

Scientists Learning More About What Causes Your Symptoms



June 2009 eNews Alert

Dear P.A.N.D.O.R.A., Inc,

A thorough understanding of the causes of your many symptoms should enable researchers to develop more effective therapies for fibromyalgia (FM). While this was obviously not the case ten to 20 or more years ago when your symptoms first appeared, the technology has evolved to the point where tailor-made medications for FM don't seem too far-fetched. Or, at least this seems plausible for your pain-related symptoms.

Although your short-term memory or fibro-fog symptoms may still be baffling to you and your doctor, researchers are trying to get a better handle on why you struggle with remembering things. But as you will read in this month's *eNews Alert*, the technology for picking up your specific sleep disorders is seriously lacking. Also, information about a new drug, particularly Savella, is of great value to patients and we hope that if you have tried this drug you will take part in our short survey on it.

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FM Brain NOT Inhibiting Pain

Physicians are accustomed to treating pain and other symptoms that they can objectively measure, and this presents a major obstacle for people with fibromyalgia (FM). While pain is supposed to be a warning signal, it has become permanent in the absence of any sign of tissue injury in people with FM. However, a recent medical report provides evidence that the pain of FM is not controlled by emotional factors.* In fact, functional MRI (fMRI) shows that the pain processing centers become less active when a painful stimulus is applied to the thumb. This is the opposite of what happens in healthy control subjects.

Although previous brain imaging studies have shown that sensory inputs to the central nervous system are magnified, the design of the current study was to focus on the pain inhibitory process. This system originates in the brain to release pain-fighting substances into the spinal cord to filter out or tone down the impact of incoming painful stimuli. Studies have shown that it doesn't work in FM patients. So this study, supported by the International Association for the

Study of Pain, was designed to see if the problems might originate in the brain.

Sixteen FM patients and 16 age-matched controls were enrolled in the study. All subjects were off of their medications and the FM group did not have any other medical condition. Pressure stimuli (anywhere from light touch to very painful) were applied to the thumb while each participant was in the fMRI scanner. A random order was used so no one could anticipate when or how intense the next stimulus would be. The amount of thumb pressure that equaled a subjective pain rating of 5 on a scale of 0 to 10 was determined for each person in the study. This enabled the research team to look at the fMRI response of each person (FM patient or healthy control) for the identical subjective pressure pain rating.

When the pain felt by each person was the same (a rating of 5), the activity of the brain regions that pertain to the emotional and sensory processing of the pain was the same in the FM group as the healthy group. This strongly argues against the possibility that emotional factors are somehow causing FM patients to perceive pain as more intense.

Looking at the brain activity for the entire range of pain ratings was most revealing. Ordinarily, brain activity increases in response to a pain stimulus, but this was not the case for people with FM. Painful stimuli lead to reduced activity in the brainstem, anterior cingulate cortex, and thalamus (the three major areas that make up the inhibitory pain system in the brain). Clearly, there is an imbalance in FM patients between incoming pain signals and the necessary activation of the brain centers to counteract or inhibit the pain. This imbalance is partly responsible for the increased pain sensitivity in FM, and the authors suggest that this brain imaging technique be used to determine if the inhibitory system balance can be restored with medications.

It should be noted that the anterior cingulate cortex has one of the highest concentrations of opioid receptors, and its activity is essential for effective opioid analgesia. Deactivation of this area could greatly compound the painful symptoms of FM. When the number of painful signals increases (pulled muscle, sore throat, over-exertion, etc.), the body's release of natural opioids (such as endorphins) or the consumption of opioid medications will have fewer receptors to act on and the pain relief will be less than normal. So while opioids do help tame the pain, this could offer an explanation as to why they are not as effective as they should be.

* Jensen KB, *et al.* [Pain](#) 144:95-100, 2009.

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Imaging the Effects of Savella

The pain inhibitory system is the suspected area where Savella (milnacipran) works to reduce pain in people with fibromyalgia. The study above shows that fibromyalgia patients have decreased activity in the brain regions believed to be involved in the pain inhibitory system, such as the thalamus and the anterior cingulate cortex. So when pain signals enter the spinal cord, the brain areas that should be actively releasing pain-fighters, such as opioids, serotonin and norepinephrine, actually become less active. This is the opposite of what happens in people without pain and provides an objective basis for why fibromyalgia patients hurt all over.

A study on the effects of Savella on pain can be read in the [Latest News section of our website](#).

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The Scoop on Savella?

The latest U.S. Food and Drug Administration approved drug to treat fibromyalgia, Savella, became available May 4. Since the release of this medication, many people have asked us for information about Savella. During the past five years of clinical trials, Fibromyalgia Network has referred to Savella by its study name “milnacipran” in several back issues.

Details about the medication, its side effects, and who may or may not be good candidates for the drug can be read in the [Latest News Archives section of our website](#).

Since Savella is a new medication in the United States, many patients and doctors have been inquiring about it. Fibromyalgia Network would like to provide you with useful feedback about this drug. If you are taking or have taken Savella, we invite your comments on this one-page survey. We hope to share these comments in an upcoming *eNews Alert*. As usual, all information contained in this survey is anonymous.

[If you have taken Savella, please click here to give us your comments.](#)

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Treating Airflow Restrictions During Sleep

Ninety-five percent of people with fibromyalgia (FM) wake up feeling unrefreshed. But don't expect a visit to a sleep lab to pinpoint your problem symptoms. Depending upon the research study you read, the prevalence of primary sleep disorders in FM and chronic fatigue syndrome (CFS) patients varies widely, but sometimes it may be as little as 18 percent.¹

Primary disorders identified by overnight sleep studies include obstructive sleep apnea, periodic limb movement sleep (PLMS), and narcolepsy. So the difficulties you face all night long are not usually caused by what scientists view as primary sleep disorders, but that does not make them any less real.

Speaking at the International Association for CFS, **Charles Lapp, M.D.**, of Charlotte, NC, says, “We just are not doing the right studies to find the sleep disorders in FM and CFS patients.” In other words, the current technology is not capable of accurately detecting the sleep problems you face each night. In the July 2009 issue of the *Fibromyalgia Network Journal* you will read about the less researched yet very common sleep disorders that Lapp finds in his FM and CFS patients, as well as his recommendations for treating them. And although upper airway resistance syndrome (UARS) is a sleep disorder that can be identified during a sleep study, many centers tend to overlook it.

“The problem,” says Lapp, “is that UARS patients do not meet the criteria for apnea, in which the airway collapses and the breathing stops.” People with UARS struggle with breathing and this causes frequent arousals associated with daytime fatigue, headaches, and irritable bowel. However, the airways don't collapse in UARS.

To better understand the difference between apnea and UARS, Lapps suggests that you consider the back of your throat to be like a tent. When you are upright, your throat is open and there is lots of air movement through the tent. If people with apnea lie down to sleep, the tent in the back of their throat collapses. They stop breathing for a moment and their oxygen levels drop, until they gasp for breath and become aroused. But, once placed on a continuous positive

airway pressure (CPAP) machine, this blows up their tent so that they breathe easily and sleep throughout the night.

“UARS is not a tent disorder because the tent never collapses and the breathing is not obstructed,” says Lapp. “UARS is more like breathing through a straw or hose. These patients struggle to breathe through a partially deflated tent and because of this they do not get deep sleep.” One study has shown that almost all FM patients have UARS and placing them on CPAP does benefit them, but not to the extent that it works for apnea patients.² “I can tell you from clinical experience that CPAP is not the answer,” says Lapp. “It helps patients sleep better, but it doesn’t cure their pain or fatigue.”

Being able to tolerate or afford CPAP is another issue for people with UARS. Health insurance companies often will restrict CPAP coverage to obstructive sleep apnea patients who are able to consistently demonstrate a 3 to 4 percent drop in blood oxygenation levels (something that doesn’t occur with UARS). Lapp says that some of his patients sleep in a recliner to keep the airways open. Aggressive treatment of acid reflux and nasal allergies, including irrigation of the sinuses with saline sprays or the use of a neti pot, is helpful. Sleeping on one’s side will also improve airflow, and you can either use a pillow wedge or arrange various sized pillows to create a ramp that props up the head if CPAP is not an option.

Although CPAP and other approaches will not cure your FM or CFS, Lapp emphasizes that it is a sleep disorder that should be addressed because patients do sleep better. In addition, he says CPAP does prevent hypertension and stroke, and reduces metabolic diseases that can lead to weight gain and diabetes. In other words, every little bit counts!

1. Reeves WC, et al. *BMC Neurol* 6:41, 2006.

2. Gold AR, et al. *Sleep* 27:459-66, 2004.

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Improving Short-Term Memory

Have you ever walked into a room to retrieve something specific when someone interrupts and asks you a question? You answer the question but forgot why you originally went into the room. Does it seem you can accomplish routine tasks very efficiently, but you tend to forget what you just read or the name of the person you were just introduced to, especially if you are distracted?

Doctors **Frank Leavitt, Ph.D.**, and **Robert S. Katz, M.D.**, of Rush Medical College in Chicago, have been studying how distractions impact the retention of memories in patients with fibromyalgia (FM) for years.¹ They found that fibro patients lose new information that is presented verbally at a rate of 44 percent greater than non-FM people who claim to have memory problems, and three times greater than healthy normal people. However, without distractions, they found the short-term verbal memory of FM patients is normal.

Now they want to find out if it is the distraction that causes an inability to remember an earlier task or perhaps some kind of fault in the initial memory process.²

Recently, the two researchers tested 91 women with FM who reported having memory problems against 43 women of similar age and education who also reported having memory problems but did not have FM. All of the women were given four tests verbally that measured their memory. In the first test (Logical Memory), the participants were asked to recall as much as they could about two stories (2 paragraphs/50 segments) immediately after hearing them. They were again asked to recall as much as they could 30 minutes later. The women earned a point for each segment of

the story they remembered. In the second test (Paired Associates), 16 words were paired up (i.e. truck/arrow) and reviewed or "rehearsed" by the participants four times. Participants then waited 30 minutes and tried to recall the word pairs again.

In the third test (ACT), the women participated in a totally unrelated "distraction" task between being given and then recalling a series of three-letter groupings. Immediately after hearing the groupings, they were asked to count backwards by threes from a specific number for at least nine seconds to cause "distraction." After counting, they were asked to recall the groupings of three letters. The ACT involved the participants in three tasks in a row (receiving new information, distraction, and recalling the new information). They were not given time to review any task in their mind before having to jump into the next task.

In the final test (RAVLT), participants were read a 15-word list of nouns (list 1) five times. Participants were asked to repeat back from memory the list after each reading. Next, a second list of 15 words (list 2) was read as a distraction and the subjects were asked to recall the words in list 2. After verbalizing the "distraction" list, participants were asked to recall the first list (the one that they rehearsed five times).

Interestingly, the fibro patients recalled information on the first two tests (Logical Memory and Paired Associates) slightly better than the non-FM patients both immediately after the test and after the 30-minute wait. In addition, the FM patients also scored slightly better on the fourth (RAVLT) test that included the repetition or rehearsal of words, even though a distraction phase (list 2) was added.

The only test in which the FM patients scored significantly worse was the ACT, which prevents rehearsal and includes a distraction phase. For the ACT, 87 percent of the patients scored in the "impaired" range. In comparison, 46 percent of the control group who claimed to have memory difficulties but were otherwise healthy scored in the "impaired" range.

Leavitt believes the act of repetition and rehearsal mechanisms in the brain are intact for FM patients and play an important role in managing distraction. "The retention of repeated information interrupted by a source of distraction is normal in patients with FM, indicating that distraction does not disrupt memory for 'well-rehearsed' information at a rate that is very similar to a healthy population following a distraction."

Leavitt and Katz think the culprit for the poor recall on the ACT test with FM patients very well may be a "weak memory trace" due to a shorter amount of processing time. In previous studies, the researchers noted that FM patients take milliseconds longer to verbally identify objects compared to healthy subjects. So when patients are spending a bit more time processing one task, they may be short-changing themselves when trying to embed a second task into memory. If they are immediately distracted following the second task, their short-term memory processes are further abbreviated.

"Presumably, distraction is more disruptive to individuals with fibromyalgia because their memory traces have not built sufficient Velcro to stick on memory on their own," write the two investigators. While additional research and other variables such as sleep, fatigue, and pain need to be considered, the theory may account for your fibro-fog.

In the meantime, Leavitt and Katz suggests that FM patients who wish to improve their ability to remember might want to review a few times what they need to recall later to create a solid, long-term memory. "Adding rehearsal practice seems to make up for losses in processing time and creates a durable memory trace that is available for later recall and less affected by distraction. One way to support memory in patients with FM may be added rehearsal."

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Life Events Linked to FM at Age 50

While geneticists are pinning down gene glitches that may make people more vulnerable to developing chronic painful conditions like fibromyalgia (FM), scientists in the United Kingdom are taking a different approach. Children born in England, Scotland, and Wales during one week in March of 1958 are part of a large ongoing database called the National Child Development Study that is being used to follow a variety of health and family-related issues. **Gareth Jones, Ph.D.**, and his team in the UK tapped into this database to determine if any adverse events that occurred by age 7 could have predicted the onset of FM in the subjects who are now age 50.*

Seventy percent of the more than 10,000 people in the database had recently completed all of the questions pertaining to pain, including filling out pain diagrams and indicating how long their pain has persisted, if they had any pain at all. The prevalence of chronic widespread pain for a minimum of three months duration (a requirement for FM) was 12 percent. This figure was the same for the men and women in the sample. This is not a surprise because many researchers in the field believe that FM occurs equally in both genders, but that the high tender point count required by the rheumatology criteria is biased toward women (so men have a more difficult time getting the diagnosis).

The health, economic, and family issues were reviewed for all subjects when they were age 7 (not just the 12 percent with presumed FM). A comparison was done between those with the widespread pain of FM and those without it. The strength of this study has to do with the fact that the medical records and family histories of the subjects at age 7 were pulled for analysis. In other words, the answers were not based on retrospective recall that can be very colored and inadequate after 43 years have passed.

Children who either had prolonged hospitalization or who were in a motor traffic accident were 1.5 to 2 times more likely to develop the chronic widespread pain similar to FM by the time they were 50. Other types of trauma, as well as abuse, family dysfunction, or economic hardship did not lead to an increased development of FM later in life.

Whiplash-type motor vehicle accidents have been documented in many studies to lead to the development of FM. In the July 2009 *Fibromyalgia Network Journal*, you will read why simple movements of the neck may worsen your fibro symptoms and which treatments are most likely to relieve this type of pain amplification (both drug and non-drugs approaches). Indeed, researchers are making progress with identifying the many sources of your pain, as well as risk factors that may lead to their development.

* Jones GJ, et al. [Pain](#) 92-96, 2009.

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Wishing you a happy and safe Fourth of July!

Kristin Thorson & the Staff of FM Network

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