talk with patients about pain and fatigue severity and the presence of other symptoms.
- Patients with chronic fatigue syndrome suffer daily, long-term, severe fatigue.
- Gulf War Illness includes chronic, medically unexplained symptoms affecting veterans and civilians involved with military duty in the Persian Gulf region.

Provided by University of Alabama at Birmingham