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Is fibromyalgia a distinct clinical entity? Historical and epidemiological evidence

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Most medical specialities have defined medically unexplained syndromes such as fibromyalgia, to categorize patients with prominent but unexplained symptoms. Other such syndromes include irritable bowel syndrome, chronic fatigue syndrome and atypical chest pain. In this chapter we present evidence to suggest that fibromyalgia is not a unique clinical entity, but shares much with these other syndromes. We use historical, clinical and epidemiological evidence to illustrate this idea. The historical data emphasize the essentially arbitrary way in which fibromyalgia developed. The clinical evidence shows the considerable overlap between patients with fibromyalgia and those with other unexplained syndromes. From an epidemiological perspective we emphasize the strong associations between symptoms such as myalgia and fatigue. We conclude by suggesting that fibromyalgia is one of many medically unexplained syndromes which have more similarities than differences between them.

Key words: fibromyalgia, medically unexplained symptoms; medically unexplained syndromes; chronic fatigue; classification; epidemiology.

Medically unexplained physical symptoms are probably the single most common reason for outpatient referrals across medical specialities[1,2] – with most studies indicating that one-third to a half of all new patients seen in secondary care have symptoms unaccounted for by defined organic disease. It is therefore not surprising that many specialities have (apparently independently) defined syndromes in which to place this troublesome group. The symptom complex for each syndrome is different – reflecting the referral practices to the different specialities. Thus rheumatologists have devised fibromyalgia, characterized by widespread pain and tender points; gastroenterologists have defined irritable bowel syndrome, characterized by abdominal pain and altered bowel habit; and cardiologists have identified non-cardiac chest pain (or syndrome X), characterized by chest pain of uncertain origin. This chapter explores the potential overlap between fibromyalgia and other unexplained syndromes.

The evidence against fibromyalgia as a distinct clinical entity comes from three sources which are explored in this chapter. We will assess clinical evidence concerning the overlap between fibromyalgia and other unexplained syndromes as seen in medical

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clinics. We will then explore epidemiological evidence from community studies confirming the dimensional rather than categorical origins of the main symptoms of fibromyalgia. However, first we shall explore the history of fibromyalgia as a diagnostic entity.

HISTORY

Patients who report diffuse muscle aches and pains have long been known in medicine. Amateur medical historians vie with each to produce the first 'description' of fibromyalgia, just as they do for chronic fatigue. More interesting is the history of the concept of fibromyalgia – the story of the label.

As is now well known, it was the British neurologist Gowers who coined the term fibrositis in 1904. Drawing attention of the clinical evidence for muscle sensitivity, he linked together lumbago and 'muscular rheumatism', introducing the term 'fibrositis' by using the analogy of cellulitis to suggest that the new condition was the result of inflammation of 'fibrous tissues of the muscles'[3] – hence a specific pathology was assumed for the new 'disease'. On the other hand, Gowers was unusual among his contemporaries for his precise use of terminology, making it clear that there was no convincing evidence for such a pathology. Whether or not he appreciated this inconsistency is unclear.

Following the lead of Gowers, physicians continued to study the phenomenon of muscle pain and tenderness. Thomas Lewis, whose reputation had been made describing effort syndrome in a previous generation, gave the concept some credibility with his work on injections of hypertonic saline into deep muscle structures. Others described tender points, trigger points and pressure points – all variations on a theme. During the 1930s and 1940s the debate oscillated to and fro – fibrositis, tension rheumatism, muscular rheumatism and other synonyms were all in common usage. None, however, was really established, the spectre at the feast always being the suspicion of psychoneurosis, as it was then called, or even frank malingering. Indeed, the historical literature confirms there has never been a time when discussion about fibrositis, fibromyalgia, neurasthenia or chronic fatigue was not concerned with organic versus psychogenic polemics.[4]

One can see the shifting boundaries and confusion in the literature on psychogenic rheumatism, which – as these areas so often are – was severely tested by the military experience. During the Second World War some doctors diagnosed fibrositis in at least 70% of those attending military hospitals with non-specific muscular complaints; others said the true proportion was nearer 5%.[5] Hence, some doctors were prepared to diagnose fibrositis in virtually anyone with musculoskeletal symptoms, others in virtually none. Psychogenic rheumatism and/or fibrositis was already seen as non-specific, associated with other symptoms such as weakness, fatigue, paraesthesiae, headaches, breathlessness and many others.[6]

In 1953 Canadian rheumatologist Wallace Graham began to shift the discourse on chronic musculoskeletal pain by arguing that it was wrong to think of fibrositis as a specific pathological entity; instead, he argued, it should be seen as a 'clinical syndrome', a syndrome of unexplained soft-tissue pain. He thus side-stepped the absence of a discrete pathology, and dramatically widened the scope and reach of the concept.

Although Graham's intervention did widen the scope of the concept, doctors then, and now, were ill at ease with such a vague concept. The cause was advanced by an influential article by internist Eugene Traut, published in 1968[7], and again when Hugh Smythe, another Canadian rheumatologist, proposed that there were indeed specific

criteria and signs for the diagnosis, namely, tender points in discrete, reproducible locations. Smythe's observations did much to overcome the reluctance of many to make the diagnosis.[8] The syndrome's popularity further increased with the emergence of an instrument, the dolorimeter, with its promise of a diagnostic 'test'.[9] No matter that commentators have drawn attention to the spurious nature of this thinking, described as 'a quasi scientific device' by Bohr[10]; the instrument, which promised 'objectivity', was an important step forward in the acceptance of the diagnosis by professionals.

Another crucial stage in the acceptance of fibromyalgia (the name which superseded fibrositis during the 1980s) by the medical community was the proposal that a specific sleep abnormality underlies the condition. This hypothesis was the result of observations made by one more Canadian rheumatologist, Harvey Moldofsky, more than 20 years ago.[11] Of ten patients with fibrositis he noted that seven had unusual alpha (fast 7.5–11 Hz) waves appearing during periods of NREM sleep. This abnormality had been previously noted in fatigued patients and had been called 'alpha-delta' sleep.[12] Moldofsky and colleagues referred to it as the 'alpha EEG NREM sleep abnormality'[11] and hypothesized that this abnormality produced the pain and possibly the fatigue of patients with fibromyalgia. The Toronto laboratory has subsequently replicated the abnormality in other samples of patients with fibromyalgia.[13] Although the finding and theory has been persuasively presented a number of questions remain unanswered: can the abnormality be reproduced in other laboratories, is it specific to fibromyalgia, and what is its causal significance?

The attempts of other laboratories to replicate this finding met with mixed success, being found by some investigators[14–17] but not others.[18–20] One possible explanation for this discrepancy is a technical point concerning EEG electrode position.[19] However, even if this explanation is correct, it remains unclear whether a valid observation is being misused by some investigators, or an artifact of muscle activity misinterpreted by others. Likewise, is it a consequence of stage 4 sleep deprivation?[21] The status of the abnormality is therefore uncertain, but its importance lies in its promise of a biological marker and a putative mechanism for what had been an elusive condition.

The end result of this process was that, by the end of the 1980s, the fibrositis/fibromyalgia concept was reasonably well established in the public imagination, and was endorsed by sufficiently large numbers of professionals to ensure its survival. It was at this time that official recognition came in the form of the American College of Rheumatologists' criteria for fibromyalgia[22], to be succeeded by the so-called 'Copenhagen Declaration'. While these definitions did improve reliability, the reasoning underlying both papers was essentially circular, and certainly did not provide any evidence for the validity of the concept.[23] Instead, 'thus a pain syndrome is said to define itself'.[24]

This minor historical excursion serves to emphasize that the historical origins of the fibrositis/fibromyalgia syndrome do not lie in any epidemiological observations, let alone any breakthroughs in the natural sciences. No new way of understanding physiological processes, nor any new imaging or other diagnostic techniques, were responsible for opening doctors' eyes to this new illness. Instead it was based solely on the clinical intuition of a few rheumatologists, often slightly peripheral to the mainstream of the profession, and invariably based on the experiences of examining small numbers of patients in specialist clinics. Moldofsky's observations apart, the drive to have fibromyalgia recognized was based on social and economic forces, and not experimental observation.

Instead, we suspect that the popularity of fibrositis, and more latterly fibromyalgia, can be traced to several sources. First of all, medical attention to the dangers of occupational activities increased towards the end of the nineteenth century, parallel

with the introduction of the first workers' compensation laws in Britain, Germany and North America.[25] Much of this activity could be seen in the field of back pain, but some of it spilled over into the more general area of non-specific muscle pain.

Second, as Shorter has pointed out, there have always been sound financial reasons for each of the medical specialities to develop their own unexplained syndrome, one which they alone are qualified to diagnose, manage, and bill for.[26]

Third, we believe, along with probably the majority of rheumatologists, that fibromyalgia occupies that grey area between medicine and psychiatry that is also occupied by chronic fatigue syndrome, irritable bowel syndrome, and many others. However, for some this uncertainty and lack of clarity is hard to accept. Some patients, and some doctors, like matters cut and dried, and equally are particularly hostile to any suggestion of a role for psychological factors. The introduction at the beginning of this century of psychogenic explanations for somatic symptoms proved unacceptable to many professionals and patients alike. Indeed, we have argued elsewhere that it was paradoxically the triumph of exclusively psychogenic explanations for the parallel condition of neurasthenia that perversely allowed the survival of an equally monolithic organically based fatigue syndrome, which persists to this day.[27]

Finally, much of the modern impetus to allow a specific fibromyalgia syndrome comes from the various compensation and social insurance schemes operating in developed countries. Few if any insurance schemes or juridical systems will allow reimbursement or compensation for general aches, pain and misery. Nearly all require a firm, medical, diagnosis, preferably one enshrined in some classification or coding system conveniently produced for that purpose. Facing a patient who is in obvious distress, and whom the doctor feels is 'genuine' (whatever that means), most of us will, with relief, make use of a label like fibromyalgia which permits our patient to receive what we feel is his or her entitlement. In a busy clinic we rarely trouble ourselves with conceptual or epidemiological niceties.

CLINICAL OVERLAPS

The most clear-cut evidence of the non-discrete nature of fibromyalgia is its overlaps with the condition known as chronic fatigue syndrome (CFS). There is considerable overlap between fibromyalgia and CFS. Some 70% of those with debilitating fatigue for more than 6 months also had persistent diffuse muscle pain.[28] Between 85 and 95%[29–31] of fibromyalgia patients complain of general fatigue. Myalgia, enshrined in the term 'myalgic encephalomyelitis', is part and parcel of CFS. Tender points, the hallmark of fibromyalgia, are also common in CFS.[32,33] Sleep disorder is common to both.[34] No essential differences emerged in a comparison of two groups labelled as CFS and fibromyalgia respectively.[35,36] Like CFS, most fibromyalgia sufferers seen in clinics are female, the commonest age group is between 18 and 45, depression is common and the prognosis in that setting is poor (see Buchwald[34]).

Formal studies confirm this overlap. Of 33 patients with primary fibromyalgia, 14 (42%) met full CFS criteria, and nine (27%) were only one item short.[37] Several authors have already commented on the comorbidity between fibromyalgia and CFS.[28,29,38–40] Even in adolescents, CFS and primary juvenile fibromyalgia syndrome are remarkably similar.[41] Current authorities now emphasize the similarities between CFS and fibromyalgia.[28,30,32]

Even the presumed infectious links, thought to be specific to CFS, are found in fibromyalgia. Some 55% of one series of fibromyalgia patients confirmed that their

illness had started with a viral illness.[36,42] A substantial minority report symptoms such as sore throats, cough, swollen lymph nodes and low-grade fevers.[35] Don Goldenberg, an academic rheumatologist practising in Boston, has been one of the most prolific authors on, and supporters of, fibromyalgia. His model of how infections might be associated with the subsequent development of fibromyalgia is very similar to those proposed by us to explain the persistence of CFS.[4] Goldenberg suggests that infection is 'one of many events that promote a maladaptive behaviour pattern which secondarily leads to fibromyalgia .... The anxiety caused by, and preoccupation with, chronic infections such as Lyme Disease may lead to avoidant behaviour and inactivity, sleep disturbances, mood disturbances, tense muscles and decreased exercise tolerance .... Societal focus on undetected agents, potential cures, new serological tests and disability ... would foster a loss of self control over one's illness'.[42]

Meanwhile, a veritable flood of papers has started to emerge listing the overlaps between fibromyalgia and virtually every other medically unexplained syndrome, including tension headache[40], chemical sensitivity[31], irritable bowel syndrome[43–45], atypical chest pain[46], gynaecological syndromes[29,47,48], temporomandibular disorders[49–51], and mitral valve prolapse.[48] In parallel, an equally large literature has evolved in reverse, commencing with another medically unexplained syndrome, such as irritable bowel or chronic fatigue syndrome, and showing the overlaps between that particular syndrome and all others, including fibromyalgia.

We have argued that one reason for this confusion is the increasing number of medical subspecialities, which has hampered systematic research, and led both clinicians and researchers to neglect the possible overlapping nature of many syndromes said to exist across medicine. We argue that all these different syndromes have more similarities than differences – the latter being largely artificial distinctions made on the basis of presenting complaint, physician interest and service configuration. This hypothesis is open to testing, and indeed we have just concluded such a study across nine medical specialities, and will report that fibromyalgia is neither a discrete disorder nor confined to rheumatological practice.[52]

Psychiatrists are now beginning to accept that, in community and primary care, the commonest mental disorders are indivisible.[53] It is only in specialist care that the discrete syndromes beloved of psychiatric classification systems become apparent. We are proposing almost the reverse. In specialist care functional somatic syndromes are indistinguishable, but different syndrome patterns may be detected in other settings.[54]

This thesis is not new. A previous generation of writers on psychosomatic issues noted the overlaps between what were then considered different psychosomatic syndromes, and also recognized the alternation or sequence of different syndromes in the same individual. Among these, Ryle's multiple visceral neuroses[55], Halliday's concept of psychosomatic affections[56] and Kissen's concept of syndrome shift[57], not only stressed these overlapping phenomena but also paid attention to psychosocial factors as precipitating causes of the syndromes. Perhaps unfortunately, none of these theories were accompanied by empirical support, and all have disappeared from current thinking on the subject. We argue that their reinstatement is overdue.

EPIDEMIOLOGICAL EVIDENCE

The epidemiology of fibromyalgia in the population has started to be clarified. Chronic muscle pain is common. A community study from the North of England found that the prevalence of chronic widespread muscle pain was 13.2%, which represents a

prevalence of 11.3% when standardized to the adult population of England and Wales.[58] Some 20% of the population in an American community survey complained of chronic regional pain, with a further 10% complaining of chronic widespread pain.[59] Fibromyalgia is less common. In a population study of 50–70 years old in Sweden, primary fibromyalgia has a prevalence of 1%.[60] In a Norwegian study, 10.5% of women aged 20 to 49 met criteria for fibromyalgia, implying both widespread muscle pain and also muscle tenderness[61,62], while 3.4% of American women and 0.5% of men met the full criteria for fibromyalgia.[59]

As with CFS, these figures depend upon the exact criteria employed, and may represent arbitrary boundaries where none exist in nature. There is convincing evidence that fibromyalgia is not a discrete entity, but is part of a continuum from no muscle pain to severe pain with tender points.[58,63,64] Indeed, the authors of a large Finnish population study[65] found little evidence for a discrete disorder called fibromyalgia, concluding instead that it represented the extreme end of 'the different (though correlated) dimensions of illness, pain and mental distress'.

That myalgia may not be specific for either fibromyalgia or CFS is not surprising because it is a common somatic symptom in its own right. In a population study 14% of subjects aged between 18 and 45 complained of muscle pain at rest, and 22% complained of muscle pain after exercise.[66] Myalgia was closely associated with fatigue. Those who reported muscle pain were more than three times more likely to experience substantial fatigue than those who did not. Many people find it difficult to distinguish between the two experiences, since the experience of painful muscles merges with the sense of painful weariness that is one expression of fatigue.

The most convincing evidence comes from epidemiological studies from both Britain and the United States which continue to produce evidence against the existence of a discrete disorder labelled fibromyalgia.[43,58,59,67] For example, Peter Croft and colleagues from the Arthritis and Rheumatism Council Epidemiology unit at Manchester found tender points were related not only to pain, but also to fatigue and sleep problems. Tender points were instead a marker for general distress.[58,67] Indeed, when a quantitative rather than a qualitative approach is taken in clinical populations, much the same is found there as well[68] – leading Fred Wolfe to conclude that the 'tender point count functions as a 'sedimentation rate' (ESR) for distress'.[68]

The difficulties of defining fibromyalgia and CFS, and hence estimating their prevalence, reflect the differences between categorical and dimensional approaches to classification, and the limitations of the former. A categorical approach assumes that there is an entity called fibromyalgia. At some stage researchers will discover either a unique set of symptoms or a pathological marker which will enable the clinical boundaries of the syndrome to be delineated. This is the approach that underlies much of the current research effort in both fibromyalgia and CFS. Yet identifying either a unique symptom profile or validating a laboratory test continues to prove elusive.

The alternative is that there is no categorical condition called fibromyalgia, CFS or any other name. The evidence that fatigue is dimensionally distributed in the community, and that no cut-off exists to separate normal from abnormal fatigue, is overwhelming.[4] Rather than list all the studies confirming the dimensional nature of fatigue or myalgia, we will state that we are unaware of any study that shows the opposite. A helpful analogy is with hypertension, which is simiarly distributed in the community, with no single point at which blood pressure becomes abnormal, but instead a gradually increasing risk of adverse consequences. The nature of hypertension was famously debated by Platt, who proposed a categorical solution, and Pickering, who did not. It was Pickering's views that prevailed.

The two views are not totally incompatible. Continuing the analogy with hypertension, it can be argued that although the population studies do not find much evidence of a categorical syndrome of excessive fatigue, nor of a disease called hypertension, discrete causes do exist for both. In specialist practice cardiologists are always alert to the possibility of renal or endocrine causes of hypertension, such as renal artery stenosis or phaeochromocytoma, although their public health impact is slight. Likewise, severe hypertension is associated with a distinct constellation of pathology (e.g. damage to the kidneys, eyes, heart and brain). Similarly, discrete diseases associated with severe fatigue and myalgia also exist, some known, and no doubt others yet to be identified. The role of epidemiology is to put them into a population perspective. Thus we must always be alert to the possibility that at some future date some cases of fibromyalgia will cease to be 'medically unexplained' in a discrete sense, but it seems unlikely that a single cause will be identified for the more common clinical situation.

At present most thinking on fibromyalgia follows a 'Platt' model, but we favour a 'Pickering' view, and suggest that fatigue and myalgia syndromes are arbitrarily created syndromes that lie at the extreme end of the spectrum of polysymptomatic distress. Definitive evidence to support or refute this view will come from primary care or community samples, not the study of specialist populations. A study that takes the extreme end of the spectrum, represented by selected samples of patients referred to rheumatology or pain services, and compares them with non-fatigued controls, will produce a Platt categorical solution but for spurious reasons.

Researchers interested in the problem of fibromyalgia have drawn similar conclusions from a series of epidemiological studies confirming the dimensional nature of muscle pain and tender points in the community, and the similar difficulties of defining an arbitrary syndrome.[58,59,43,67]

The example of hypertension has other lessons for those concerned with the study of myalgia. First, although myalgia is a dimensional variable that cannot be easily separated from normal experience, it can still be associated with specific disease processes, and requires understanding and treatment. Hypertension, even if labelled 'essential', is clearly not benign, and can be associated with both morbidity and mortality. No physician would hesitate to introduce vigorous treatment for high blood pressure. So it is with myalgia. Because one cannot detect a clear-cut division between 'normal' muscle pain and the suffering of patients with fibromyalgia, this no more invalidates the latter than the dimensional view of blood pressure invalidates the medical importance of severe hypertension.

Practice points

- the diagnosis of fibromyalgia has evolved out of rheumatologists' need to categorise patients with unexplained musculoskeletal pain
- other disciplines have created similar medically unexplained syndromes dominated by symptoms pertaining to their speciality
- patients with fibromyalgia have many symptoms related to other bodily systems
- there is considerable overlap between fibromyalgia and other unexplained syndromes, such as chronic fatigue syndrome. These syndromes have more similarities than differences
- there are no specific biological markers which have been demonstrated to separate fibromyalgia from other syndromes

In this brief review we have argued that current definitions of fibromyalgia have evolved out of specialist clinical practice and there is little evidence that such classifications 'carve nature at its joints'. The definition reflects more of the need for specialists to allocate patients whose symptoms are unexplained to a distinct category than any truth based on population or laboratory studies. It should therefore come as no surprise that fibromyalgia overlaps with other medically unexplained symptoms and syndromes, such as CFS. While narrowly defined syndromes such as fibromyalgia may be convenient in clinical practice, such syndromes have more similarities than differences.

Research agenda

- population based studies are required to understand the overlap between symptoms in the community
- hospital based studies are required to understand common factors between medically unexplained symptoms and syndromes presenting to different specialities

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