What's the Big Deal with Small Fibers?

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t the end of a winding road of neurons stretching from the cerebral cortex to the spinal cord to the dorsal root axon, extends the smallest and among, evolutionarily, the oldest nerve fibers in the human body. These tiny, ancient axons reach into the crevices of our organs, through the marrow of our bones, and near our skin's surface. At no thicker than five micrometers, they don't get too much attention in the world of neurology. Yet new research is uncovering just what the big deal is with these small fibers.

Tens of millions of Americans have been diagnosed with fibromyalgia, chronic fatigue, or chronic pain. On average, receiving these diagnoses takes four years, but for patients with this "mystery pain," a diagnosis is far from an answer. The cause of these syndromes has baffled doctors for decades, and, without a known cause, there is no known route for treatment. Recently, however, some researchers have looked in a small place to find big answers.

Small nerve fibers include C-fibers and A-delta fibers. Most

nerve fibers are coated with myelin sheath, a fatty insulating layer that helps neurons conduct signals. A-delta fibers and C-fibers, however, have little to no myelin and are involved in many biological activities since they extend to diverse regions of the body. One of their primary roles is in the perception of pain. The A-delta fibers are lightly myelinated, allowing

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for the transmission of faster signals to the spinal cord, and subsequently to the brain. These fibers account for the sensation of acute, sharp pain. C-fibers, on the other hand, are slower in their signaling due to their lack of myelination. C-fibers transmit a sensation of dull, diffuse pain. They

also play a role in temperature

sensation, touch, and vibration. Not only do small nerve fibers send signals to the brain, but some (C-fibers, specifically) also receive messages from the brain. They help regulate the autonomic functions of the body, including digestion, sweating, heart rate, and bladder control. When the end of small nerve fibers degrades and there is a reduction in the number of fibers, it is known as small fiber polyneuropathy. The prefix poly is used because of the multitude of body regions and systems these small fibers reach. Given the extensive range of functions small nerve fibers take on, it becomes clear that their dysfunction could manifest in a variety of ways, making these neuropathies challenging to diagnose. The symptoms of small fiber polyneuropathy are broad and vary from patient to patient. Common symptoms include fatigue, generalized body pain, poor circulation, faintness, exercise intolerance, headaches, gastrointestinal abnormalities, and even issues involving irregular heart rate, sweating patterns, and brain

Small nerve fibers help regulate the fog. Anne Louise Oaklander, autonomic functions of the body, MD, Ph.D., and director of Massachusettes General including digestion, sweating, heart Hospital's Nerve Unit noted rate, and bladder control. that many of the patients she had diagnosed with this small fiber polyneuropathy were tests. At that point, a path to treatment is revealed. also previously diagnosed In the last few years, progress has been rapid in this field, but with fibromyalgia, which shares many symptoms. Oaklander's lab did there is still more work to be done. Doctors must know to examine the a prospective study that found that 41% of patients previously labeled individual patient's underlying cause whether it be diabetes, infections like with fibromyalgia have evidence of small-fiber polyneuropathy as the Lyme disease, or autoimmune disorders, and outline an individualized underlying cause of their symptoms. Many other studies have gone on approach to treatment. The current atmosphere in medicine does not to publish similar results. She notes that while 41% is surely not an allow for this type of attention given to an individual patient. The core of absolute, providing a subset of the fibromyalgia population with a reason progress in this field lies in spreading this information to both patients, for their symptoms may help narrow down the other possible causes of doctors and empowering patients to understand their illness, and seeking fibromyalgia. the answers, treatment, and medical attention they deserve. There are a number of causes for small-fiber polyneuropathy including autoimmunity, diabetes, and chemotherapy. Unlike fibromvalgia, the causes are known and treatable. One of these causes is new to the field, and effecting a subset of the population never before

associated with neuropathies: autoimmune-associated small-fiber neuropathy in children.

Small nerve fibers are key players in immune signaling and

activation when damage (pain) is detected. Since communication with the immune system is so vital, they must be able to come in contact with the immune system. This contact is quite uncommon for a neuron. Most neurons are protected from immune "attack" via the bloodnerve barrier in the periphery (or blood-brain barrier in the brain). While the interaction of small nerve fibers and immune cells is crucial, it leaves a striking vulnerability for autoimmune attack. It is precisely the autoimmune attack on these fibers that results in what is known as autoimmune-associated small-fiber polyneuropathy.

Receiving the diagnosis of small-fiber polyneuropathy reveals a glorious path for treatment. Thanks to the work of Dr. Oaklander's lab and clinic, information about causes and subsequent treatments for the condition is now available to patients and doctors on her website, neuropathycommons.com. Once the root cause is determined, treatment is almost always an option.

Diagnosis of fibromyalgia, chronic pain, and chronic fatigue typically carry a great deal of stigma and frustration for patients. Individuals with these conditions are plagued by pain on an ongoing basis, with no real understanding of why or how they are feeling this way. Many doctors often tell patients that their condition is a result of a depressed or anxious mental state, failing to recognize that the mental state is more often than not a result of long-term debilitating pain than a cause of it. This inaccurate perception has been amplified by the disproportionate effects of fibromyalgia on women and historically disproportionate presence of male doctors. Due to this prevailing stigma, Dr. Oaklander acknowledges the importance of outlining objective diagnostic criteria.

In most cases, objective diagnosis is made with a small skin biopsy, usually taken from the leg under local anesthetic. Labs count the number of small C and A-delta nerve fibers. Doctors can determine whether or not the patient has neuropathy (a reduced number of neurons) by comparing the patient's numbers to healthy controls. In this way, patients are given objective validation of their pain. The diagnosis is also made with autonomic nervous function testing, nerve conduction testing, standard neurological examination, and clinical history. After diagnosis, it's time to identify the cause, which is usually done with various blood