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Fibromyalgia Linked to Extensive Brain Inflammation

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STORY AT-A-GLANCE

- Brain scans of fibromyalgia patients have offered hard evidence that the pain they experience is real; their threshold for tolerating pain impulses is substantially lower than that of most individuals
- Recent research shows fibromyalgia patients tend to have severe inflammation in their body, including their nervous system and brain
- The cannabinoid receptor that produces the "high" in response to THC in marijuana also helps regulate inflammatory reactions in your brain
- The signal that instructs glial cells to stop their inflammatory activity is endocannabinoids, which work by binding to cannabinoid receptors on certain neurons
- With age, your natural production of endocannabinoids decreases, which then leads to impaired immune response regulation and chronic inflammation

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Fibromyalgia, characterized by chronic, widespread pain is an often-debilitating condition that primarily affects women. While as many as 10 million Americans have fibromyalgia, its cause remains a mystery.

Brain scans of fibromyalgia patients have offered hard evidence that the pain they experience is indeed real — mainly because their threshold for tolerating pain impulses

is substantially lower than that of most individuals. But the mechanism causing this lowered pain threshold is still unknown.

Some experts, such as Dr. Frederick Wolfe, the director of the National Databank for Rheumatic Diseases and the lead author of the 1990 paper that first defined fibromyalgia's diagnostic guidelines, believe fibromyalgia is mainly a physical response to mental and emotional stress.

But while stress and emotions may indeed play an important role, more recent research shows fibromyalgia patients tend to have severe inflammation in their body, including their nervous system and brain.

Signs and Symptoms of Fibromyalgia

Diagnosis can be a challenge, but the updated case definitions of fibromyalgia, issued in 2010 and later simplified in 2012, claim to correctly diagnose about 83% of cases.[1] Originally, the condition was thought to be a peripheral musculoskeletal disease. Today, fibromyalgia has become increasingly recognized as a neurobiological problem causing central pain sensitization.

Unfortunately, there are currently no laboratory tests available for diagnosing fibromyalgia, so physicians primarily depend on patient histories, reported symptoms and physical exam findings. Classic symptoms of this condition include:

- **Pain —** The key marker of fibromyalgia is pain, which is profound, widespread and chronic. Pain inside of your elbows and knees, collarbones and hips is indicative of fibromyalgia when it's present on both sides.

  People also frequently report pain all over their bodies — including in their muscles, ligaments and tendons — and the pain tends to vary in intensity. It has been described as deep muscular aching, stabbing, shooting, throbbing and twitching.

  Neurological complaints add to the discomfort, such as numbness, tingling and burning. The severity of the pain and stiffness is often worse in the morning.

Aggravating factors include cold/humid weather, nonrestorative sleep, fatigue, excessive physical activity, physical inactivity, anxiety and stress.

- **Cognitive impairment —** So-called "fibro-fog" or foggy-headedness is a common complaint.
- **Fatigue —** The fatigue of fibromyalgia is different from the fatigue that many people complain of in today's busy world. It is more than being tired; it's an all-encompassing exhaustion that interferes with even the simplest daily activities, often leaving the patient with a limited ability to function both mentally and physically for an extended period of time.
- **Sleep disruption —** Another major part of the diagnostic criteria for this condition is some type of significant sleep disturbance. In fact, part of an effective treatment program is to make sure you're sleeping better.

  Medical researchers have documented specific and distinctive abnormalities in the Stage 4 deep sleep of fibromyalgia patients. During sleep, they are constantly interrupted by bursts of awake-like brain activity, limiting the amount of time they spend in deep sleep.
- **Other symptoms —** Other common symptoms include irritable bowel and bladder, headaches and migraines, restless leg syndrome and periodic limb movements, impaired memory and concentration, skin sensitivities and rashes, dry eyes and mouth, anxiety, depression, ringing in the ears, dizziness, Raynaud's Syndrome and impaired coordination.

Conventional treatment typically involves some form of pain medication, and perhaps psychotropic drugs like antidepressants. I don't recommend either as they fail to address the cause of your problem. Many fibromyalgia sufferers also do not respond to conventional painkillers, which can set in motion a vicious circle of overmedicating on these dangerous drugs.

Brain Inflammation — Another Hallmark of Fibromyalgia

Using PET imaging, an investigation[2] by researchers at Massachusetts General Hospital and Karolinska Institutet in Sweden revealed the presence of widespread brain inflammation in patients diagnosed with fibromyalgia.[3,4]

Earlier research[5] conducted at Karolinska Institutet also discovered high concentrations of cytokines (inflammatory proteins) in the cerebrospinal fluid, suggesting fibromyalgia patients have inflammation in their nervous system as well.[6]

The team at Massachusetts General Hospital, meanwhile, has previously shown that neural inflammation, and glial cell (immune cells) activation specifically, plays a role in chronic back pain. Animal studies have also offered evidence for the hypothesis that glial cell activation can be a cause of chronic pain in general.[7]

Here, they found that when glial cells in the cerebral cortex were activated, the more aggressive the activation, the greater the fatigue experienced by the patient. As reported by Medical Life Sciences:[8]

> *"The current study first assessed fibromyalgia symptoms in patients using a questionnaire. A PET tracer was then used, that is, a radioactive marker which binds a specific protein called translocator protein (TSPO) that is expressed at levels much above the normal in activated glial cells, namely, astrocytes and microglia …*
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> *[G]lial activation was found to be present at significantly higher levels in multiple brain areas in patients who had fibromyalgia than in controls. Glial cell activation causes inflammatory chemicals to be released, which cause the pain pathways to be more sensitive to pain, and promote fatigue …*
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> *One area showing higher TSPO binding in direct proportion to the self-reported level of fatigue was the cingulate gyrus, an area of the brain linked to emotional processing. Previous research has reported that this area is inflamed in chronic fatigue syndrome."*

Brain Inflammation Linked to Loss of Brain Cells

In related news, German researchers investigating inflammation mechanisms in the brain have found that as mice get older and regulation of inflammatory responses become increasingly impaired, they start losing brain cells.[9]

Interestingly, the cannabinoid receptor type 1 (CB1), which produces the "high" in response to tetrahydrocannabinol (THC) in marijuana, also helps regulate inflammatory reactions in your brain. In short, chronic brain inflammation is in part driven by the CB1 receptors' failure to respond. To understand how this works, you need to know a little bit about how microglial cells work.

Microglial cells are specialized immune cells found in your central nervous system, including your spinal cord and brain. These immune cells respond to bacteria and are responsible for clearing out malfunctioning nerve cells. They also signal and recruit other immune cells when needed and trigger the inflammatory response when necessary.

Problems arise when the inflammatory response becomes dysregulated and overactive. In the brain, the inflammation can easily damage healthy brain tissue. The "brake signal" that instructs glial cells to stop their inflammatory activity is endocannabinoids, and the endocannabinoids work by binding to certain receptors, including CB1 and cannabinoid receptor type 2 (CB2).

Immune Cells Communicate, Influence Inflammatory Response

Curiously, microglial cells have virtually no CB1 and very few CB2 receptors, yet they still react to endocannabinoids. The present study was designed to investigate this puzzling riddle. As it turns out, there's a type of neuron that does contain a large number of CB1 receptors, and it appears that it is the CB1 receptors on these specific neurons that control microglial cell activity.

In other words, it appears microglial cells do not communicate with nerve cells directly; rather, they release endocannabinoids, which then bind to CB1 receptors found in nearby

neurons. These neurons in turn communicate directly with other nerve cells. So, the brain's immune response is regulated in an indirect manner rather than a direct one.

Now, what happens with age is that your natural production of endocannabinoids decreases, which then leads to impaired immune response regulation and chronic inflammation. As noted by coauthor Dr. Andras Bilkei-Gorzo:[10]

> *"Since the neuronal CB1 receptors are no longer sufficiently activated, the glial cells are almost constantly in inflammatory mode. More regulatory neurons die as a result, so the immune response is less regulated and may become free-running."*

Earlier research[11] by this same team found that THC can help restore cognitive function in older brains, and the current study also hints at THC-containing cannabis may have valuable neuroprotective benefits in older people by quelling brain inflammation and preventing loss of brain cells. As the study was done on mice, further research is needed to confirm that the same mechanisms apply to humans, but it's compelling nonetheless.

Are You Living an Inflammatory Lifestyle?

Your diet can either promote or decrease inflammation. For example, foods that increase the inflammatory response in your body include:

- Sugar, especially processed corn syrup
- Synthetically produced trans fats
- Processed vegetable and seed oils, high in oxidized omega-6 fat
- Processed meats
- Refined carbohydrates

Meanwhile, marine-based omega-3 fats have powerful anti-inflammatory effects, and are crucial for healthy brain function in general. Antioxidant-rich fruits and vegetables

are also important for controlling inflammation, as is optimizing your vitamin D to a level of 60 to 80 ng/mL, ideally through sensible sun exposure.

In addition to anti-inflammatory and immune-boosting properties, vitamin D receptors appear in a wide variety of brain tissue, and researchers believe optimal vitamin D levels may enhance important chemicals in your brain and protect brain cells by increasing the effectiveness of glial cells that help nurse damaged neurons back to health.

A number of ubiquitous chemicals have also been implicated in inflammation, so if you struggle with fibromyalgia you'd be wise to take a close look at your choice of foods, household and personal care products. As mentioned earlier, getting enough high-quality sleep is another key treatment component for fibromyalgia.

Ketogenic Diet Massively Decreases Brain Inflammation

Research[12] published last year suggests ketogenic diets — which are high in healthy fats and low in net carbs — are a particularly powerful ally for suppressing brain inflammation, as ketones are powerful HDAC (histone deacetylase inhibitors) that suppress the primary NF-κB inflammatory pathway.

As explained by Medical Xpress,[13] the defining moment of the study[14] came when the team "identified a pivotal protein that links the diet to inflammatory genes, which, if blocked, could mirror the anti-inflammatory effects of ketogenic diets."

A ketogenic diet changes the way your body uses energy, converting your body from burning carbohydrates for energy to burning fat as your primary source of fuel. When your body is able to burn fat, your liver creates ketones, which burn more efficiently than carbs, thus creating far less reactive oxygen species and secondary free radicals that can damage your cellular and mitochondrial cell membranes, proteins and DNA.

Animals (rats) used in this study were found to have reduced inflammation when the researchers used a molecule called 2-deoxyglucose (2DG) to block glucose metabolism and induce a ketogenic state, similar to what would occur if you followed a ketogenic

diet. By doing this, inflammation was brought down to levels near those found in controls.

Suppressing Inflammation Improves Pain

Senior study author Dr. Raymond Swanson, a professor of neurology at UCSF and chief of the neurology service at the San Francisco Veterans Affairs Medical Center, commented on the results, saying:

> *"I was most surprised by the magnitude of this effect, because I thought ketogenic diets might help just a little bit. But when we got these big effects with 2DG, I thought wow, there's really something here.*
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> *The team further found that reduced glucose metabolism lowered a key barometer of energy metabolism — the NADH/NAD+ ratio — which in turn activated a protein called CtBP that acts to suppress activity of inflammatory genes."*

The study also pointed out that a ketogenic diet may relieve pain via several mechanisms, similar to the ways it's known to help epilepsy.

> *"Like seizures, chronic pain is thought to involve increased excitability of neurons; for pain, this can involve peripheral and/or central neurons. Thus, there is some similarity of the underlying biology,"* the authors stated, adding:
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> "*A major research focus should be on how metabolic interventions such as a ketogenic diet can ameliorate common, comorbid and difficult-to-treat conditions such as pain and inflammation."*[15]

Cyclical Ketosis for Optimal Health

Eating a ketogenic diet doesn't have to be complicated or painful. My book "Fat for Fuel" presents a complete Mitochondrial Metabolic Therapy (MMT) program, complemented

by an online course created in collaboration with nutritionist Miriam Kalamian, who specializes in nutritional ketosis.

The course, which consists of seven comprehensive lessons, teaches you the keys to fighting chronic disease and optimizing your health and longevity. In summary, the MMT diet is a cyclical **ketogenic diet**, high in healthy fats and fiber, low in net carbs with a moderate amount of protein.

The cyclical component is important, as long-term continuous ketosis has drawbacks that may actually undermine your health and longevity. One of the primary reasons to cycle in and out of ketosis is because the "metabolic magic" in the mitochondria actually occurs during the refeeding phase, not during the starvation phase.

Ideally, once you have established ketosis you cycle healthy carbs back in to about 100 to 150 grams on days when you do strength training. MMT has a number of really important health benefits, and may just be the U-turn you've been searching for if you're struggling with a chronic health condition. You can learn more by following the hyperlinks provided in the text above.

Address Emotional Contributors

Since fibromyalgia is a chronic condition, it becomes emotionally challenging in addition to the physical challenges it imposes on your life. Having a game plan to deal with your emotional well-being is especially important if you suffer from any chronic disease.

If you have fibromyalgia, you might be able to trace it back to a triggering event, or you might not. Any traumatic experience has the potential to linger in your mind for a lifetime. You can have the perfect diet, the perfect exercise routine, and an ideal life; but if you have lingering unresolved emotional issues, you can still become very sick.

A tool that can help release this emotional sludge is the Emotional Freedom Techniques (EFT). If you are a regular reader of my newsletter, this won't be an unfamiliar term to you. EFT is a form of bioenergetic normalization. If you have fibromyalgia, this is

something that is going to be extremely helpful. You can do this yourself, at home, and it takes just a few minutes to learn. For a demonstration, see the video above.

Sources and References

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