

A Holistic Explanation for the Fibromyalgia Enigma: Autonomic Nervous System Dysfunction

By Manuel Martínez-Lavín, M.D.
Instituto Nacional de Cardiología Mexico
(National Cardiology Institute of Mexico)

This article discusses scientific evidence supporting the notion that **all** fibromyalgia (FM) features can be explained on the basis of autonomic (sympathetic) nervous system dysfunction. On this basis, a holistic approach for FM treatment is proposed.

My first argument is that FM is a multi-system illness. This means that FM symptoms are not limited to the muscles as the name fibromyalgia may suggest. It is obvious that this illness also produces dramatic manifestations in different organs and systems of the body. The most frequent associated complaints are: fatigue, sleep disorders, morning stiffness, headache, a numbness and tingling feeling in the extremities, restless legs, anxiety, dryness in the mouth, cold-clammy hands, irritable bowel, mental fogging, and cystitis. So, any valid theory attempting to explain FM mechanisms should first give a coherent explanation for the presence of these disparate symptoms in the same patients. When we started our FM research at the National Cardiology Institute of Mexico, our working hypothesis was that all of the above-mentioned features could be explained on the basis of autonomic nervous system dysfunction.

What Is the Autonomic Nervous System?

The autonomic nervous system (ANS) is the portion of the nervous system that controls the function of the different organs and systems of the body. For instance, it regulates body temperature, blood pressure, heartbeat rate, and bowel and bladder tone, among many other variables. It is "autonomic" because our mind does not govern its performance; rather, it works below the level of consciousness. One striking characteristic of this system is the rapidity and intensity of the onset of its action and its dissipation. Centers located in the central nervous system (brain stem, hypothalamus, and thalamus) and in the spinal cord activate the ANS. These centers also receive input from the limbic system and other higher brain areas. This means that the ANS is the interface between mind and body functions. These connections enable the ANS to be the main component of the stress response system in charge of fight-or-flight reactions.

The ANS works closely with the endocrine system (the hormonal system), particularly the hypothalamic-pituitary-adrenal axis. Another endocrine axis closely related to the ANS involves growth hormone secretion.

The peripheral autonomic system is divided into two branches; sympathetic and parasympathetic. These two branches have antagonistic effects on most bodily functions, and their proper balance preserves equilibrium. Thus, the ANS represents the *ying-yang* concept of ancient eastern cultures. Sympathetic activation prepares the whole

body for *fight or flight* in response to stress or emergencies; in contrast, parasympathetic tone favors digestive functions and sleep. The sympathetic autonomic branch extends from the brain stem to the spinal cord and features rich sympathetic nerve tissue in the neck and pelvic areas (important facts for FM research). From the spinal cord, the sympathetic nervous system goes to our internal organs and to the extremities. At the skin level, sympathetic activity induces cold clammy hands, mottled skin, and *piloerection* (goose flesh).

The action of the two branches of the ANS is mediated by *neurotransmitters*. *Adrenaline* (also known as *norepinephrine*) is the predominant sympathetic neurotransmitter whereas *acetylcholine* acts in the parasympathetic periphery.

Until recently, the action of this extremely dynamic ANS has been difficult to assess in clinical practice. Changes in breathing pattern, mental stress, or even posture alter immediately and completely the sympathetic/parasympathetic balance. Nevertheless, with the introduction of a new powerful cybernetic technique named *heart rate variability analysis*, the outlook has changed dramatically.

What is Heart Rate Variability Analysis?

This technique is based on the fact that the heart rate is not uniform but varies continuously from beat to beat by a few milliseconds. The periodic components of this endless heart rate variation are dictated by the antagonistic impulses that the sympathetic and parasympathetic branches have on the heart. Cybernetic recording of this constant variability is able to estimate both sympathetic and parasympathetic activity. The elegance of this method resides in the fact that all measurements are derived from electrocardiograms, so patients are subjected to no discomfort whatsoever.

Heart rate variability analysis is not a test that a patient can readily obtain from practicing physicians. So far, this test is largely confined to research centers.

Our Research on Fibromyalgia

We have used heart rate variability analysis to estimate ANS function in patients with FM. We have found that such patients have changes consistent with relentless hyperactivity of their sympathetic nervous system which continues 24 hours a day. Very interestingly, in a different study, we subjected FM patients to a simple stress test which involved having them stand up. Their overworked sympathetic nervous system became unable to further respond meaning that the system was already exhausted.

It is known that as we stand up, blood tends to pool in the lower parts of the body. In normal circumstances, there is an immediate sympathetic surge that compensates for this blood shift and maintains normal blood circulation to the head. People with FM clearly have an abnormal response, and their sympathetic nervous system fails to respond properly. It is pertinent to mention that researchers from different parts of the world have confirmed these abnormal heart rate variability findings in patients with FM.

Based on this research, we proposed that *dysautonomia* (the medical term for ANS dysfunction) is frequent in patients with FM. Such *dysautonomia* can be characterized as a sympathetic nervous system that is persistently **hyperactive** but **hypo-reactive** to stress. Furthermore, we propose that such *dysautonomia* explains all FM features. Our ANS findings fully agree with previous ground-breaking research on sleep disorders and hormonal abnormalities in FM.

Dysautonomia Explains All FM Features

Sympathetic *hypo-reactivity* provides a coherent explanation for the constant fatigue and other symptoms associated with low blood pressure, such as dizziness, fogginess, and faintness. This phenomenon can be compared to what would happen to a constantly forced engine that becomes unable to speed up in response to further stimulation.

Relentless sympathetic *hyperactivity* also explains the sleep disturbances associated with FM. It is known that parasympathetic tone predominates during deep sleep stages and that seconds before awakening episodes there is a sympathetic surge. Our concurrent studies of polysomnography and heart rate variability analyses have shown that FM people have relentless nocturnal sympathetic hyperactivity associated with constant arousal and awakening episodes.

Sympathetic *hyperactivity* may also explain the cold, clammy hands (pseudo Raynaud's phenomenon) and the constant dryness in the mouth often seen in persons with FM. Investigators who have directly studied irritable bowel syndrome and interstitial cystitis have also reported alterations which are consistent with sympathetic hyperactivity.

The relationship between FM and anxiety and/or depression also deserves special mention. It is clear that FM patients frequently have these two conditions. It hardly could be any other way in persons suffering from chronic intense pain. Unfortunately, the psychological component associated with multisystem FM features has led some physicians to diagnose these patients with pejorative labels such as hypochondriasis or hysteria. In recent years, new labels have been applied, such as "health seeking behavior" or "somatization". In my opinion, these labels are totally misplaced and do not help by any means in understanding the causes that lead to FM. The fact that there is a psychological component to FM does not diminish the validity of the diagnosis nor make patients guilty for their own suffering. The key issue in FM research is not whether there is a psychological component; the key issue is why these persons have so much pain. **(It is the pain, stupid !!!)**. There is ample evidence to sustain the fact that FM pain is real as attested by different studies demonstrating very high levels of the powerful pain-transmitting *substance P* in the cerebrospinal fluid of patients. According to our model, anxiety could be either the cause or the effect of sympathetic hyperactivity. It should be noted that any normal person injected with adrenaline becomes jittery and anxious.

However, we have to address the key FM issue: how to explain its defining features (i.e., widespread pain and tenderness at palpation on specific anatomical points). We

propose that these key features can be explained by the mechanism known in medicine as *sympathetically maintained pain*. This type of pain is characterized by its frequent onset after trauma, by its independence of any tissue damage, and by the presence of *allodynia* (the medical term for pain elicitation with light touch) and *paresthesias* (the medical term for burning, tingling sensations). *Sympathetically maintained pain* is a type of neuropathic pain. This means that the problem lies in the pain-transmitting nerve itself. Examples of neuropathic pain are post-herpetic neuralgia, diabetic neuropathy, and reflex sympathetic dystrophy. We have suggested that FM is a generalized form of reflex sympathetic dystrophy. Unfortunately, these types of neuropathic pain respond poorly to the usual analgesic/anti-inflammatory medications.

Sympathetically maintained pain syndromes have strong experimental foundations. Studies performed in animals have shown that trauma may trigger relentless sympathetic hyperactivity and that in such instances the pain-transmitting nerves are altered and abnormally activated by norepinephrine (a phenomenon known as *norepinephrine-evoked pain*), thus starting a vicious cycle of sympathetic hyperactivity and pain.

FM has clear *sympathetically maintained pain* features. As discussed before, there is relentless sympathetic hyperactivity. There is frequent onset after physical or psychological trauma. There is widespread pain without underlying tissue damage accompanied by *allodynia and paresthesias*. The typical FM tender points reflect a state of generalized allodynia. It should also be noted that most FM tender points are located in the neck area, a zone very rich in sympathetic interconnections. Nowhere else in the body are the sympathetic cell bodies so near to the skin. Our recent findings (see sidebar) show that injections of tiny amounts of norepinephrine induce pain in FM patients, thus reinforcing the notion that FM is *a sympathetically maintained pain syndrome*.

Treatment of Dysautonomia in Fibromyalgia

The realization of dysautonomia in FM demands a holistic approach for its treatment. We are not dealing with a localized ailment; rather, it is our main regulatory system that is not working properly.

Dysautonomia provides a plausible explanation for the reported beneficial effects of interventions such as cognitive-behavioral therapy and graded aerobic exercises. These disciplines improve FM symptoms and also improve resting autonomic tone.

It also seems wise to ask patients to avoid the intake of adrenaline-like substances such as nicotine, caffeine-containing soft drinks, and coffee. Liberal intake of mineral water may help symptoms related to low blood pressure such as fatigue, dizziness, and faintness.

For this chronic illness with multiple complaints, is important to refrain from excessive use of medications. *Therapy should be individualized and remain under a physician's supervision*. Medications should be directed to improve sleep and autonomic balance. The main FM symptom, widespread pain, should be eased with

centrally acting analgesics. Anti-inflammatory medications have little beneficial effects. It is clear that current analgesic therapy is insufficient in many cases. We have to direct our attention to anti-neuropathic medications, but again, currently available compounds are not satisfactory in many instances. Different types of anti-neuropathic drugs are in the developmental stage, and there is reason to believe that these new medications will also be effective for FM pain. There is much to be learned about the possible beneficial effects of eastern relaxation disciplines on ANS balance and on FM symptoms.

In conclusion, we can be optimistic. The FM enigma is in the process of being better understood. I am convinced that scientific evidence will eventually disprove FM non-believers. Both patients and health care providers have to be daring and move away from the decrepit medical paradigm that views any illness without obvious structural damage as non-existent or as belonging to the realm of psychiatry. We need to adopt a scientifically holistic paradigm that recognizes the tight mind-body interactions in any chronic disease state. We have to be imaginative and develop different treatments for FM based on the unfolding new knowledge.

About the Author: Manuel Martínez-Lavín, M.D. graduated as a physician from the National University of Mexico. He did his postgraduate training in Internal Medicine at St. Louis University in Missouri and in Rheumatology at Scripps Clinic in La Jolla, California. He is certified in Internal Medicine and Rheumatology by the American Board of Internal Medicine. He is currently Chief of the Rheumatology Department at the National Cardiology Institute of Mexico. He has published over 60 research articles in scientific, peer-reviewed journals. His research interest focuses on cardiovascular involvement in rheumatic diseases.