If fibromyalgia did not exist, we should have invented it. 
A short history of a controversial syndrome

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SUMMARY
Fibromyalgia is a recent disease, and some physicians remain doubtful about its reality. The history of fibromyalgia is a story of controversies: the fight between subjectivity and cartesianism, and between old mind and body concepts. Fibromyalgia represents the emblematic condition of unexplained medical symptoms, far from well-defined diseases with objective biomarkers. In this review we will follow the fibromyalgia story along the ages and sciences to better understand this complex pain disorder, between soma and psyche, and between medicine and psycho-sociology and to demonstrate that fibromyalgia exist, we have not invented it.

Key words: Fibromyalgia, fibrositis, myalgia, tender points.

INTRODUCTION

Fibromyalgia is a recent disease (1), and some physicians remain doubtful about its reality. In 1926, Hunter had already stated that “it requires a little courage to present a paper on this subject, for fibrositis, or myalgia, has no generally recognised pathology and the term has in the past been used very loosely to cover many pathological conditions” (2). In fact, the name “fibromyalgia” is recent, proposed by Hench (3) in 1976, but the story began long before this labelling.

Over time, its story has been influenced by current concepts, from muscle to psychology, from genetics to hormones, and finally with important findings related to the neurosciences.

We will follow this story along the ages and sciences to better understand this complex pain disorder, between soma and psyche, and between medicine and psycho-sociology.

This story aims to demonstrate that patients have existed all throughout the centuries, and that if fibromyalgia did not exist, we should have invented it.

At the beginning: greek and roman literature “Joint pain is driven by the brain”

The history of pain medicine and rheumatology is very old, and it is possible to find interesting concepts and descriptions of pain in ancient Greek literature. In 410 BC, Hippocrates (430-380 BC) described the “Rheuma Theory”: a mechanism of pain where the brain sends liquid to the lower limb, and when there is more liquid, there is more pain. Rheuma means fluid in Greek, and in fact, the Rheuma theory explains the influence of the brain on the body (4).

It is interesting to note that this concept is close to the recent concepts of central sensitization. Hippocrates was one of the first to consider that pain is not a punishment but a natural phenomenon. He also described the use of nonpharmacological tools to relieve pain: cold and hot application, and plaster (4).

After Hippocrates, Theophrastes (372 BC-287 BC), a Greek physician who was one of Aristoteles disciples, described widespread pain conditions. Theophrastes published the “characters” where he described a feature of general pain in muscles and ten-
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The very first medical description of fibromyalgia in Renaissance times
Guillaume de Baillou (1538-1616) was a physician (Dean of the University of Paris medical faculty, 1580), and founder of modern epidemiology who revived Hippocratic medical practice in Renaissance Europe. He was the first to define the term “rheumatism” in its modern sense. In 1592, he published a book “Liber de rheumatismo”, in which there are some descriptions of muscular pain close to fibromyalgia. This is probably the very first medical description of fibromyalgia.

Starting to establish pathophysiology: fibromyalgia as a muscle disorder
In the 19th century, the first pathophysiological approaches emerged, and fibromyalgia was described as “muscular rheumatism.” In the 19th century, concomitantly, several European authors described similar clinical syndromes with widespread pain localised in the muscles.

The tender points
The tender points were described by Valleeix in France, in 1841 (7). He described referred pain triggered while certain painful points were palpated. Just after, in 1858, in Great Britain, Inman described a muscular localised pain independent of innervation and also “referred pain” (8). Concomitantly, in Germany, Florrie (1843) (9) described nodules in the muscles with pain induced by pressure and in 1903, Cornelius (10) described “nervous points” in the muscle, with pain influenced by weather and emotions.

Toward the description of fibrositis
There have been concomitant descriptions of features of widespread pain, mostly related to muscles.

In 1876, in Sweden, Hellday described myositis (11). In 1904, Gowers (12) introduced the term “fibrositis” to describe the inflammation of fibrous tissue in his description of low back pain. In the same year, the pathologist Stockman (13) first reported evidence of inflammatory changes in the fibrous, intramuscular septa (a thin membrane that divides two soft masses of tissue) in biopsies from patients.

However, subsequent studies of muscle biopsies have failed to reproduce Stockman’s findings of inflammation, and the term “fibrositis” is therefore considered a misnomer (14).

After the description of fibrositis, Telling described nodular fibromyositis (15) and was the first to try to unify different disorders with different names, describing the same pathophysiological entity. Cyriax, a British physician, widely known as the father of orthopedic medicine. He believed that muscle pain derived from nerve impingement due to disc degeneration and also reported more precise fibrositis features (16). In 1952, Janet Travell coined the word “myofascial” and the myofascial pain syndrome (17).

All these theories on the muscle pathophysiology have not been confirmed, and only muscle microcirculation and metabolic abnormalities have been found (18).
The end of the 19th and the start of the 20th century: the golden era of psychology

The end of the 19th century and the 20th century can be considered as the era of psychology, with several schools of psychology. Among the most famous: in North America (William James), in Austria (Sigmund Freud, Joseph Breuer), France (Jean-Baptiste Charcot), and Germany (Wilhelm Wundt). This was also the specific rise of psychoanalysis with Freud and his disciples.

Neurasthenia

A very interesting condition, surprisingly very close to the ACR 2010 criteria of fibromyalgia has been described in 1869 under the name of neurasthenia, described by G.M. Beard (19) (Figure 1, Table I).

Psychogenic and psychosomatic rheumatism

In this line, fibromyalgia was considered a psychological disorder, with several new labels: myofibrositis mimicking other diseases (20), psychogenic rheumatism (21), and allergic myalgia (22) (Figure 2).

Post-traumatic pain

The Second World War was a period in which several descriptions were reported in male soldier patients. In 1942, Savage (23) demonstrated that in 2,727 visiting soldiers, 307 had rheumatic symptoms, and among them 52% had fibrositis. In 1947: Boland (21) described “psychogenic rheumatism” in the army, with the description of this new clinical entity involving 24% of soldiers attending his hospital. There were biological and imaging abnormalities, and the clinical picture was considered linked to psychological stress. This is very close to another syndrome, described 50 years later, in 1991, the Gulf War syndrome (24). Finally, recent studies have not confirmed that fibromyalgia is a psychological disorder. Indeed, there are more anxiety and more depression in fibromyalgia, but also in all other chronic syndromes compared to healthy controls (25). Anxiety and depression increase when related to medical symptoms without identified pathology (26).

There is no proven specific psychological feature or traits associated with fibromyalgia (27), whereas cognitive dysfunction and inefficient coping are severe (28).

From the 1950s, the stress theory: is fibromyalgia syndrome a stress-induced disorder with changes in the stress hormones?

Many years after the theory of stress originated by the famous endocrinologist Hans Selye, in the 50s, there have been several studies on endocrine abnormalities of the hypothalamic-pituitary-adrenal (HPA) axis in fibromyalgia. These theories describe endocrine abnormalities of the hypothalamic-

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Table I - Criteria for neurasthenia described by Beard (1869).

<table>
<thead>
<tr>
<th>Condition</th>
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<tr>
<td>Cephalalgia</td>
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<tr>
<td>Insomnia, nightmares</td>
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<tr>
<td>Rachialgia, coccygodynia</td>
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<tr>
<td>Fatigue, mainly in the morning, with muscular atrophy</td>
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<tr>
<td>Dyspepsia</td>
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<tr>
<td>Sexual disorders and dysfunction</td>
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<td>Psychological asthenia</td>
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<td>Memory loss</td>
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pituitary-adrenal (HPA) axis that result in a blunted adrenal cortisol response to ACTH with lowered 24-hour free cortisol levels in many patients with fibromyalgia (29). Other theories have looked at IGF1 and GH levels in fibromyalgia patients. They have found low insulin-like growth factor (IGF1) in one-third of patients, resulting in decreased nocturnal growth hormone (GH) secretion (30). In fact, hormonal dosages are not indicated for clinical use in patient care, but may have an impact on therapeutic approaches since several studies have demonstrated relevant effect of GH treatment in fibromyalgia (31).

**The golden times: recognition of the disease, development of criteria, but still controversies**

Between the 1970s and the 90s, recognition of the disease was an important step for patients but also for physicians: the disease received a name, diagnostic criteria, and assessment tools.

**Naming the disease and official integration in the disease classification**

In 1976, the Nobel Prize winner Hench described the term “fibromyalgia” as a non-articular rheumatism. In 1990 the World Health Organization recognised fibromyalgia. Fibromyalgia was integrated into the International Classification of Diseases (ICD-10) in the chapter on non-articular rheumatic diseases, with unknown aetiology, under the code M79-0. In 1987, the American Medical Association (AMA), recognized FMS as a true illness and a major cause of disability. In 1992, at the Second World Congress on Myofascial Pain and Fibromyalgia in Copenhagen, a consensus statement on fibromyalgia was agreed and published in The Lancet under the name “Copenhagen Declaration 1992” (32).

**Concomitantly, several classification criteria have been proposed**

In 1972, the first criteria to be proposed were published by Smythe (33). In the 1980’s, another researcher, Yunus, further clarified fibromyalgia by proposing the need for a unified classification system as well as the first diagnostic criteria. He was the first to popularize the word ‘fibromyalgia’ and in 1981 the Yunus criteria were released (34). Lastly, Wolfe et al. in 1990 published the most famous criteria under the name of ACR 1990 Classification Criteria (35).

**Several tools to assess fibromyalgia**

The first tool to assess fibromyalgia, the Fibromyalgia Impact Questionnaire (FIQ), was developed in the late 1980s by Burckhardt, Clark and Bennett at Oregon in Portland USA (36). Since that time FIQ has been extensively used as one of the main indexes of therapeutic efficacy in fibromyalgia. OMERACT, an independent organization primarily dedicated to rheumatoid arthritis developed its first workshop on fibromyalgia in 2004 (37) to define important and relevant research domains.

**Some controversies have emerged**

Immediately after 1990, when the American College of Rheumatology (ACR) classification criteria for fibromyalgia (35) were published, controversies emerged.

![Figure 3 - Tender points. American College of Rheumatology (ACR), 1990.](image_url)
ACR1990 criteria were primarily classification but not diagnostic criteria: the value of 11 tender points out of 18 was discussed, and important symptoms such as fatigue, sleep disturbances, and cognitive dysfunction are not included in the ACR criteria (38) (Figure 3).

**Sleep as a pathophysiological explanation**
Sleep disorders have been recently considered an important comorbid condition in fibromyalgia. In the 1970s, Moldofsky (39) performed the first scientific sleep studies in fibromyalgia and demonstrated the links between sleep disorders and fibromyalgia. The association between musculoskeletal symptoms and a non-REM or stage 4 sleep disturbance was demonstrated. Moldofsky proposed that fibrositis be considered a “nonrestorarive sleep syndrome.” Although not specific to fibromyalgia, this irregular sleep pattern may be an important factor contributing to the severity of disease manifestations.

**In the 21st century, is everything genetically driven?**
As in many diseases, a genetic predisposition has been evoked in fibromyalgia. An interesting study demonstrated familial aggregation in fibromyalgia (40). Much research, especially in Israel, has tried to identify genetic factors that may predispose to fibromyalgia (41). Most of the targets that have been studied are related to serotonin receptors and transporters, enzymes like COMT (42), and dopamine receptors.

**The last chapter: the era of neurosciences: fibromyalgia is a dysfunctional disorder? A neuropathic pain?**
The 21st century can be considered the century of neurosciences, since there have been major findings in that scientific area.

**CNS imaging: fibromyalgia is real!**
CNS imaging has presented an important step for physicians in that it demonstrates that specific changes are observed in the patients’ brain (43), suggesting to all physicians that finally fibromyalgia is real (Figure 4).

**Is fibromyalgia a neurological condition?**
Concomitantly, other authors have suggested that fibromyalgia could be part of neuropathic disorders (44), and several works have investigated central nervous system changes in fibromyalgia (45). For example, there are modifications in the neuromediators, increased levels of substance P and nerve growth factor, and lowered levels of serotonin.

**Is fibromyalgia a dysfunctional pain syndrome?**
Not yet validated, but in discussion, the classification of pain disorders may incor-
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Fibromyalgia: a never ending story?
The recent history of fibromyalgia is now very dynamic in several ways:

Diagnostic criteria. The new criteria, released by the ACR in 2010 (49) 20 years after the first classification criteria, tried to abandon tender point examination and establish diagnostic and severity criteria. To date, these criteria are not validated and still in discussion.

Therapeutic approaches. There is a growing discrepancy between Europe and North America in the availability of drugs for the treatment of fibromyalgia. The FDA (50) has approved 3 pharmacological treatments for pain in fibromyalgia: duloxetine, milnacipran and pregabalin, although EMA has rejected all the same dossiers, for different reasons, including the small number of European patients, weak efficacy (very small effect-sizes), and no evidence of a dose-effect relationship. These discrepancies also reflect the different social health systems.

Management recommendations. Although there is no drug licensed for fibromyalgia in Europe, several recommendations have been published: in 2006, EULAR developed recommendations (51), but other recommendations have been published in Germany and Spain.

Screening tools. Several screening tools have been developed to detect fibromyalgia more easily in clinical practice. A tool dedicated to screen fibromyalgia via phone calls has been proposed by Canadian authors: the LFESQ (52) as well as a simple tool to screen fibromyalgia in clinical practice, the FiRST (Fibromyalgia Rapid Screening Tool) (53).

Epidemiological data. Fibromyalgia epidemiological studies have represented an important step in demonstrating the prevalence of the disease. Most of these studies have led to similar data. In the US, fibromyalgia is estimated at around 3% of the adult population (52,54). In Europe, the prevalence of fibromyalgia is also estimated between 1.6% in France (55) and 2.6% in whole Europe (56).

CONCLUSIONS

In conclusion, the history of fibromyalgia is a story of controversies: the fight between subjectivity and cartesianism, and between old mind and body concepts. Fibromyalgia represents the emblematic condition of unexplained medical symptoms (57), far from well-defined diseases with objective biomarkers. It is the far end of medicine, sociology and psychology, addressing difficult questions to medical science. This exciting scientific history is not finished, but we do hope that this history will come to a time when patients will no longer be stigmatised. Even if no one denies that patients exist, there are still many “fibroskeptical” physicians and, as in the 1920s, the question “is fibromyalgia real?” remains. It is time that medicine recognizes these patients and their condition, without any prejudice and with the best scientific evidence.

REFERENCES

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