

Fibromyalgia Syndrome
A Pathoneurological Basis of Disease

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Abstract

Fibromyalgia (also known as fibromyalgia syndrome, or FMS) is a condition which causes its victims to suffer a wide range of symptoms, most notably chronic musculoskeletal pain. Although the causes of fibromyalgia remain unknown, recent advances help elucidate the underlying pathophysiologies of this condition, and show that it is likely not a musculoskeletal condition, but rather a pathoneurological condition.

Fibromyalgia Syndrome

A Pathoneurological Basis of Disease

Introduction

One condition which has continued to increase in the public's awareness is fibromyalgia syndrome (FMS), better known as fibromyalgia. Although many people have heard of fibromyalgia, however, few have a good understanding of this mysterious, painful condition. Even now, fibromyalgia's origins remain unknown, and this has historically led researchers to label it a psychosomatic condition. However, as research has progressed, new data has evolved to validate the claims of those suffering from fibromyalgia, indicating this condition merits further research in order to develop a cure.

While fibromyalgia was studied as early as the 1600s, as muscular rheumatism, and later in the 1800s, as hysterical paroxysm, its definite symptoms appear to have been first diagnosed in 1904, when it was called fibrositis. At that time, fibrositis was just a general word for pain that seemed to derive from muscle fibers due to inflammation. Much later, the name evolved from fibrositis to fibromyalgia, as the understanding of the condition began to increase, and researchers realized that it was not an inflammatory disease. In the 1970s, a modern understanding of this condition began to take shape, when it was described simply as pain in many locations with multiple pressure points, or highly localized areas of increased sensitivity to pressure. During this time period, medical researchers assumed that this was an autoimmune disease, and tried to identify its pathophysiology. However, they failed to find anything wrong with the autoimmune system (even during the 1990s). At this point, many researchers began to believe that fibromyalgia was in fact a psychosomatic condition.

In 1981, studies demonstrated that there was a list of eighteen consistent pressure points in addition to a common set of symptoms. Although many of the symptoms tended to be subjective (namely, the severity of pain experienced by the patient), the list supported the belief that fibromyalgia was a specific condition, and not simply a figment of the patient's imagination. This belief was reinforced in the late 1980s, when researchers noted that serotonergic drugs were consistently effective, because they helped to reduce pain (as measured with questionnaires). It wasn't until 1990, however, that the American College of Rheumatology (or the ACR) established the first diagnostic criteria. Since then, as new technology has developed, researchers have identified specific parts of the body (in particular, the central nervous system) which appear to be affected among patients suffering from fibromyalgia. This has given greater credence to the actuality of the disease (Inanici & Yunus, 2004).

Incidence

It has previously been reported that women are seven times more likely than men to develop fibromyalgia. However, studies have indicated that while 0.068 percent of men are likely to develop FMS, only 0.113 percent of women develop it (Weir et al., 2006). This means that women are only 1.6 times more likely to develop FMS than men. Overall, it is estimated that there is a prevalence of about two percent of the American population (Seidel & Muller, 2011)

Symptoms

Part of what makes fibromyalgia such a controversial disease (and why many medical professionals over the years have labeled it psychosomatic) is its diverse and complex list of symptoms. As a syndrome, fibromyalgia has many possible symptoms

which could indicate FMS, and most occur independently of each other. In addition, these symptoms often occur with other conditions, such as arthritis or chronic fatigue syndrome. Complicating the matter, these symptoms often come and go between periods of intense expression and less severe expression. For example, a patient may experience a higher level of severe pain for a time, only to return to experiencing milder pain. Because of this diversity, no two people with fibromyalgia experience exactly the same symptoms (and especially not for the same durations of various intensities). Chronic pain remains the most underlying consistent symptom of all expressions of fibromyalgia and is often musculoskeletal in nature, affecting muscles, fasciae and joints. However, fibromyalgia syndrome is often accompanied by a host of other symptoms that frequently affect various parts of the body.

Pain

Chronic pain is the most prevalent symptom of fibromyalgia. However, this pain rarely remains in one location, but spreads widely throughout the body, and often moves to different locations. Patients often report experiencing intense pain in the arm, for example, but later, in the lower back. Apart from this chronic pain, those suffering from fibromyalgia also experience high levels of pain after even mild trauma. In fact, a bump or a squeeze, which may cause the average person mild discomfort for a few seconds, tends to hurt those with fibromyalgia for up to a few minutes. A study conducted in 2004 demonstrated via MRIs that those with FMS do in fact feel more pain from stimuli than healthy controls (Giesecke et al., 2004). In addition to the chronic pain and the low pain tolerance, those with fibromyalgia frequently have a host of pressure points throughout the body which are especially sensitive to touch, and where pain often congregates

(Blumenstiel et al., 2011; Wilbarger & Cook, 2011). It is also interesting to note that among patients with FMS, EEGs (or electroencephalograms) demonstrate a quicker response to pain than in healthy controls. EEGs involve attaching electrodes to a patient's head in order to measure brain activity during various stimuli. In a study performed in 2000, EEGs of healthy controls were compared to those of FMS patients during a cold pressor test, where the test subject immerses a hand into ice water for a definite period of time. Those with FMS consistently reported the pain as "intolerable" sooner than healthy test subjects, and the EEGs indicated a higher level of brain activity in a shorter amount of time, thereby indicating that the FMS patients felt pain sooner in a quantitative manner (Stevens, Batra, Kotter, Bartels, & Schwarz, 2000).

Confusion

Apart from the pain, another characteristic of fibromyalgia is something often referred to as "fibro fog." In high-stress situations, such as events with lots of background noise or flashing lights, many of those who suffer from fibromyalgia begin to lose mental acuity. This can manifest itself in two forms. In severe cases, it can occur as mild memory loss (wherein patients have difficulty recalling information, such as common words for objects). However, it can also be seen as slow or "cloudy" thinking. This includes a drawn out decision making process as well as poor choices. To someone viewing a patient, the most notable characteristic of fibro fog is slow reflexes. Many patients who have experienced fibro fog describe it as a "zoned out" feeling, and a certain inability to do anything about it, much like when the average person is severely sleep deprived.

Stress

Another primary characteristic of FMS is high levels of stress. While some people speculate that stress causes the onset of fibromyalgia, others consider stress a symptom. In reality, this aspect of fibromyalgia is a lot more controversial, since some people simply hide stress better than others, or apply different standards to describe a stressful situation. Regardless, stress produces many effects, one of which seems to be sudden changes in emotion. Those with fibromyalgia frequently suffer from a significantly greater amount of anxiety (measured with surveys and questionnaires) than an average healthy individual, and quickly begin to worry about things that could go wrong, especially in stressful situations.

Insomnia

Many FMS patients report difficulty sleeping at night. Again, many researchers disagree as to whether this is due to pain or other conditions, or whether this causes the other symptoms. Regardless, sleep deficiency decidedly alters the lifestyle of fibromyalgia patients. First, it exacerbates the other symptoms (which are often aggravated among healthy individuals who don't get enough sleep). Second, it adds to the psychological factor among FMS patients, who often report having anxious thoughts as they lie awake at night.

Depression

One of the more crippling aspects of FMS is the emotional toll it takes on its victims. This most frequently occurs as depression. While researchers have observed physiological reasons for this depression, many fibromyalgia patients also express discouragement at the prospect of living an entire life with the symptoms (especially the

pain) of their illness. As with the other associated symptoms, however, depression tends to oscillate in its severity.

Associated Conditions

In addition to the characterizing symptoms already mentioned, another factor in fibromyalgia is that it is associated with many other diseases. Most of these associated conditions are stress-related, which means that they may share a common cause with FMS.

One of the most commonly associated conditions is known as IBS, or irritable bowel syndrome. IBS demonstrates a prevalence ranging anywhere from 30-70% among FMS patients, as opposed to the typical 10-20% occurrence among healthy individuals (Sperber & Dekel, 2010). Characterized by abdominal pain, cramping, and inconsistencies in bowel movements, IBS is similar to what the average person experiences during times of high anxiety, such as before public speaking. In fact, IBS may be more related to stress than anything else. A study conducted in 2008 demonstrates a correlation between psychosocial factors (including anxiety and sleep problems) and presentations of IBS, increasing the probability that IBS and FMS could share a common stress related etiology (Nicholl et al., 2008).

Another associated condition is GERD, or gastrointestinal esophageal reflux disease, which occurs when stomach acids “leak up” into the esophagus. This is most commonly experienced as heartburn, and causes sleep disturbances due to pain.

Another commonly associated condition is arthritis. Known for causing joint pains, arthritis manifests itself very similarly to fibromyalgia. This is one reason why fibromyalgia is so difficult to detect, since many other conditions explain, in part, FMS’s

symptoms. Arthritis adds to the pain that FMS patients feel in their joints, and can even cause joint degeneration.

Fibromyalgia also includes a host of other associated conditions, including Crohn's disease, chronic fatigue syndrome, hypothyroidism, and carpal tunnel syndrome. However, due to the length of the list, patients with FMS typically have just a few of the associated conditions.

Diagnosis

Given fibromyalgia's tendencies to look like other conditions, it is a very difficult condition to diagnose. Not only does fibromyalgia vary in how it manifests pain, but pain itself is also incredibly subjective, varying from person to person according to his or her pain tolerance. In reality, most doctors have accepted that fibromyalgia must be diagnosed by a process of elimination. However, there are also two other positive tests commonly used in its diagnosis.

Diagnosis Via the Elimination Process

As for the elimination process, some of the most commonly performed tests are blood tests, including rheumatoid factor (RF) to test for rheumatoid arthritis among other things, or a complete blood count (CBC) to rule out other potential diseases, such as lupus, anemia, or polymyalgia rheumatica. Additional tests, such as erythrocyte sedimentation rate (ESR), may also be ordered to confirm the CBC's negative results. In addition, there are blood tests searching for specific chemicals or proteins, such as checking TSH levels in the blood to rule out hypothyroidism. Negative results from these tests help to support a diagnosis from two other sets of inconclusive positive test results.

ACR Test

The first positive test created, called the ACR test (American College of Rheumatology test, developed in 1990), simply tests the number of pain-inducing pressure points in a patient. In total, there are eighteen pressure points from which to choose, as seen in Figure I. A doctor uses discernment in how much pressure to apply (though always less than nine pounds of force), and if a patient reports significant pain with mild pressure in at least eleven of the eighteen points, the test is positive for fibromyalgia. While the specific cause for these painful pressure points remains unknown, it is clear that they are frequently in similar, localized areas on the body. Modern medicine has deemed the ACR test insufficient to diagnose FMS, however, and this has led caregivers to develop other tests to assist in making a diagnosis.

WPI/SS

More recently, another method has been developed which includes two facets. First, there is a widespread pain index (WPI). For this, the patient chooses which parts of his or her body have hurt within the past week from a list of nineteen body parts. For each part listed, the patient receives a score of one, producing a total score ranging from zero to nineteen. Secondly, there is a symptom severity score (SS score). In this scoring system, the patient ranks the severity from zero to three in four different categories, including fatigue, waking up unrefreshed, cognitive symptoms (such as anxiety or fibro fog), and a fourth area, somatic symptoms in general. For the first three, a simple score is given between zero and three. For the fourth, the patient chooses from among forty-one general somatic symptoms, and tallies “points” from that (0-10 symptoms is roughly equal to one point, 11-24 symptoms is about equal to two, and 25+ is approximately equal to

three).

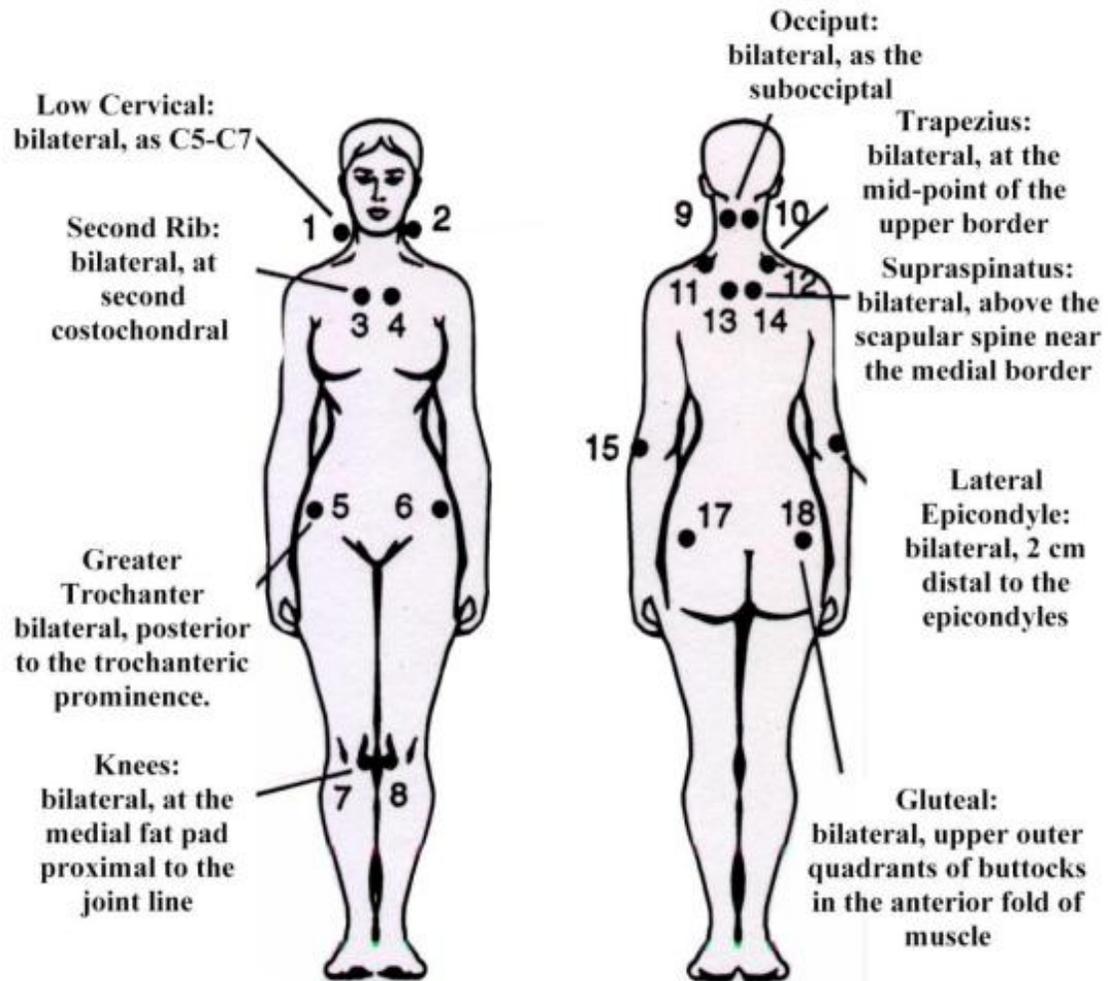


Figure I: Pressure Points in Fibromyalgia Syndrome. As can be seen, there are eighteen pressure points listed. A patient with at least eleven of these is diagnosed as positive for fibromyalgia according to the ACR test (Garcia, E., Godoy-Izquierdo, D., Godoy, J.F., Perez, M. & Lopez-Chicheri, I, 2007).

Given the scores from the WPI test and the SS score, a three part criteria was developed. First, the symptoms must have persisted for at least three months. Second, there must be no other disease that can explain the symptoms (which is why the negative tests must be run). Third, either the WPI score must be greater than or equal to seven with

an SS score greater than or equal to five, or the WPI score must be between three and six with an SS score greater than eight (Wolfe & Hauser, 2011).

The advantage offered by the second method (that is, the WPI/SS) is that it is more consistent than the ACR test. In addition to the ACR test's fluctuations based on how hard a doctor applies pressure (which is very difficult to replicate uniformly), many doctors simply cannot pinpoint the pressure points. Based on the difficulties associated with performing the ACR test, it is now recommended that caregivers use both the ACR test and the WPI/SS score tests (both in conjunction with the process of elimination), but that they rely more heavily on the latter.

Pathophysiology

The causes of fibromyalgia have yet to be understood from a biochemical or molecular biological perspective. Many researchers have speculated about what actually causes the body to respond to stress the way bodies of FMS patients do, but the answer has so far eluded them. However, recent discoveries describing the pathophysiologies of FMS patients may lead to a better understanding of this condition.

Decaying Gray Matter

Interestingly, research has demonstrated that those suffering from fibromyalgia seem to lose more gray matter in the brain than the average person. Researchers in Quebec, Canada have used voxel based morphometric analysis of gray matter in magnetic resonance images to compare brains from FMS patients with those of healthy individuals as controls. Morphometric analysis simply measures the volume and shape of the organ of interest and its subparts. Voxel based morphometry uses scanning techniques (in this case, MRI) as well as statistics to determine the size of the organ of interest. The

researchers found that patients with fibromyalgia lost on average about nine and a half times as much gray matter per year compared to a typically healthy individual. From a neurological perspective, this leads to the appearance of aging at a faster rate with regards to the brain, with about a three times greater age-associated decrease in gray matter. However, researchers haven't yet discovered the cause for this loss in gray matter (Kuchinad et al., 2007; Robinson, Craggs, Price, Perlstein, & Staud, 2011). Regardless, the correlation between decreasing gray matter volume and chronic pain has been observed in more instances than just those of patients suffering from FMS (Wood, 2010). In fact, the decrease in brain matter has also been observed in patients who are diagnosed with bipolar I disorder (Li et al., 2011).

Regions of the brain which tend to experience the greatest impact are the cingulate, insular and medial frontal cortices, and the parahippocampal gyri (Kuchinad, et al., 2007). The cingulate, a part of the limbic system, plays a key role in the formation of emotions and may help explain the difficulty some FMS patients have controlling their emotions. In addition, it is a major pain regulator of the brain, and an alteration in its function could explain the low pain tolerance of FMS patients. The insular cortex takes part in a wide range of functions, including social emotions, "emotional tasks with cognitive demand" and pain management (Phan, Wager, Taylor, & Liberzon, 2002; Robinson, et al., 2011). Interestingly, the insular cortex also plays a role in irritable bowel syndrome (IBS), a major associated symptom of fibromyalgia, by altering pain perception of the rectum (Song et al., 2006). The frontal cortex is important in general cognitive processes, including motor responses and social responses. Multiple studies indicate that there is a strong association between altered frontal cortex function and

several psychiatric conditions including depression, schizophrenia, and obsessive-compulsive disorder (Jaracz & Rybakowski, 2005; Tamminga & Buchsbaum, 2004). As for the parahippocampal region, research indicates that it is involved with topographical learning and that in some cases, damage can be associated with schizophrenia (Aguirre, Detre, Alsop, & D'Esposito, 1996; McDonald et al., 2000). However, this doesn't seem to match any of the commonly reported symptoms of FMS, which may indicate other areas of the brain also assist in topographical learning.

Decreased Pain Inhibition

Of all the pathophysiologies associated with fibromyalgia, one of the most keenly observed is a decrease in pain inhibition. Using various techniques (such as thermal scanning or MRI), researchers have observed brain activity during mild physical trauma in patients with FMS compared to healthy individuals, and have found an irrefutable increase in pain sensitivity (Normand et al., 2011). Again, researchers have yet to discover why FMS patients are unable to inhibit pain as efficiently as healthy individuals, and whether the condition stems from the peripheral nervous system, the spinal cord, or the brain. However, one study has shown, via functional MRI scans, that healthy individuals have significantly higher levels of connectivity in the amygdala, hippocampus, brainstem, and especially the rostral anterior cingulate cortex (Jensen et al., 2012). Again, since these play significant roles in pain moderation, it seems plausible that the telltale FMS symptom of chronic pain may stem from a pathoneurological source.

Chemical Imbalances

Serotonin. One of the best known neurotransmitters, serotonin (also called 5-HT for 5-hydroxytryptamine), seems to be involved in FMS. Multiple studies have suggested

that serotonin levels in the brain may be lower than normal among patients with fibromyalgia (Neeck, 2000). Since serotonin is the “feel good” neurotransmitter, it is fairly obvious that a decrease in its concentration could cause some of the symptoms of FMS. However, there is some debate among researchers as to what causes the low serotonin levels in FMS patients. A study done in 1999 seemed to indicate that there may be a correlation between FMS and 5-HTT, a serotonin transporter which was previously assumed to be responsible for the low serotonin levels (Offenbaecher et al., 1999). There are two primary types of the degenerate repeat polymorphic region of the gene which encodes serotonin, 5-HTTLPR (serotonin-transporter-linked polymorphic region), a long allele (L) and a short (S), and the study seemed to indicate the those with FMS were predisposed to having an S/S genotype, which other studies have demonstrated leads to a susceptibility to depression. A more recent study, however, suggests that there is no significant correlation between 5-HTT and FMS. This study found that among one hundred and twenty volunteers (half were normal healthy candidates and the other half had been diagnosed with FMS), the percentages of the genotypic variations were similar in both the FMS patients and the healthy candidates (Gursoy, 2002). Another study, performed in 2012, also indicates that there is little to no correlation between fibromyalgia and 5-HTT, but does reveal a strong association between FMS and the expression of a serotonin receptor, 5-HT_{2A}, and specifically its T102C polymorphism (Y. H. Lee, Choi, Ji, & Song, 2012). Interestingly, many other studies have found that an over expression of this specific polymorphism is often associated with suicidal tendencies (Du, Faludi, Palkovits, Bakish, & Hrdina, 2001; Vaquero-Lorenzo et al., 2008).

Brain-derived neurotrophic factor. A second factor which may play a significant role in fibromyalgia is known as brain-derived neurotrophic factor, or BDNF. BDNF has previously been demonstrated to play a role in depression and anxiety (Lang et al., 2005; Montag, Reuter, Newport, Elger, & Weber, 2008). To study this relationship, serum levels of BDNF were measured in both healthy controls and FMS patients during periods with varying intensities of depression, measured with the NEO-Five Factor Inventory (a personality test to measure, among other things, neuroticism, which is the tendency towards anxiety), and the State-Trait Anxiety Inventory, also measuring anxiety. Interestingly, there seemed to be a correlation between decreased levels of serum BDNF and the severity of the patients' depression (Lang, et al., 2005; Nugraha, Korallus, & Gutenbrunner, 2013). However, a separate study demonstrated that disrupting the signaling pathways involving BDNF did not induce depression, but did decrease responses to antidepressants (measured again with questionnaires). This suggests that a shortage of BDNF may not be the sole cause of depression, but that increasing BDNF concentrations may be a target for antidepressant drugs, in order that other antidepressants can be more effective. (Martinowich, Manji, & Lu, 2007).

Treatment

Sadly, once a diagnosis has been given, many individuals begin to experience despair, since there are currently no cures for fibromyalgia (given that researchers are still unsure what causes it). At best, various medications and treatments are administered in order to reduce the severity of symptoms, but that is all that doctors can currently do, as is often the case with diseases. However, the field of palliative care (which simply reduces the severity of the symptoms) for FMS patients offers a wide range of treatment

plans which seem to significantly reduce suffering, including: medications, lifestyle changes, and alternative medicinal treatments

Medications

Obviously, since the cause of fibromyalgia remains unknown, there is a limit to the effectiveness of medications. As is the case with many diseases, caregivers are simply unable to cure the problem itself and must resort to masking it. With FMS, however, it is even more difficult to alleviate the symptoms, since it is a syndrome with such a wide range of symptoms. Regardless, medications can provide partial relief from many of the symptoms associated with fibromyalgia, including: pain, anxiety, and insomnia.

Analgesics. One such class of medication is, obviously, analgesics. While many over the counter drugs (such as acetaminophen, tramadol, and ibuprofen) provide initial relief, more powerful analgesics (like morphine or codeine) are periodically administered to better control pain. Because some of these more powerful analgesics are potentially addictive, they may not be the best solution, however. Patients with fibromyalgia seem to be particularly sensitive to codeine, and often experience nausea. In addition, many pain medications can cause drowsiness and difficulty concentrating, which mimic one of the major symptoms of fibromyalgia anyway, making these drugs less beneficial to an FMS patient.

However, some analgesics do offer hope. For example, one class of analgesics which shows a lot of promise is the 5-HT₃ receptor antagonists (Seidel & Muller, 2011). 5-HT₃ receptors are ligand-gated ion channels, which when activated by an agonist (such as serotonin) have been shown to cause nausea, vomiting, seizures and, more importantly for FMS, excitation of the nociceptive neurons (if the receptors are located in the

peripheral nervous system). As a result, an antagonist to 5-HT₃ can in essence “calm” the excited neurons, leading to a decrease in hyperalgesia, or pain sensitivity. Administration of 5-HT₃ antagonists is currently favored for FMS patients who have physical pain (presumably from nociceptors), but no psychological distress.

Antidepressants and anti-anxiety medications. Other classes of drugs often prescribed to FMS patients are antidepressants and anti-anxiety medications, which help with the more psychological aspects of fibromyalgia. As for the antidepressants, many classes of drugs seem to have positive results, although some are more beneficial than others. One class that seems to be useful is serotonin reuptake inhibitors, such as duloxetine and venlafaxine, usually prescribed for major depressive disorder (MDD) and general anxiety disorder (GAD).

In addition to general serotonin reuptake inhibitors, specific serotonin reuptake inhibitors (which exclusively prevent the degradation of serotonin) may be tried, such as: fluoxetine, paroxetine, and citalopram. Interestingly, although these drugs tend to produce a weaker effect, they often have a higher tolerability profile, meaning fewer patients with FMS experience adverse effects, such as allergic reactions, nausea, or other side effects, when they take these drugs (Dharmshaktu, Tayal, & Kalra, 2012).

Simply administering serotonin directly has also shown to produce some positive effects on depression and insomnia (Juhl, 1998). Anti-anxiety medications, such as Klonopin, can also help by reducing restlessness (especially at night) and by activating pain inhibitors in the body to facilitate sleep.

Non-steroidal anti-inflammatory drugs. Non-steroidal anti-inflammatory drugs (NSAIDs) are sometimes offered by doctors in lieu of analgesics, since inflammation has

historically been assumed to play a major role in the pain. However, these often produce minimal results, which is why many caregivers no longer believe that fibromyalgia is an inflammatory disease. (The ineffectiveness of NSAIDs does at least offer researchers a clue as to the origins of fibromyalgia, and indicates that this disease likely does not stem from a purely musculoskeletal derangement).

Hypnotic drugs. Since many FMS patients report experiencing non-restorative sleep and since many of the symptoms found in FMS are considerably exacerbated by a lack of deep sleep, an obvious answer would be to administer sleeping pills. However, many sedative drugs have proved ineffective in providing quality sleep. This could be due to a decrease in what are called “sleep spindles” in patients with FMS (Landis, Lentz, Rothermel, Buchwald, & Shaver, 2004). When an individual is asleep, disruptions are typically mitigated by short periods of intense brain activity known as sleep spindles, which seem to help maintain tranquility, almost as though the brain is choosing not to wake up. This could explain why simply putting patients to sleep seems ineffective at providing quality rest, since the pills don’t necessarily cause a deeper sleep. As of yet, researchers have not discovered what causes sleep spindles, or why some people tend to have more than others, and are examining drugs that may boost their frequency.

Anticonvulsant drugs. Two of the most commonly prescribed medications for fibromyalgia are pregabalin and gabapentin. However, these two drugs are classified as antiepileptic drugs, and are administered predominantly to epileptics. Some research suggests that both seem to be relatively effective, although they do have significant adverse effects, including dizziness, somnolence and dry mouth (Tzello et al., 2010). Regardless, pregabalin is the better known drug and seems to be safe (Straube, Derry,

Moore, & McQuay, 2010), making it the drug of choice. Researchers are beginning to suspect that antiepileptic drugs (AEDs) may act by binding to the alpha2-delta subunits of a voltage gated calcium ion channel (Weissmann, Di Guilmi, Urbano, & Uchitel, 2013). This is relevant to FMS because these drugs, which reduce epileptic neuronal hyperexcitability as well as neuropathic pain, may have a common pathway (possibly in the Ca²⁺ ion channel) (Bialer, 2012).

Lifestyle Changes

In addition to medications, other simple treatment plans, like the pharmaceuticals, only reduce the severity of the symptoms. Also, there is disagreement among those with fibromyalgia as to which of the changes have the greatest impact. Regardless, many FMS patients attest to the value of lifestyle habits in reducing symptoms, even though these dramatic changes are often the most difficult for the FMS patient to continue to make.

Dietary changes. One of the easiest changes in lifestyle that can be made by an FMS patient is an alteration in his or her diet. However, these recommendations can change dramatically from individual to individual. For example, many women find that chewing ice helps, while others find relief with a specific drink, such as a Diet Coke or (rarely) coffee. Since the effects of a food or drink vary considerably, it seems plausible that these may function better in reducing stress than by producing a specific physiological effect.

Some dietary changes seem to have value for other reasons as well. For example, a study conducted in 2000 demonstrated a *strong* correlation between a vegan diet and an improvement in fibromyalgia symptoms, including reduced joint stiffness, higher quality of sleep, and less pain (measured with both a general health questionnaire and a

rheumatologist's questionnaire) (Kaartinen et al., 2000). Other rheumatoid patients given a vegan diet, specifically those rich in antioxidants, lactobacilli, and fiber, also experienced significant reductions in their pain (Hanninen et al., 2000).

Two other diet studies which omit specific food groups seem to make an impact. In the first, test subjects participated in a modified elimination diet, eating predominantly rice protein powder and consuming a higher amount of phytonutrient-rich medical food. These FMS patients scored better in many pain and health questionnaires, and even seemed to have higher pain tolerance for up to five tender points (Lamb et al., 2011).

A second study reported a few cases (which do seem to be rare exceptions) in which patients actually seemed to suffer from an excess of aspartame in their diets. By removing aspartame from the diets of these patients (many of whom had been taking aspartame supplements), the chronic pain disappeared almost entirely, even after years of pain. The pain would then reappear with the reintroduction of aspartame into the patients' diets (Ciappuccini, Ansemant, Maillefert, Tavernier, & Ornetti, 2010). Although these cases appear unusual, the removal of aspartame is an easy treatment for those whom it affects.

Exercise. Despite the fact that vegan diets do seem to play a role in pain management for FMS patients, more recent studies suggest that these benefits may occur because these diets induce weight loss. One study in particular demonstrated a strong correlation between BMI and the number of pressure points a FMS patient has, as well as a connection between total levels of cholesterol and triglycerides and pain experienced by those with fibromyalgia (Cordero et al., 2013).

In addition, other exercises have been shown to alleviate both immediate and long-term pain. One specific exercise which seems to be beneficial is swimming. A study performed in 2012 demonstrated that low intensity swimming in warm water led to an immediate decrease in the pain experienced by participants. It is interesting to note that this seemed to have a greater effect on older women and on those with greater pain (Segura-Jimenez et al., 2012). Other review studies have also noticed a trend that both aquatic exercise and balneotherapy (that is, bathing in warm water or water massages, etc.) assist in minimizing pains associated with FMS (Verhagen, Cardoso, & Bierma-Zeinstra, 2012).

However, not all of the benefits of exercise are entirely physical. Many studies have demonstrated that long term exercise and stretching provide psychological stability and health (Sanudo, Galiano, Carrasco, de Hoyos, & McVeigh, 2011). In large part, this could be the result of an interesting finding that has been clearly demonstrated over the past decade: exercise increases brain-derived neurotrophic factor concentrations (Johnson & Mitchell, 2003; M. C. Lee et al., 2013; Oliff, Berchtold, Isackson, & Cotman, 1998). As previously mentioned, BDNF may play a role in some of the psychological factors associated with FMS. As a result, an increase in exercise could clearly lead to a better mindset.

An additional study which may have implications for FMS suggests that exercise increases the concentrations in the brain of both vascular endothelial growth factor (VEGF) and insulin-like growth factor type 1, as well as increased connectivity between the bilateral hippocampus and the bilateral middle temporal gyrus, demonstrating that exercise does in fact alter the brain (Voss et al., 2013). The hippocampus and middle

temporal gyrus, both parts of the temporal lobe, seem to play a role in emotional control and linguistic comprehension, among other things. This could help explain why exercise can have such positive effects on FMS patients (although exercise tends to help even healthy individuals considerably).

Sleep pattern management. Perhaps one of the biggest factors, however, seems to be getting enough sleep. Although, as noted previously, medications are insufficient to consistently and effectively provide restful sleep, some patients with FMS are able to enhance their own sleep quality. Others with FMS have reported sleeping more restfully by changing their environment before going to bed (that is, turning off all lights, making sure there will be no noises, etc.). If patients with FMS also spend time thinking about positive things before going to bed, anxiety may be reduced, leading to more restorative sleep.

Alternative Treatment

Stress reduction. A major factor in the treatment of fibromyalgia is helping its victims learn how to manage stress. There is a plethora of techniques for managing stress, and different victims of FMS will advocate different techniques. Perhaps one of the most popular techniques is receiving muscle massages, which has little research supporting its efficacy, but is commonly recommended by those with FMS (Field et al., 2002).

Another technique for reducing stress (although often less frequently supported by medical practitioners) is meditation. Despite the negative connotations often associated with meditation due to its religious aspects, several studies have demonstrated an improvement in pain experienced by those with FMS who practice various forms of meditation (Liu et al., 2012; Schmidt et al., 2011).

Conclusion

Summary

Fibromyalgia syndrome is an increasingly well-known condition. However, many aspects of this condition remain shrouded in mystery. While medical professionals have developed lists of common symptoms, or associated diseases, and have established a standardized diagnostic procedure for fibromyalgia, researchers have yet to determine what actually causes this condition, or even all the abnormalities in the body which are associated with FMS. However, certain pathophysiological tendencies have been established and many palliative treatments have been considered and tested.

Discussion

Traditionally, rheumatologists have been the physicians most often responsible for diagnosing and treating fibromyalgia syndrome, since they are most familiar with the frequently associated joint and muscle conditions. However, a closer look at the pathophysiology behind FMS, as well as the treatments which seem to be most effective, indicates that this condition is predominantly pathoneurological in nature, whether in chemical imbalances (such as serotonin or BDNF) or in hyperexcitable sensory neurons. In light of these findings, neurologists rather than rheumatologists may be better equipped to take the lead in research and new drug development.

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