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Mini Review

Fibromyalgia and the Brain Microbiome

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What is a microbiome?

Our stomach microbiome is a collection of all the bacteria that exist in our digestive system and help us digest food. Only in our intestines there are about 100 trillion bacteria (bacteria, viruses, fungi and more), similar to the number of cells we have in our entire body!

Your microbiota is unique to you and affects how your body reacts to different foods.

Fibromyalgia is a chronic disease that causes widespread pain, with patients often experiencing extreme fatigue, sleep disturbances, depression and headaches. Fibromyalgia patients have brain inflammation. Using PET brain imaging, researchers from Karolinska Hospital (Sweden) and Massachusetts (USA) have now shown that glial cells - cells of the immune system of the central nervous system - are activated in the brains of fibromyalgia patients.

Recent studies indicate that the brain microbiome populations [1] (Gut, Blood, Brain, Eye for example) may cause this neurodegenerative disorder as it is as in the illnesses - AD, PD, DM2 and many more, that currently lack remedy. This awakes the hope for the cure of these diseases.

Is insulin resistance the cause of fibromyalgia?

Despite the hard effort [2], the nature of FM is unknown, so there is no known disease treatment for this condition. We know that the majority (if not all) patients with FM belong to a distinct population that can be separated from controls by their levels of glycated hemoglobin A1c (HbA1c), a host marker of insulin resistance (IR). This was proven by analyzing the data after introducing age-corrected stratification into a constant regression model. This treatment strategy showed very significant differences.

Brain inflammation reported (For first time) in Fibromyalgia, The story at a glance

Brain scans of fibromyalgia [3] patients offered substantial evidence that the pain they were experiencing was real; Their tolerance threshold for pain impulses is significantly lower than that of most people. Recent studies have shown that fibromyalgia patients tend to suffer from severe inflammation in their body, this includes their nervous system and particularly their brains. The cannabinoid receptor that produces the "high" in response to THC in marijuana. Also helps regulate inflammatory responses in the brain. The signal reserved for glial cells to stop their inflammatory activity is endocannabinoids, which work by binding to cannabinoid receptors on individual neurons. With age, the natural production of endocannabinoids decreases, which then leads to a lack of immune response and chronic inflammation.

The diagnosis of FM is based on the identification of a characteristic cluster of symptoms, while excluding other potential sources of pain [4]. The diagnostic criteria for FM rely on selfreported symptoms [5]. The lack of criteria for objective diagnosis is a source of frus-

tration among patients and doctors and adds to the possible reasons for wrong diagnoses. In two retrospective cohorts of patients were diagnosed with FM. The rate of false positive diagnoses. The patients with chronic fatigue syndrome, which shares some characteristic features with FM, have been shown to have altered gut microbiome and metabolic profiles [6]. In conclusion, changes in the microbiome have been reported in a number of rheumatological diseases, including rheumatoid arthritis and spondyloarthropathy. Indirect evidence suggests that the gut microbiome may be altered in FM patients: a change in small intestinal permeability has been reported in a cohort of FM and complex regional pain syndrome (CRPS) patients; In a small cross-sectional study of FM patients, a clear metabolic signature of urine was demonstrated, which can be attributed to the gut microbiome modifications [7-9].

Introduction

We want to think of fibromyalgia (FM) as a disease of the central nervous system, but the focus tends to eliminate the accumulating evidence of problems in the body.

We don't think of fibromyalgia as an inflammatory disorder. It is true that overt signs of inflammation are quite rarely found in patients with FM, but research suggests that inflammatory factors may play a role.

Then there are the mitochondria. Mitochondrial dysfunction is a real possibility for chronic fatigue syndrome, but I have rarely associated it with FM or pain. However, it turns out that many studies, indicate that mitochondrial dysfunction can indeed play a significant role in fibromyalgia.

Researchers, studied at the Massachusetts General Hospital (MGH) in collaboration with the Karolinska Institute team in Sweden - have for the first time documented the widespread inflammation in the brains of patients with the poorly understood situation called 'fibromyalgia'. The report was published online in "Brain", Behavior and Immunity.

More about this source text required for additional translation information [10].

Can fibromyalgia be a mitochondrial disease?

Introduction

Fibromyalgia and neurodegeneration

Before [11], fibromyalgia is considered non-degenerative, meaning that biological structures have not been damaged or destroyed as they are known in other neurological diseases such as multiple sclerosis or Alzheimer's disease. However, this research suggests that fibromyalgia may, in fact, involve some neurological degeneration of structures in the central nervous system. This, together with earlier research on damage to small nerve fibers in the skin, may mean that the degeneration is not limited to the central nervous system, but may extend to the peripheral nervous system, involving the nerves in the limbs, hands and feet. The term neurological disorder is used for any condition caused by dysfunction in part of the brain, expressed in physical and/or psychological symptoms. Are free radicals and antioxidants in primary fibromyalgia an oxidative stress disorder? The "neurological disorders" are diseases of the brain, spinal cord and the nerves connecting them. The disorders include: epilepsy, Alzheimer's disease and dementia, stroke, migraine and other headaches, multiple sclerosis, Parkinson's disease, neurodegeneration, brain tumors, traumatic disorders of the nervous system and brain disorders. Lots of bacteria, viral, microbiome [12,13] symptoms may occur due to the infection itself, or due to an immune response. People tend to associate FM with the Eoxin toxin. Eoxin is a member of the CC family of chemokines, so named because of their two conserved N-terminal cysteines (although natural eotaxin preparations appear to contain N-absorbing truncated forms lacking two or three amino acids). The

genes encoding these chemokines are clustered on chromosome 17. The hallmark of CC chemokines is usually their ability to attract and activate inflammatory leukocytes, particularly lymphocytes, monocytes, eosinophils and basophils, as some stromal cells such as endothelial muscle and certain cells.

Fibromyalgia (FM) is a common syndrome, typical by chronic joint pain, fatigue and impaired sleep, it is very challenging to diagnose and demanding to treat.

Comparing FM patients to separate controls applying differential analysis, substantial differences were found in the abundance of microbial components. The difference in microbial composition was understood by variables associated with FM more than any other local or environmental variable and correlated with clinical parameters of FM. Consistent with the observed change in metabolized butyrate species, serum metabolite analysis focused on differences in serum levels of butylate and propionate in FM patients. Using machine learning algorithms, the composition of the microbiome only allowed a classification of patients, and controls (ROC AUC 87.8%). This is the first publication of a change in gut bacteria with noncomb pain. This paves the way for further studies, elucidates the pathophysiology of FM, develops diagnostic aids and enables examining new treatment methods.

The relationship between fibromyalgia, the optic nerve and neurodegeneration

Fibromyalgia has always created problems for doctors. We have pain, but no apparent cause. If this research is accurate, which we won't know until it is replicated, it could be that our pain is coming from a very reliable source. After all, neuropathic pain has been recognized for a long time. Suddenly it makes our "mysterious" pain not mysterious at all. On the other hand, it opens new doors for investigation.

If we have damaged nerves, then why? What causes the damage? Potential candidates could include autoimmunity, which would involve the immune system turning around and destroying nerves as if they were bacteria, problems with the body using substances to grow or maintain nerves. Researchers have long considered the possibility of autoimmune fibromyalgia, but so far we have no significant evidence to support it. Now that researchers have discovered real damage, they may have better insight into where to look for autoimmune activity.

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Cannabigerol (CBG) protects neurons and minimizes inflammation in neurodegenerative diseases

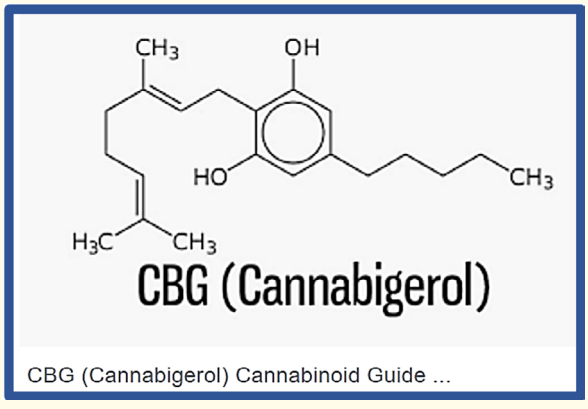

Figure 1

It was demonstrated [14]. Your body goes from burning carbohydrates for energy to consuming fat as the main fuel source. When our body is able to digest fat, our liver creates ketones [15], which are digested more efficiently than sugars, thus creating much less reactive oxygen species and secondary free radicals that can damage cellular mitochondria, proteins and DNA.

The animals (rats) used in this study found that they had reduced inflammation. When the scientists used a molecule called 2-deoxy-glucose (2DG) to block glucose metabolism and induce a ketogenic state [16]. Similar to what happens if you follow a ketogenic diet. By doing so, inflammation was brought to levels close to those found in controls.

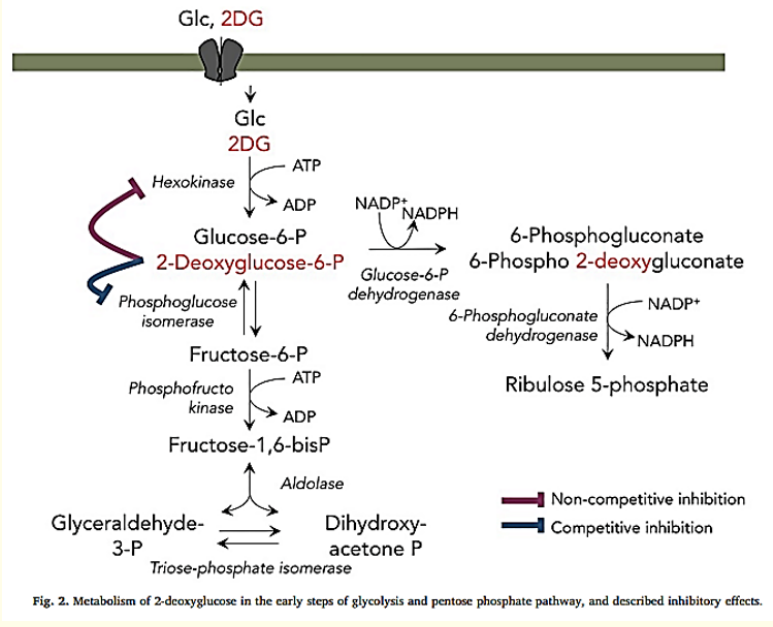

Figure 2: *Perspective cellular toxicity of the metabolic inhibitor 2-deoxyglucose and associated resistance mechanisms. https://www.ecronicon.com/ecpt/pdf/ECPT-07-00390.pdf.*

However, we can protect our intestines. That's the tantalizing finding of a new study [17] recently published and reveals a way in which mice - and possibly humans - can control the composition and behavior of their gut population - the microbiome. Such a prospect raises the widely held notion that the complex ecosystem of bacteria inhabiting our guts actually acts as our puppet master, altering the brain's biochemistry even as it tends to our immune system, warding off infection and helping us break down our big burger and fries.

Bibliography

1. Thuy Doan., *et al*. "Paucibacterial Microbiome and Resident DNA Virome of the Healthy Conjunctiva"; Doan T, Akileswaran". *Andersen Investigative Ophthalmology and Visual Science* 57 (2016): 5116-5126.
2. Pappolla MA., *et al*. "Is insulin resistance the cause of fibromyalgia? A preliminary report". *PLoS ONE* 14.5 (2019): e0216079.
3. https://www.thepaincenter.com/news/new-study-shows-yoga-decreases-fibro-pain
4. Häuser W., *et al*. "Fibromyalgia. " Facts and myths pertaining to fibromyalgia". *Nature Reviews Disease Primers* 1 (2015): 15022.
5. Huang Q., *et al*. "The oral and gut microbiomes are perturbed in rheumatoid arthritis and partly normalized after treatment". *Nature Medicine* 21 (2015): 895-905.
6. Newberry F., *et al*. "Does the microbiome and virome contribute to myalgic encephalomyelitis/chronic fatigue syndrome?" *Clinical Science London English* 1979 132 (2018): 523-542.
7. Hernandez CJ. "The Microbiome and Bone and Joint Disease". *Current Rheumatology Reports* 19 (2017): 77.
8. Goebel A., *et al*. "Altered intestinal permeability in patients with primary fibromyalgia and in patients with complex regional pain syndrome". *Rheumatology Oxford England* 47 (2008): 1223-1227.
9. Mansfield KE., *et al*. "Identifying patients with chronic widespread pain in primary care". *Pain* 158 (2017): 110-119.
10. https://www.massgeneral.org/News/pressrelease.aspx?id=2296
11. http://fibrowomen.com/fibromyalgia-the-optic-nerve-and-neuro-degeneration/
12. Minerbi Amir., *et al*. "Altered microbiome composition in individuals with fibromyalgia". *Pain Management Resource Center* 18 (2019).
13. Ludovic Giloteaux., *et al*. "Reduced diversity and altered composition of the gut microbiome in individuals with myalgic encephalomyelitis/chronic fatigue syndrome". *Microbiome* 4 (2016): 30.
14. https://www.prohealth.com/library/cannibigerol-cbg-protects-neurons-and-reduces-inflammation-in-neurodegenerative-disease-43904
15. Shimon Shatzmiller., *et al*. "Obesity Diabetes and Ketoacidosis in Elderly". *EC Pharmacology and Toxicology* 7.11 (2019): 01-20.
16. ClotildeLaussel and Sébastien Léon."Cellular toxicity of the metabolic inhibitor 2-deoxyglucose and associated resistance mechanisms". *Biochemical Pharmacology* 182 (2020): 114213.
17. Shirong Liu., *et al*. "The Host Shapes the Gut Microbiota via Fecal MicroRNA". *We Cell Host and Microbe* 19 (2019): 32-43.

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