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Opinion Letter

Body Pain and the Microbiome

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What Is A Microbiome?

Your stomach microbiome is a collection of all the bacteria that exist in our digestive system and help us digest food. In our gut alone we have around 100 trillion of the microbes (bacteria, Viruses, fungi and other sorts), similar to the number of cells we have throughout our body! Your microbial world is unique to you, and affects how your body responds to different foods.

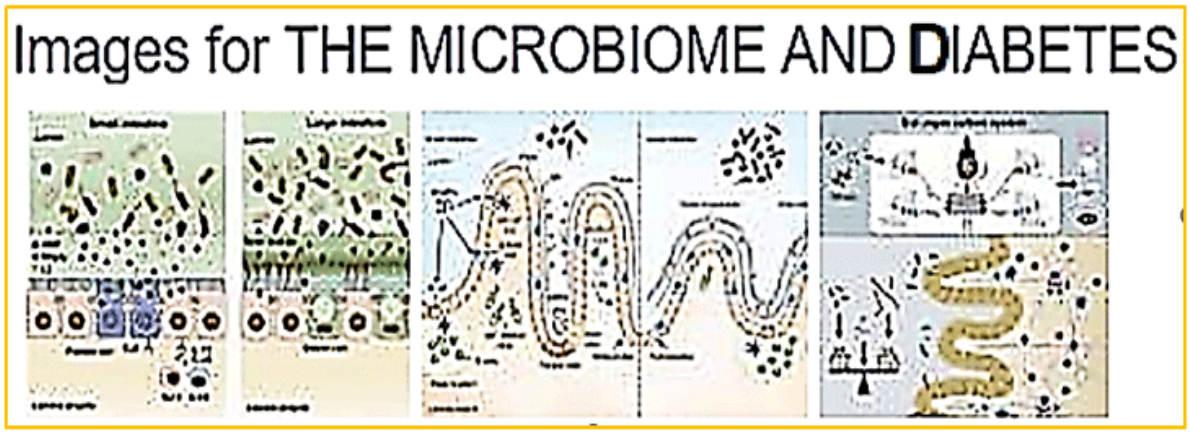

Figure 1

More images for The Microbiome And Diabetes And Fibromyalgia Shatzmiller Shimon Letter to the Editor Department of Chemical Biology, Ariel University, Ariel, Israel The body's Microbiota supports local mucosal immunity Increasingly recognized as an essential modulator of Systemic immune system. The exact role of the intestines Microbiotics in bacterial pneumonia, for example, however, is Unknown. With 425 million people in the world suffering, living with diabetes, chances are you have a family or friend who has this chronic illness. One of the main risks for DM2 (Diabetes Melitus type 2) is obesity. Changes in gut microbiota have been associated with the appearance of obesity and type 2 diabetes in humans. So this raises the question: can trigger the gut microbiota trigger, prevent or manage type 2 diabetes? And if so, how?. Diabetes is a chronicdisease that might be associated with other neurodegenerative diseases. On the mechanistic association between type 2 diabetes (T2DM) and Alzheimer's disease (AD). The underlying causes of CNS complications caused by diabetes are multifactorial and they understand relatively little although it is now clear that the blood-brain barrier (BBB) damage plays a significant role in CNS-dependent disorders of diabetes. Changes in plasma glucose levels (hyperglycemia or hypoglycemia) have been associated with transfer functions from years of BBB (eg glucose, insulin, choline, amino acids etc.), integrity (tight junction disorder) and oxidative stress in the CNS microSillaries. The latter two are involved in a potentially causal role for activation regulation of the receptor for advanced end glycation products (RAGE). This type I protein membrane also transports amyloid beta (Aβ) from the

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blood to the brain over the BBB thus, the association between type 2 diabetes (T2DM) and Alzheimer's disease (AD, also known as "type 3 diabetes.") Hyperglycemia is associated with progression of ischemia Brain, resulting in improvement of secondary brain injury. Type 2 diabetes (T2D) is a widespread metabolic Report image.

Microbiome and Fibromyalgia Chronic Pain

Fibromyalgia is a chronic disease that causes widespread pain, with patients often experiencing extreme fatigue, sleep disorders, depression and headaches. Patients with fibromyalgia have inflammation of the brain. Using PET brain imaging, researchers at Karolinska (Sweden) and Massachusetts (USA) Hospitals have now shown that glial cells - the central nervous system immune cells - are activated in the brains of patients with fibromyalgia. Recent research indicates that the cerebral microbiome populations [1] (Gut, Blood, Brain, Eye for example) may cause this neurodegenerative disorder as it does in the AD, PD, DM2 and many more diseases that lack remedy. This raises the hope for the cure of these diseases.

Is Insulin Resistance the Cause of Fibromyalgia?

Despite extensive research [2], the nature of FM is therefore unknown, there Treatment is not a change in a disease known for this situation. We know that most (if not all) Patients with FM belong to a separate population that can be separated from the control group by their glycated hemoglobin A1C (HbA1c) levels, a host marker of insulin resistance (IR). This has been demonstrated by analyzing the data after introducing age patching stratification to a linear regression model. This strategy showed very significant differences.

Brain Inflammation Reported For First Time in Fibromyalgia, a Story at a Glance

Brain scans of fibromyalgia [3] patients have offered substantial evidence that the pain they experience is real; Their threshold of suffering pain impulses is significantly lower than that of most people Recent studies showed that fibromyalgia patients tend to have severe inflammation of their bodies, including their nervous system and brain The cannabinoid receptor that produces the "high" in response to THC in marijuana also helps regulate brain inflammatory responses The signal reserved for glial cells to stop their inflammatory activity is endocannabinoids, which work by binding receptors to cannabinoids on individual neurons With age, the natural production of endocannabinoids decreases, which then leads to immune response deficit and chronic inflammation. The diagnosis of FM is based on the recognition of a typical cluster of symptoms, while excluding other potential sources of pain [4]. The diagnostic criteria for FM rely on self reported symptoms [5]. The lack of objective diagnostic criteria is a source of frustration among patients and clinicians, and adds to the possible reasons for incorrect diagnoses. In two retrospective cohorts of patients diagnosed with FM, the rate of false positive diagnoses. Patients with chronic fatigue syndrome, which shares some characteristic features with FM, were shown to have altered the gut microbiome and metabolomic profiles [6]. Summing up, in several rheumatologic diseases, including rheumatoid arthritis and spondyloarthropathies, microbiome alterations have been reported [7]. Indirect evidence hints that the gut microbiome may be altered in FM patients: Altered small intestinal permeability was reported in a cohort of FM and complex regional pain syndrome (CRPS) patients [8] in a small cross-sectional study of FM patients, a distinct urine metabolomic signature was demonstrated, which could be attributed to gut microbiome alterations [9].

Foreword

We tend to think of fibromyalgia (FM) as the central nervous system disease, but the focus tends to eliminate the growing evidence of problems in the body.We do not tend to think of fibromyalgia as an inflammatory disorder. It is true that visible signs of inflammation are quite rarely found in patients with FM, but studies suggest inflammatory factors may play a role.Then there are the mitochondria. Mitochondrial dysfunction is a real possibility of chronic fatigue syndrome, but I have rarely connected it with FM or pain. It turns out, however, that many studies - most of them minor - indicate that mitochondrial dysfunction can indeed play a significant role in fibromyalgia. Researchers, in a study by the Massachusetts General Hospital (MGH), in collaboration with the team of the Karolinska Institute in Sweden - first documented widespread inflammation in the brains of patients with a poorly understood condition called fibromyalgia. Their report was published online in Brain, Behavior and Immunity [10]. Can fibromyalgia be a mitochondrial disease?

Introduction

Fibromyalgia and Neurodegeneration

Before [11], fibromyalgia is considered non-degenerative, meaning that no biological structures have been damaged or destroyed as they are known in other neurological diseases such as multiple sclerosis or Alzheimer's disease. However, this study suggests that fibromyalgia may, in fact, involve some neurodegeneration in structures within the central nervous system. This, combined with earlier research on damage to small nerve fibers in the skin, can mean that degeneration is not confined to the central nervous system, but may extend the peripheral nervous system, which involves the nerves in the limbs, hands, and legs. The term neurological disorder is used to any condition caused by dysfunction in the part of the brain, resulting in physical and/or psychological symptoms. Is Free radicals and antioxidants in primary fibromyalgia an oxidative stress disorder? The "neurological disorders"

are an illness of the brain, spinal cord, and nerves that connect them. These disorders include epilepsy, Alzheimer's disease and dementia, stroke, migraine headaches and other headaches, multiple sclerosis, Parkinson's disease, neurodegeneration, brain tumors, traumatic disorders in the nervous system and brain disorders. Many bacterial, viral, microbiomal [12,13] infections can affect the nervous system. Neurological symptoms may occur due to the infection itself or due to an immune response. People tend to relate FM with a toxin Eoxin. Eoxinis a member of the CC family of chemokines, so called because of their two conserved N-terminal Cysteine N (although the natural eotaxin preparations seem to contain N-absorbent cut forms lacking two or three amino acids). The genes that encode these chemokines are grouped on chromosome 17. The hallmark of CC chemokines usually is their ability to chemoattract and activate inflammatory leucocytes, especially lymphocytes, monocytes, eosinophils and basophils, as well as some stromal cells such as endothelial muscle and some cells. Fibromyalgia (FM) is a common syndrome, characterized by chronic joint pain, fatigue and sleep impairment, it is challenging to diagnose and challenging to treat. When comparing FM patients to separate controls using differential abundance analysis, significant differences were found in the number of bacterial components. The difference in microbial composition was explained by FM-related variables more than any other local or environmental variable and correlation with clinical parameters of FM. Consistent with the observed change in metabolizing butyate species, targeted serum metabolites analysis of differences in serum levels of butyate and propionate in FM patients. Using computerized learning algorithms, the microbiome composition allowed only the classification of patients and controls (ROC AUC 87.8%). To our understanding, it is the first publication of the microbial change in the intestines with non-combat pain. This observation paves the way for additional studies, clarifies the pathophysiology of the FM, develops diagnostic aids and allows for the examination of new treatment methods.

The Relationship between Fibromyalgia, the Optic Nerve, and Neurodegeneration

Fibromyalgia has always posed problems for doctors. We have pain, but there is no apparent reason. If this study is accurate, which we will not know until it is replicated; it can be that our pain comes from a very credible source. After all, neuropathic pain is recognized for a long time. Suddenly, this makes our "mysterious" pain not mysterious at all. On the other hand, he opens new doors for interrogation. If we have damaged nerves, then why? What causes damage? Potential candidates can include autoimmune, which will include the immune system going wild and distroying the nerves as if they were microbes, problems with the body using substances to grow or maintain nerves. Researchers have long assessed possible autoimmune fibromyalgia, but so far we have no substantial evidence for it. Now that researchers have discovered real damage, they may gain better insight into where to look for autoimmune activity. They may also be able to detect deficiency or inefficiency in how nerves are kept. Diagnostic tests, it's too early to say whether eye disorders can lead to a more objective test than we currently have. If so, it will be a significant advance in how fibromyalgia is identified. Because thinning was worse in more severe cases, it could provide a marker for doctors to monitor treatments as well as progress. It is also possible that these discoveries can lead to targeted treatments. We will not know the full impact of this study for some time, as any progress in diagnosis and treatment will have to come after further research or confirm or contradict the findings.

Cannibigerol (CBG) Protects Neurons and Minimizes Inflammation in Neurodegenerative Diseases

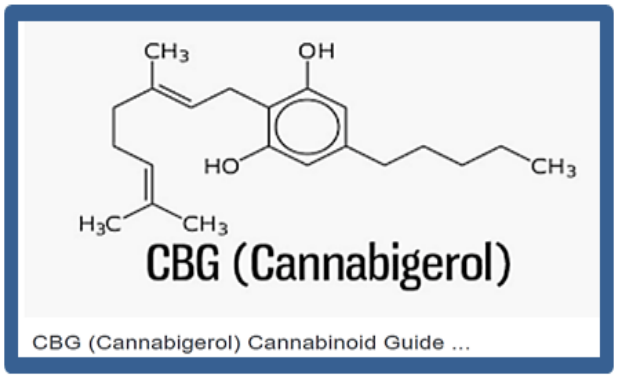

Figure 2

It was demonstrated [14] that VCE-003.2 is neuroprotective against neuronal prophylactic damage in the in vivo model of PD and in neutron cell models of neuron film. These effects may be PPAR receptors, although in silicon and in vitro experiments, it is highly recommended that VCE-003.2 targets PPAR by acting on two binding sites in LBP, one that is sensitive to T0070907 and another that is not affected by this PPAR ΝΝ antagonist (Alternate link site).

A massive ketogenic diet reduces brain inflammation [15]

A study published last year suggests ketogenic diets - which are high in healthy fats and low in net carbohydrates - are an especially potent ally for suppressing brain inflammation, as ketones are potent HDAC (histone deacetylase inhibitors) that suppress NF-κB primary inflammatory pathway. As explained by Medical Xpress, 13 the constitutive moment of the study came when the team identified an essential protein linking the diet to inflammatory genes that, if blocked, may reflect the anti-inflammatory effects of ketogenic diets. A catogenic diet changes the way your body uses energy, converting your body from burning carbohydrates for energy to consuming fat as

the primary source of fuel. When our body is able to burn fat, your liver creates ketones, which burn more efficiently than carbohydrates, thus creating much less reactive oxygen species and secondary free radicals that can harm your cellular mitochondrial cells, proteins and DNA. The rats used in this study found that they reduced inflammation when the researchers used a molecule called 2-deoxyglucose (2DG) to block glucose metabolism and cause a catatonic state, similar to what happens if you follow a ketogenic diet. By doing so, inflammation was brought to levels near those found in controls. It is possible to keep our gut in check after all. That's the tantalizing finding from a new study [16] published recently that reveals a way that mice-and potentially humans can control the makeup and behavior of their guticrobes population - the microbiome. Such a prospect upends the popular notion that the complex ecosystem of germs residing in our guts essentially acts as our puppet master, altering brain biochemistry even as it tends to our immune system, wards off infection and helps us break down our supersized burger and fries. The increasing load of intermittent pain disorders has attracted increasing interest from researchers and clinicians learn the sources of pain from internal organs. The viscera Pain is a complex and heterogeneous disorder that can Range from the mild discomfort of indigestion to the agonizing pain of kidney pain, usually disproportionately affects women more than men [17,18]. the most common Forms of abdominal pain are classified as functional disorders in the gastrointestinal tract (FGID) such as the Irritable Bowel Syndrome (IBS), which exceeds 40 billion USD Costs and affects about 10-15% of the estimated US and European populations [19,20]. Interstitial pain disorders to exert enormous pressure on the health system and they are related to psychological distress, sleep disorders and sexual function, which affects everyone negatively Quality of life of the patient [21]. Moreover, both aging and gender affect the progression of pathology and pain in the gut, With IBS reported twice more frequently than in women Men [22]. Fibromyalgia affects 2-4% of the population [23] and has no known cure. Symptoms include fatigue, sleep difficulties, and cognitive difficulties, but the disease is clearly characterized by joint chronic pain [24,25].In a paper in the journal Pain, a Montreal-based research team showed for the first time that there are changes in bacteria in the digestive tract of people with fibromyalgia. About 20 different bacterial species were found in larger or smaller amounts in the microbiomes of the participants suffering from the disease than in healthy creation. Analysis of the Gut Microbiome Reveals Significant Differences between Men with Chronic Prostatitis/Chronic Pelvic Pain Syndrome [26,27] and Controls. A chronic cause of prostatitis / chronic pain and pain syndrome is a common disorder with different etiologies and clinical features. The intestinal microbium is a metabolic active ecosystem associated with systemic conditions (the gut-brain axis). We assume that intestinal microbium will show changes between people with chronic pelvic pain syndrome. Materials and Methods We identified people with chronic pelvic pain syndrome and controls that were asymptomatic or had only urinary tract symptoms. After a rectal examination, the tip of the dirty glove was immersed in sterile saline and stored in ice. The severity of the symptom was measured with the NIH-Chronic Prostatitis Symptom Index and clinical phenotype with UPOINT. Total DNA was extracted from a pellet of samples. The MiSeq sequence of specific bacteria and 16S rRNA capture was carried out. Taxonomic and bioinformatics tests were performed using principal coordinate analysis, QIIME and LEFSealgorithms.The results were 25 patients and 25 controls with complete data. (Chronic pain in the pelvis was 52.3 vs control of 57.0 years, p = 0.27) in patients with pain syndrome and chronic pain. Median symptom was median 48 months, chronic prostatitis symptom index was 26.0 and meant of UPOINT was 3.6. Of UniFrac revealed closer clusters of controls in space that differed from broader clusters of cases (p = 0.001) with cases of (P = 0.001) Compared to controls, 3 exhibits were overrepresented in cases and 12 were incorrectly represented, such as Prevotellabacteria [28].Conclusions: People with chronic pelvic pain syndrome have less significant diversity of microbial collections than controls , And lower sections of Prevotella, with sufficient separation to be used as a potential biomarker.The microbial of the intestines may serve as a biomarker and potential therapeutic ability in the chronic pelvic pain syndrome. Purpose: Chronic prostatitis / chronic pain syndrome is a common disorder with different etiologies and clinical features. The intestinal microbium is a metabolic active ecosystem associated with systemic conditions (the gut-brain axis).Chronic prostatitis / chronic pain syndrome is a common disorder with different etiologies and clinical features. The intestinal microbium is a metabolic active ecosystem associated with systemic conditions (the gut-brain axis). We assume that intestinal microbium will show changes between patients with chronic pelvic pain syndrome and controls. We examined patients with chronic pelvic pain syndrome and controls that were asymptomatic or had only urinary tract symptoms. After a rectal examination, the tip of the dirty glove was immersed in sterile saline and stored in ice. The severity of the symptom was measured with the NIH-Chronic Prostatitis Symptom Index and clinical phenotype with UPOINT. Total DNA was extracted from a pellet of samples. The MiSeq sequence of specific bacteria and 16S rRNA capture was performed. Opioids are the gold way of treating pain; however, their clinical use is impaired by the development of hyperalgesia tolerance when used chronically. Moreover, prolonged use of opioids may lead to negative emotional states that exacerbate the emotional disorders already present in the chronic pain population. This work shows that inflammation in the brain contributes to this adverse effect, although the mechanism that drives central inflammation is still unclear. Recent reports have shown that neuronal stimulation observed in other psychiatric conditions can be caused by disruptions to the microbiota in the gut along an abnormal signaling axis of the brain [10].An analysis of the human microbiology continues to reveal new associations that have not been realized in the past

between microbial disbiosis and disease. "Romantic approaches" to bacterial identification using dependent cultural methods enable practitioners to recognize the presence of changes in mass and diversity of the microbial and identification of correlations with disease processes. While some of these diseases were have been extensively studied and well defined in their etiology and treatment methods (colorectal cancer), others provided much more significant challenges both in diagnosis and treatment. Such a condition, chronic Prostatitis / chronic pelvic pain syndrome (CP / CPPS), has a number of etiological and beneficial contributions From inflammation, inflammation, central nervous system (CNS) changes, stress, central-all sensitivity Factors that play essential roles in the interplay between the human body and its microbial. Not an individual the cause of CP / CPPS has been identified and this is most likely a syndrome with multifactorial factors. It Heterogeneity and ambiguity are sources of significant frustration for patients and suppliers alike. Although In multiple attempts, treatment of chronic prostatitis with monotherapy saw limited success, ieHe thought because of his heterogeneous nature. Phenotypic approaches are to classify the disease as well Direct CP / CPPS treatment has proved helpful in these patients but still questions about etiology. A new microbiology study found correlations between symptom scores and disease severity and the degree of dysbiosis in urine and intestines (stool) microbiomes in these patients compared to unliced Controls. These findings present the abilities of new diagnostic and therapeutic targets for CP / CPPS patients [9].

Microbiome and Migraine Chronic Pain

Migraine [29] is a recurrent primary headache that affects 17% of women and 5% -8% of men. Migraine sensitivity is multifactorial with genetic, hormonal and environmental factors all playing an important role. The physiopathology of migraine is complex and yet not fully understood. Many neuropeptides, neurotransmitters and brain pathways were involved. Referring to the enormous mechanisms and pathways in migraine, a wide range of morbidity and morbidity (eg, cardiovascular, psychiatric and other neurological diseases) are closely related to migraine. Recent reports demonstrate an increased occurrence of gastrointestinal disorders (GI) in patients with migraine compared to the general population. Helicobacter pylori infection, irritable bowel syndrome, gastro paresis, liver disorders, celiac disease and changes in the microbiota have been associated with migraine. A number of mechanisms involved in the gastrointestinal axis, such as chronic inflammatory response with inflammatory and as active mediators to the circulatory system, microbiota modulation in the intestine of the ventricular ventricle and autonomic and interactive nervous system dysfunction, associations. However, the exact mechanisms and pathways associated with the intestinal axis in the migraine brain should be fully clarified. In this review, we review the existing literature that links migraine with gastrointestinal disorders. We discuss possible physiopathological mechanisms, clinical implications, as well as a number of future areas of interest in research. Although previous studies identified a link between gastrointestinal disorders and migraines [30], the exact role of crosstalk-gut-brain - the transmission of signals between the intestines and brain-in migraines is unknown. If his model is successful, Tao hopes that this will lead to a better understanding of the abdominal brain crosstalk and how disruption of the gut microbiota can cause migraine.

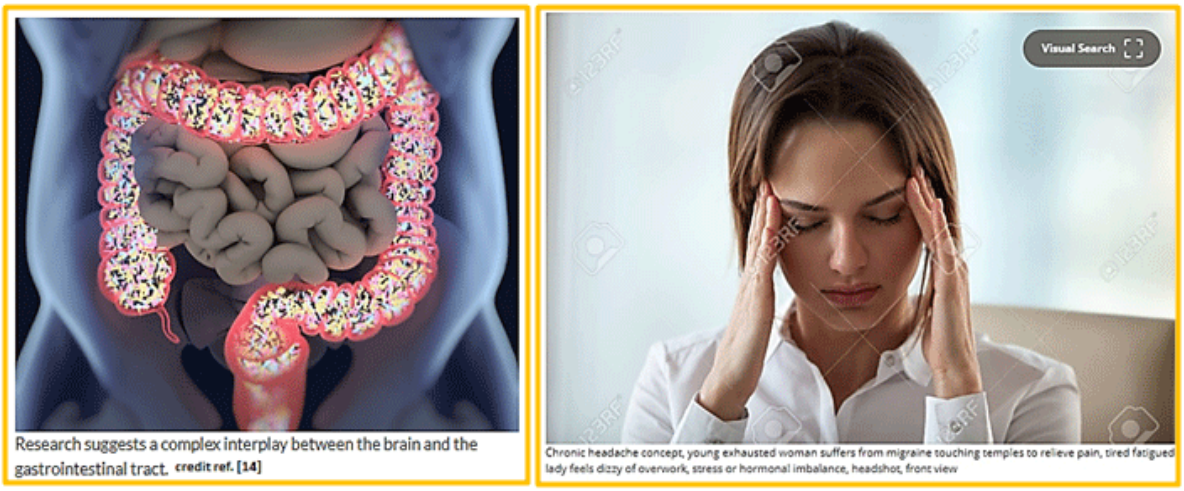

Figure 3

Chronic headache concept, a young exhausted woman suffers from migraine touching temples to relieve pain, the tired fatigued lady feels dizzy of overwork, stress or hormonal imbalance. Many know that bacteria can cause diseases and infections, but not all bacteria are harmful. In fact, your stomach is just one of many parts of the body full of "good" bacteria. This bacterial population - known as the gut microbiota - works hard to maintain a healthy body and normal functioning. However, when the gut microbiota is disturbed from its regular routine, there can be side effects. Migraines are the most common disease in the world, with more than 37 million people in the United States. Although migraines can significantly affect the way of life, these types of headaches are often undiagnosed and contreated. This is due to the lack of a clinically relevant animal model for migraine headaches. Without a clinically relevant model, it can be challenging to learn about how to treat and prevent migraines. It is reported that compounds containing nitrates found in certain foods - usually processed meats, leafy vegetables, chocolate and some wines - as well as preservatives and nitrates may trigger migraines as a byproduct, but the possible mechanical link between nitrates, intestinal microbial and the likelihood of experiencing migraines is unknown .A recent study found that migraine patients have higher levels of oral bacteria involved in processing nitrates, making them more susceptible to migraine. The researchers used high-throughput (RRNA) 16S ribosomal ribonucleic acid (RRNA) technologies to determine whether there was a link between nitrate-reducing bacteria in oral and oral samples and migraines. The presence and recurrence of nitrate, nitric and nitrogen reductase genes were determined by predictive phytochemicals from 172 oral tests and 1,996 faecal samples of healthy participants in the group of Gutt's American agents and were associated with self-migraine. Migraine sufferers had higher levels of nitric reductase, nitrite and nitrogen (NO) genes - all involved in nitrogen exchange - in the expected metagenomics in both oral and fecal samples (these genes showed a more significant increase in vocal samples than stool samples). These results suggest that microbes in the mouth may contribute to the efficient decomposition of nitrate contained in food and preservatives, which are eventually converted into nitric oxide in the bloodstream and cause the blood vessels in the brain and scalp to expand.In addition, the study showed that streptococcus and pseudomonas genera were grown in oral micrographs of migraines compared to non-migraines; Both have the potential to reduce nitrate. Rothiamucilaginosa and Haemophilusparainfluenzae have also shown differential patterns of abundance in the oral microglia of migraines and non-migraines, and these bacteria have been reported here and here as significant nitrate substitutes in the human mouth.It shows for the first time a potential link between bacteria, migraines and nitrate - nitrite and nitrogen by reporting the higher prevalence of oral migraines in people with migraines than in the mouth of non-migraines. Despite being only a correlation study, this work offers a possible explanation of why some patients are more sensitive than others to migraines and why some foods appear as triggers for migraines [31]

Chemicals to Treat Pains of Finromyalgia

Fibromyalgia (FMS) is chronic pain syndrome. Reasonable pathogenesis of the disease is the unclear and pursuit of measurable biomarkers for objective identification of affected individuals is a continuation Effort in FMS research. Our goal was to perform explorative metabolomics research [31] to clarify the A global metabolite profile of patients with FMS, and [32] to investigate the potential of this metabolite. Fibromyalgia and neuropathic pain [33,34] are two similar diseases. Information in order to increase the existing medical practice in diagnosing the disease is needed. Patients with diabetic neuropathy (DPN) and fibromyalgia (FM) differ significantly in pathogenic factors and the spatial distribution of perceived pain. One could ask whether, despite these apparent differences, similar exceptional deviations and pain qualities exist in both entities. We assumed the same sensory sense Symptoms might be associated with similar mechanisms of creating pain. The goals are [35] to compare and [36] to identify similarities and differences in sensory symptoms the two entities. In a pilot study, only a poster was presented per year Meeting of Rheumatology Society of Britain [37] Richards and co-workers (2001) reported muscle Metabolites identified in the urine of fibromyalgia patients May to indicate muscle damage. Muscle pain symptoms [38] are the most common cause of chronic disability, and muscle biopsy is often performed to achieve a diagnosis when hemangiomas have a myopatic source. However, the role of muscle biopsy in fibromyalgia is quite controversial. This examines the reported studies to assess whether there are changes in the muscle, whether these changes produce pain, and if a muscle biopsy helps in a diagnostic panel of fibromyalgia. Morphological and metabolic changes exist in the muscle of patients with fibromyalgia, but they are not specific and do not suffice for a specific diagnosis. However, the results obtained so far indicate the role of external factors in maintaining pain intensity. Therefore, it is advisable to have a better understanding of peripheral muscle change that can open up new therapeutic strategies. Although not by Set up a study of metabolomics, their metabolites targeted tests of urine by NMR (nuclear magnetic resonance Spectroscopy) revealed significant levels of creatine in Fibromyalgia syndrome (FMS) Patients and increase (t-test $p < 0.05$) urinary excretion of Choline, Taurine, Citrate and *Trimethylamine N-Oxide* (TMAO) [39] with respect to corresponding controls. The first metabolomics study on FMS, reported at 2013 [40], used 50 µl blood samples collected on blood (Whatman 903 protein keeps the snap apart Card, GE Healthcare, Westborough, MA, USA) from Patients diagnosed with FMS (n = 14), osteoarthritis (OA, n = 15) and rheumatoid arthritis (RA, n = 12). Samples were dry and then transferred to the laboratory for infrared spectroscopy and infrared

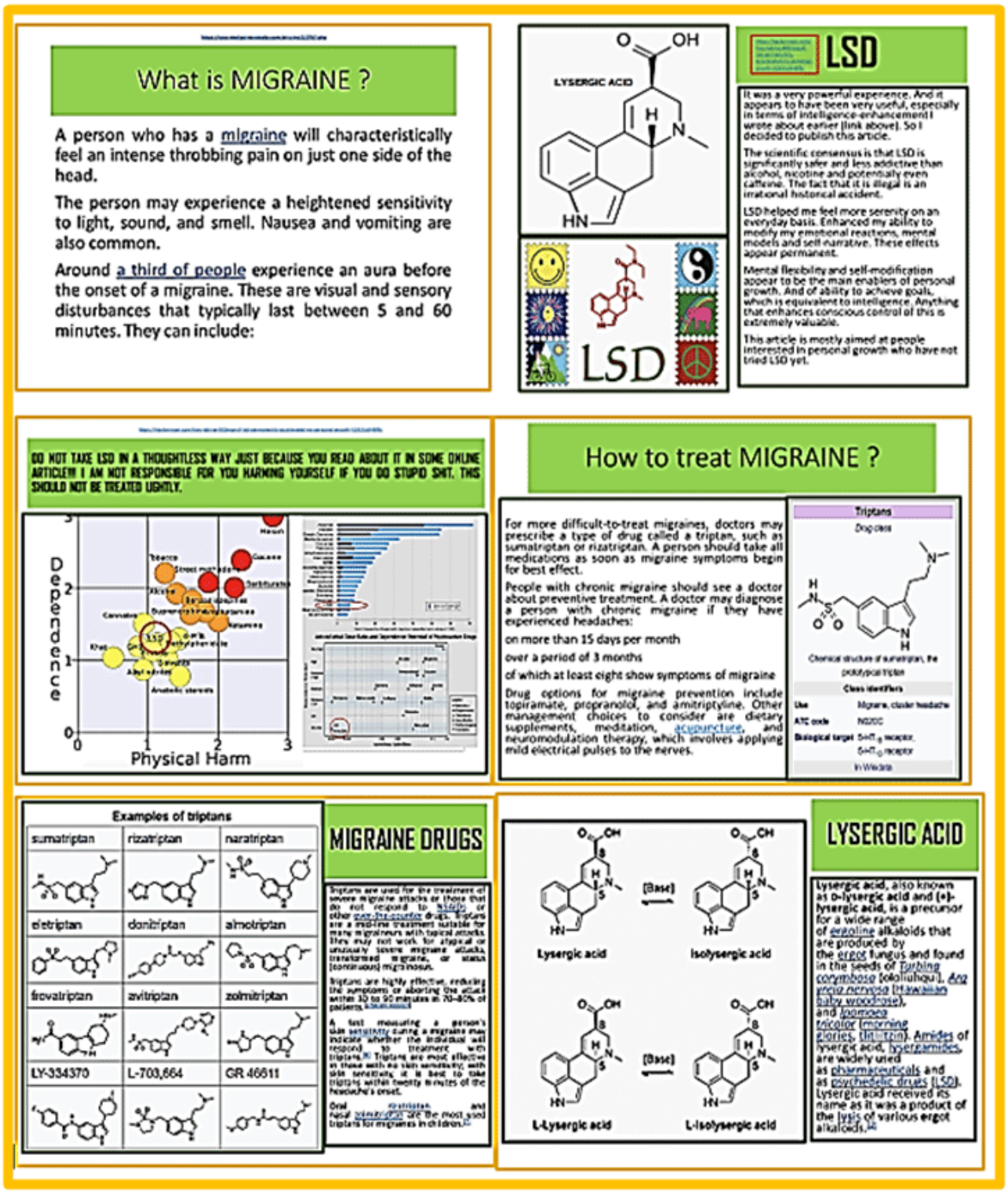
What is MIGRAINE ?
A person who has a migraine will characteristically feel an intense throbbing pain on just one side of the head.
The person may experience a heightened sensitivity to light, sound, and smell. Nausea and vomiting are also common.
Around a third of people experience an aura before the onset of a migraine. These are visual and sensory disturbances that typically last between 5 and 60 minutes. They can include:
LYSERGIC ACID
LSD
It was a very powerful experience. And it appears to have been very useful, especially in terms of intelligence-enhancement I wrote about earlier [link above]. So I decided to publish this article.
The scientific consensus is that LSD is significantly safer and less addictive than alcohol, nicotine and potentially even caffeine. The fact that it is illegal is an irrational historical accident.
LSD helped me feel more serenity on an everyday basis. Enhanced my ability to modify my emotional reactions, mental models and self-narrative. These effects appear permanent.
Mental flexibility and self-modification appear to be the main enablers of personal growth. And of ability to achieve goals, which is equivalent to intelligence. Anything that enhances conscious control of this is extremely valuable.
This article is mostly aimed at people interested in personal growth who have not tried LSD yet.
LSD
DO NOT TAKE LSD IN A THOUGHTLESS WAY JUST BECAUSE YOU READ ABOUT IT IN SOME ONLINE ARTICLE!!! I AM NOT RESPONSIBLE FOR YOU HARMING YOURSELF IF YOU DO STUPID SHIT. THIS SHOULD NOT BE TREATED LIGHTLY.
Dependence
Physical Harm
How to treat MIGRAINE ?
For more difficult-to-treat migraines, doctors may prescribe a type of drug called a triptan, such as sumatriptan or rizatriptan. A person should take all medications as soon as migraine symptoms begin for best effect.
People with chronic migraine should see a doctor about preventive treatment. A doctor may diagnose a person with chronic migraine if they have experienced headaches:
on more than 15 days per month
over a period of 3 months
of which at least eight show symptoms of migraine
Drug options for migraine prevention include topiramate, propranolol, and amitriptyline. Other management choices to consider are dietary supplements, meditation, acupuncture, and neuromodulation therapy, which involves applying mild electrical pulses to the nerves.
Triptans
Examples of triptans
sumatriptan
rizatriptan
naratriptan
eletriptan
donitriptan
almotriptan
frovatriptan
avitriptan
zolmitriptan
LY-334370
L-703,664
GR 46611
MIGRAINE DRUGS
LYSERGIC ACID
Lysergic acid
Isolysergic acid
D-Lysergic acid
D-Isolysergic acid
[Base]
Lysergic acid, also known as D-lysergic acid and (+)-lysergic acid, is a precursor for a wide range of ergoline alkaloids that are produced by the ergot fungus and found in the seeds of Turbina corymbosa (ololiuhqui), Ipomoea violacea (tlitliltzin), and Ipomoea tricolor (morning glories, tlitliltzin). Amides of lysergic acid, lysergamides, are widely used as pharmaceuticals and as psychedelic drugs (LSD). Lysergic acid received its name as it was a product of the lysis of various ergot alkaloids.

Figure 4

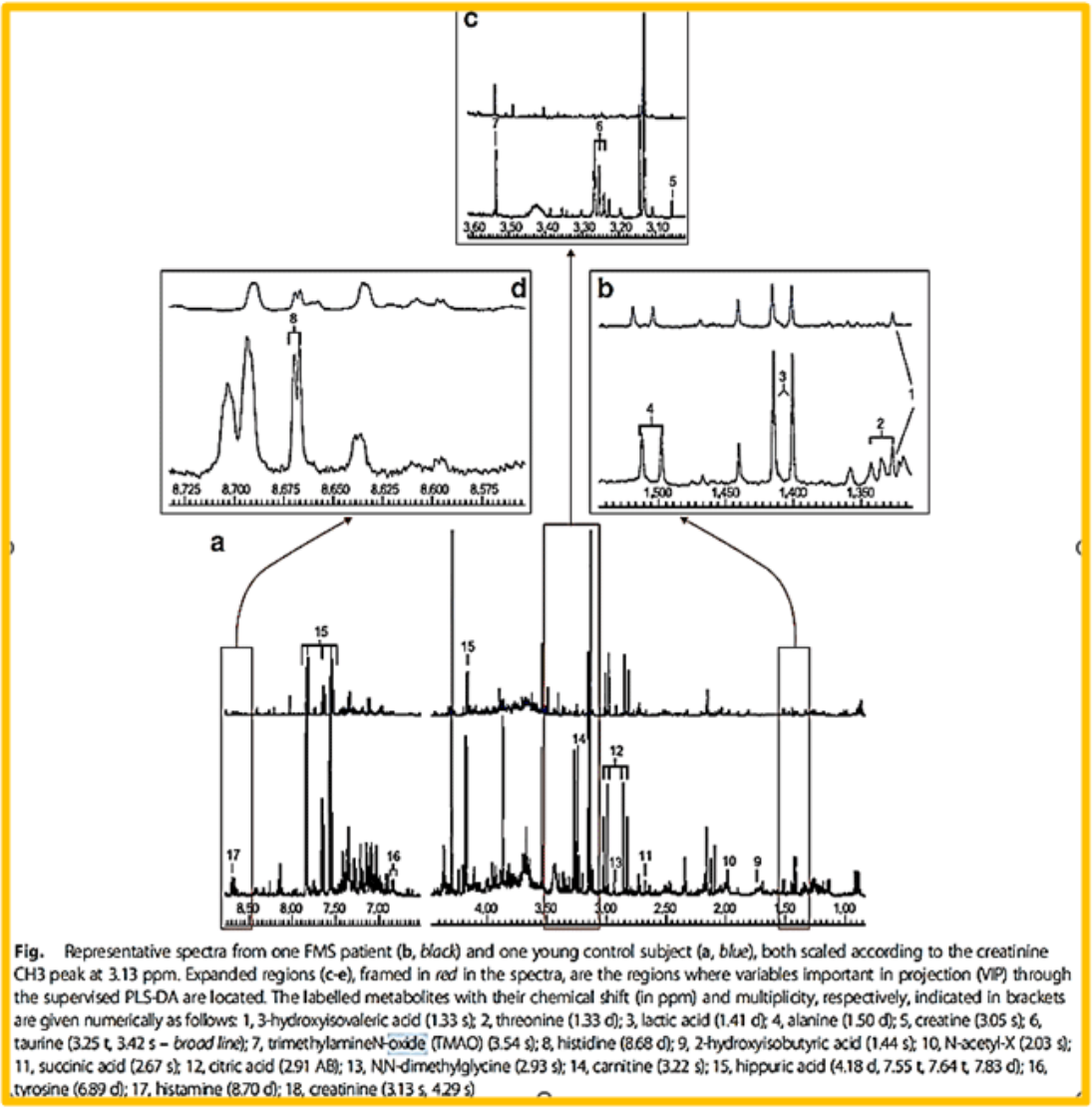

Fig. Representative spectra from one FMS patient (**b**, *black*) and one young control subject (**a**, *blue*), both scaled according to the creatinine CH3 peak at 3.13 ppm. Expanded regions (**c-e**), framed in *red* in the spectra, are the regions where variables important in projection (VIP) through the supervised PLS-DA are located. The labelled metabolites with their chemical shift (in ppm) and multiplicity, respectively, indicated in brackets are given numerically as follows: 1, 3-hydroxyisovaleric acid (1.33 s); 2, threonine (1.33 d); 3, lactic acid (1.41 d); 4, alanine (1.50 d); 5, creatine (3.05 s); 6, taurine (3.25 t, 3.42 *s – broad line*); 7, trimethylamineN-oxide (TMAO) (3.54 s); 8, histidine (8.68 d); 9, 2-hydroxyisobutyric acid (1.44 s); 10, N-acetyl-X (2.03 s); 11, succinic acid (2.67 s); 12, citric acid (2.91 AB); 13, NN-dimethylglycine (2.93 s); 14, carnitine (3.22 s); 15, hippuric acid (4.18 d, 7.55 t, 7.64 t, 7.83 d); 16, tyrosine (6.89 d); 17, histamine (8.70 d); 18, creatinine (3.13 s, 4.29 s)

The NMR analysis of Urine metabolites from "Fibromyalgia syndrome" (FMS) Patients. TMAO (□-3.55) in top © square

Figure 5

micro-infrared (IRMS).

Another analysis. RA and OA groups appeared to be Metabolic similar, but different from metabolites Profile of FMS. The IRMS approach was not unequivocal Identify the metabolites responsible for the diagnosis of Spectral differentiation, although changes in tryptophan It seems the metabolites are involved.

Treating Pain with Drugs

This review is one of the series on drugs used to treat chronic neuropathic pain. Estimates of the population prevalence of chronic pain with neurophysiological components ranged from 6% to 10%. Current treatment options for neuropathic pain. A significant benefit for just a few people, often with side effects that outweigh the benefits. There is a need to explore other treatments. Options, with different mechanisms of action for treating conditions with chronic neuropathic pain. Cannabis has been used. For milenia [41,42] to reduce pain. Cannabis plants are now promoted by some patients and their supporters to treat any kind of chronic pain.

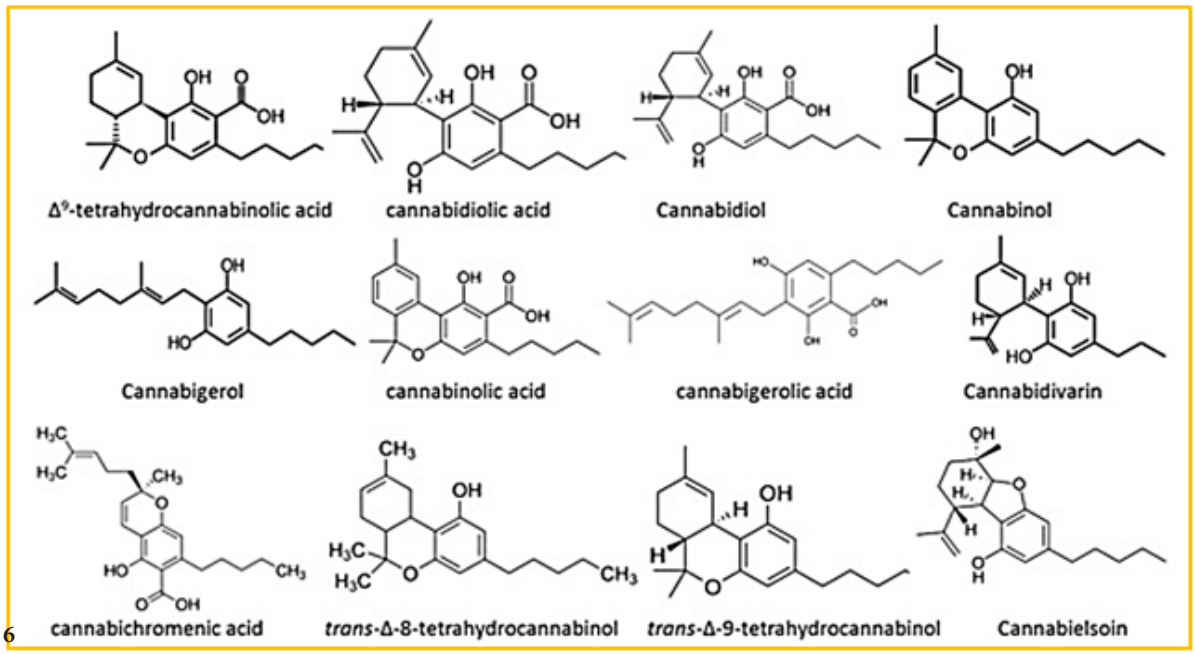

Figure 6

The primary sorts of natural cannabinoids belong to the families of the cannabigerol-type, cannabichromene-type, cannabidiol-type, cannabinodiol-type, tetrahydrocannabinol-type, cannabinol-type, cannabitriol-type, cannabielsoin-type, isocannabinoids, cannabicyclol-type, cannabicitran-type, and cannabichromanone-type [43]. Although the healing properties of cannabis species have been known for centuries, interest rates on its primary active metabolites as therapeutic alternatives to several pathologies Has increased in recent years [12]. The potential use of this revolution has been around the world regarding the public Health, production, use and sale of hashish, and led in general to changes in legislation in part States. The scientific progress and concerns of the scientific community were beneficial Understanding of cannabis derivatives as pharmacological options in a number of conditions, such as Appetite stimulation, pain management, skin pathologies, anticonvulsant therapy, neurodegeneration Diseases and in The ethical implications of their use and the ways of the manager, even in the adverse health field Consequences and death attributed to marijuana consumption, which represent some of the cases Which consist of the use of these compounds as therapeutic drugs. This review Understand the primary secondary metabolites of cannabis, approaching their therapeutic potential applications, as their potential health risks, in order to differentiate consumption as recreation Drugs. Analytical methodologies will also focus on their analysis, in order to assist Medical professionals and toxicologists in cases where these compounds exist.

The Microbiome Diabetes and Fibromyalgia

The body's Microbiota supports local mucosal immunity increasingly recognized as an essential modulator of Systemic immune system. The exact role of the intestines Microbiotics in bacterial pneumonia, for example, however, is Unknown. With 425 million people in the world living with diabetes, chances are you have a family or friend who has this chronic illness. One of the main risks for DM2 (Diabetes Melitus type 2) is obesity [44,45]. Changes in gut microbiota have been associated with the appearance of obesity and type 2 diabetes in humans. So this raises the question: can trigger the gut microbiota trigger, prevent or manage type 2 diabetes? And if so, how? Diabetes is a chronicdisease that might be associated with other neurodegenerative diseases [46]. On the mechanistic association between type 2 diabetes (T2DM) and Alzheimer's disease (AD). The underlying causes of CNS complications caused by diabetes are multifactorial and they understand relatively little although it is now clear that the blood-brain barrier (BBB) damage plays a significant role in CNS-dependent disorders of diabetes. Changes in plasma glucose levels (hyperglycemia or hypoglycemia) have been associated with transfer functions from years of BBB (eg glucose, insulin, choline, amino acids etc.), integrity (tight junction disorder) and oxidative stress in the CNS microSillaries. The latter two are involved in a potentially causal role for activation regulation of the receptor for advanced end glycation products (RAGE). This type I protein membrane also transports amyloid beta (Aβ) from the blood to the brain over the BBB thus, the association between type 2 diabetes (T2DM) and Alzheimer's

disease (AD, also known as "type 3 diabetes.") Hyperglycemia is associated with progression of ischemia Brain, resulting in improvement of secondary brain injury. Type 2 diabetes (T2D) is a widespread metabolic disorder identified by an imbalance in blood glucose level, altered lipid values and high blood pressure. Genetic components, high fat and high energy nutrition habits, and sedentary lifestyle are three major factors contributing to the high risk of T2D. Several studies have reported colon dysbiosis as a factor in the rapid progression of insulin resistance in T2D, which accounts for about 90% of all diabetes cases worldwide. The colon's dysbiosis can reshape the intestinal barrier function and mark metabolic pathways and signals, which are directly or indirectly related to insulin resistance in T2D. Thousands of microbial metabolites interact with the epithelial, liver, and heart cell receptors that characterize host physiology. Xenobiotics include nutrients, antibiotics and non-steroidal anti-inflammatory drugs that greatly influence the intestinal microbial composition and can promote dysbiosis. Any alteration of the colon can alter the host metabolism towards increased energy harvesting during diabetes and obesity. However, the specific events behind the dynamics of intestinal bacteria and their effect on host metabolism at the molecular level have not yet wholly deciphered. We reviewed the published literature to better understand the microbiota dynamics in the gut, factors that may cause dysbiosis microbiome gut and their association with Type 2 Diabetes (T2D) progression. Particular emphasis can also be made to understand the intestinal microbial induced burglary of intestinal barriers and / or tight nodes in their insulin resistance relationship [47].

The Microbiome as a Target for the Treatment of Type 2 Diabetes

The intestinal microbial is a collective term for the intestinal microbial community [48], whereas the intestinal microbium is defined as the complete collection of gut microbiota, Gutenberg University, Gutenberg, Sweden, [49]. This intestinal microbiota is not logical. Even 460-377 BC, the father of modern medicine Hippocrates declared his famous quote, "Every disease begins in the intestines." The microbial of the intestines contains a vast variety of microorganisms, which vary from bacteria, as well as from viruses, fungi, pagans, protozoa and archaea [50] serving our mature bodies. Archaea, Bacteria and Eukarya encompass the taxonomy of three areas of life [13]. The introduction of molecular techniques using a 16S gene rRNA sequence created phylogenetic information on microbial terminology. It can be used to distinguish between microbial groups in phillotypes, but is still not specific to describing bacterial species that require more advanced techniques such as a shotgun methogenic sequence. Recent estimates show that our microbiota is equal to the total number of our somatic and germ cells [51]. The proposed view of our microbiota as a symbiotic organism in our intestines has led to a new perspective that unites many lineages that can communicate with one another and design the immunomotibolistic vaccine in several ways. This intimate line of evolution has led to an integrated symbiotic relationship with a variety of abilities, including the degradation of other indigestible components of our diet, energy and nutrient harvesting, host immune system design, maintaining the integrity of the colon barrier; Xenobiotic metabolism [52,53]. Thus, the gut microbiota complements our biology in mutually beneficial ways. Fibromyalgia is a disease that leads to symptoms of pain, headaches, fatigue, constipation, etc. There are other symptoms: cognitive symptoms, irrettational sleep, etc. that lead to a decrease in quality of life. The occurrence of fibromyalgia in the United States is about 2% with the condition being seven to seven times higher in women than in men.

The Consensus of Fibromyalgia and Diabetes

There have been studies that evaluated parallel conditions that occur with fibromyalgia. One aspect is to look for the relationship of fibromyalgia with diabetes. One such study examined the prevalence of type 1 and typed 2 diabetes in patients with fibromyalgia. Frequency of fibromyalgia and other conditions Studies have assessed the incidence of fibromyalgia and other conditions have found an increased incidence of fibromyalgia among other autoimmune diseases such as lupus and Schirgen syndrome etc.

Fibromyalgia and Diabetes

It seems that patients with diabetes are more likely to be diagnosed with fibromyalgia. In addition, patients with fibromyalgia and diabetes tend to have higher levels of HbA1c in blood tests, indicating a decrease in glucose. Moreover, patients with diabetes and fibromyalgia have a higher number of tender points, increased pain scores, increased risk of sleep disorders, fatigue, and headaches [54].

Remarks

Symbionettes and compliments are not the only microorganisms the host meeting. Immune system host is continuously challenged by distinguishing beneficial bacteria Pathogens. The interactive role of pugs [55] and fungi [56] in the gut microbiota composition is also getting more attention. Although still well understood, the microbiota and intestines the host immune system have co-evolved so profoundly that they are can affect our immune well-being. It seems in mice without the germ, where the absence of microbiota leads Defects in the development and function of the immune system [57]. It described a dynamic maturation of the intestines the microbiome and host immune system is the host microbe determination Interactions and influence on susceptibility to infection, Inflammatory and autoimmune diseases [58]. This is one of the hardest and challenging problems from the pharmaceutical industry: to discover new non-opioid drugs that will ease these pains.

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