Fibromyalgia syndrome and depression: common pathways

Fibromyalgia is a musculoskeletal pain disorder which predominantly affects women and is often associated with depression. Both conditions have much in common, so assessment and treatment of physical and mental health symptoms with dual-acting medications and other appropriate interventions would seem advantageous.

Fibromyalgia is a common, poorly understood, debilitating chronic pain syndrome, which by definition lasts longer than 3 months. The cause is unknown although the usual possibilities of genes, viruses, physical trauma, hormones, autoimmune disease and stress have all been implicated.

In 1995 the authors wrote in this journal: 'Fibromyalgia syndrome (FMS) is characterised by generalised aches, pains, tender points, stiffness and fatigue, yet, despite increasing recognition of this syndrome as a clinical entity, its aetiology remains obscure. There is now increasing evidence that FMS represents a distinct rheumatic disorder and should not be regarded as a somatic illness secondary to psychiatric disorder' (Dunne and Dunne, 1995). Time has borne this statement out.

How common is it?

Fibromyalgia is seen predominantly in women, with onset usually between the ages of 20–50 years. Less commonly, children, older adults and the elderly are affected. Despite an increased awareness of the syndrome it is estimated that 75% of sufferers go undiagnosed (Clauw et al, 2011). In some rheumatology clinics the prevalence may be as high as 20%: the condition is also more severe in such settings (Langford and Gilliland, 2008).

Clinical symptoms

Three key symptoms occur in nearly all patients, namely pain, fatigue and sleep disturbance. Pain is felt in deep tissues which include ligaments, joints and muscles. Often it is severe enough to limit a patient's ability to carry out ordinary household chores and/or lead to work abstinence. It is felt predominantly in the neck and back, lower cervical and lumbar spine respectively (i.e. the axial skeleton). Described variously as dull, boring, burning or diffuse, it is often associated with hyperalgesia (exaggerated prolonged response to pain from a noxious stimulus). Other patients feel exhausted and miserable because of unbearable, sometimes multifocal pain, which may wax and wane in a migratory fashion. Poor sleep aggravates the pain through tiredness and exhaustion. There is a generalized decrease in the pain perception threshold, reflecting discrimination of a nociceptive quality, for example, touch, warmth, cold. These phenomena can be demonstrated clinically by pressure algometry (dolorimetry) or in research settings with quantitative sensory testing using pressure, heat, cold or electricity as stimuli. Fibromyalgia pain radiates diffusely from the axial skeleton over large areas of the body, predominantly involving muscles, musculoskeletal junctions and joints (arthralgia without actual synovitis).

Tender points are a measure of hyperalgesia (there is no tissue damage) although the role of tender points in the diagnosis has been challenged and not all physicians agree on whether 11 of 18 tender muscular points stipulated in the original criteria need be present (Wolfe et al, 1990). Besides, tenderness is also present in non-muscular sites, such as the thumb.

There is the danger that patients may be stigmatized as malingerers because there is no obvious explanation for their chronic symptoms. Anxiety, stress and depression brought about by fibromyalgia syndrome add to the misery and no doubt personality and cognitive factors come into play (Dunne and Dunne, 1995; Williams and Gracely, 2006). Other symptoms include generalized stiffness and digestive upsets. As with other rheumatic conditions, musculoskeletal symptoms are anecdotally aggravated by dampness and poor weather conditions, and the pain seems to improve in dry, hot climates. Medications may alleviate the pain and tenderness, although not completely. Some common tender points are shown in *Figure 1*.

Doctors should be aware of the limitations inherent in using tender sites when diagnosing fibromyalgia syndrome because so many symptoms often overlap with other, related disorders (osteoarthritis, for example) which can complicate the clinical picture (Goldenberg, 2009). Stiffness in the joints is present on awakening and may persist throughout the day in some patients. Some patients with typical symptoms may

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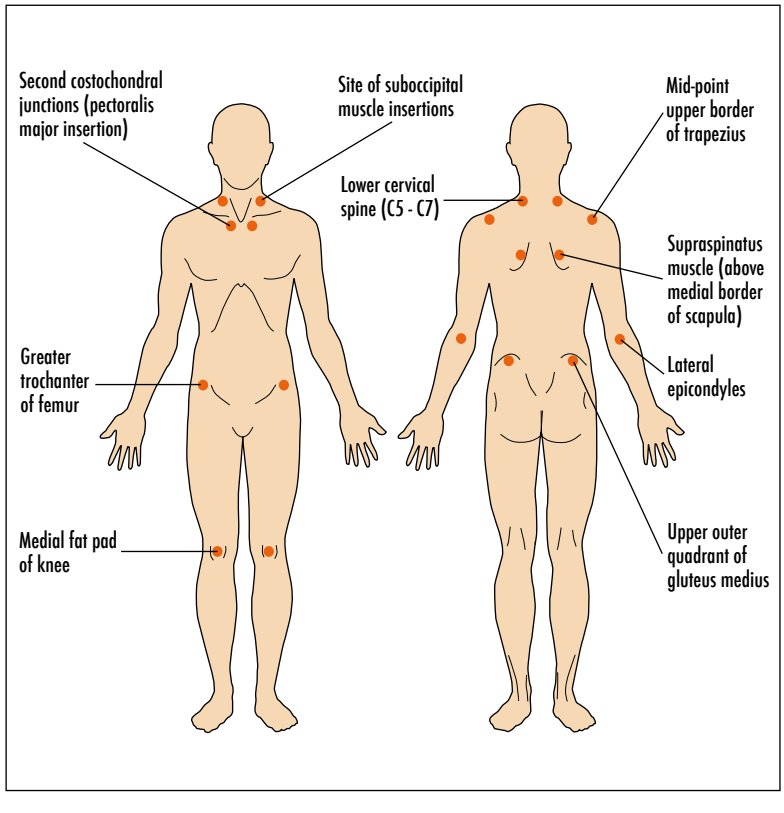
have only four to six tender points when seen in a clinical setting. Fatigue, sleep problems and cognitive changes may present predominantly. Paraesthesiae (abnormal sensory sensations) or dysaesthesiae (painful sensations) of the extremities sometimes occur (Doherty and Jones, 1995).

Non-restorative or unrefreshing sleep with frequent wakening is present in most patients, with disruption of stage 4 deep sleep (non-rapid eye movement), although this phenomenon is also seen in healthy individuals, for example, with loud noise. Sleep studies show a slow wave alpha rhythm. The sleep problems are not necessarily the result of pain, anxiety or depression, and although concurrent mood disorders occur in about 30% of patients (Hudson et al, 1992), psychiatric illness is not necessary for fibromyalgia syndrome to develop. Suicide behaviour was increased in one survey. Mental health disorders do not cause fibromyalgia although it is conceivable that prolonged stress could lower one's tolerance to pain (Calandre et al, 2011). There is no objective muscular weakness or neurological disorder to account for the symptoms. For example, involvement of the supraspinatus muscle of the shoulder would limit initial abduction of the arm because of pain, not weakness.

Cognitive function is sometimes described as 'fibrofog' and may be a primary symptom of fibromyalgia, reflecting impairments in working memory (a form of short-term memory), episodic (memory for events), and semantic memory (memory for words, rules, language).

Figure 1. Common hyperalgesic tender sites.



Other patients may present with weight fluctuations, allergic symptoms (for example, nasal congestion) and hypersensitivity to environmental stimuli (odours, bright lights, loud noises). Non-cardiac chest pain, dyspepsia, headache, abdominal cramping (irritable bowel syndrome), temporomandibular pain (jaw and facial tenderness), chronic pelvic pain, skin problems (dry or itchy) and dysmenorrhoea are other unusual features. Syncope or dizziness, shortness of breath, urinary frequency and urgency (irritable bladder) occasionally occur. Studies vary but approximately 20–30% of patients with rheumatoid arthritis and 50% of patients with systemic lupus erythematosus have fibromyalgia; therefore recognition and treatment of both illnesses need to be addressed (Yunus, 2008) (*Table 1*).

Diagnosis

The diagnostic criteria have been modified since the original criteria were set out (Wolfe et al, 1990). Some remain unchanged, for example, symptoms must have been present for at least 3 months, and the patient should not have another disorder that would otherwise explain the pain. The new criteria are designed to be used as an alternative to the 1990 criteria rather than to supersede them, i.e. both sets of criteria are valid. The original criteria were developed as a research tool whereas the 2010 criteria are thought to be better for diagnostic use in routine clinical practice (Wolfe et al, 2010).

The chronic widespread pain generally characteristic of fibromyalgia syndrome should be present in two contralateral quadrants. Nowadays the tender site test has been replaced with a widespread pain index and symptom severity scale. The former is determined by counting the number of areas on the body where the

Table 1. Symptoms of fibromyalgia syndrome

Condition	% of fibromyalgia syndrome symptoms
Muscular pain	100
Fatigue	96
Insomnia	86
Joint pains	72
Headaches	60
Restless legs	56
Numbness and tingling	52
Impaired memory	46
Leg cramps	42
Impaired concentration	41
Nervousness	32
Depression (major depression)	20

From Wolfe et al (1990)

patient has felt pain in the last week. The checklist includes 19 specified areas. The symptom severity score is determined by rating on a scale of 0–3 (three being the most pervasive) the severity of three common symptoms namely, fatigue, insomnia (90% of sufferers) and cognitive symptoms (memory and concentration). An additional three points can be added to account for other symptoms such as numbness, dizziness, nausea, irritable bowel syndrome or depression. The final score is between 0 and 12. To meet the criteria for a diagnosis of fibromyalgia a patient would have seven or more pain areas on the widespread pain index and a symptom severity score of 5 or more; or three to six pain areas and a symptom severity score of 9 or more (Wolfe et al, 2011).

The length and complexity of some scales preclude their use in ordinary clinical practice and simpler scales have been devised to quantify symptom severity (excluding cognitive dysfunction), for example the 7-item VASFIQ scale. This scale accurately quantifies global fibromyalgia severity by identifying significant symptoms of tiredness or fatigue, sleep disturbance, anxiety or depression, and enables a quicker assessment in busy outpatient clinics (Boomershine et al, 2011).

The fibromyalgia impact questionnaire is a 10-minute self-administered instrument with each question given a maximum score of 10, and therefore an overall 100 as top score. It covers all the various symptoms characteristically associated with fibromyalgia syndrome and has been extensively validated (Burckhardt et al, 1991; Bennett, 2005).

Diagnostic variants

The term fibromyalgia is not ideal although it is well known and often described by patients as such. It was previously called fibrositis which is a misnomer because it is not an inflammatory disorder. Symptoms of fibromyalgia do not respond to steroids. Other terms, for example, idiopathic diffuse pain syndrome or idiopathic musculoskeletal disorder, do not offer any further clarity. It has also become evident that in primary care a tender point count is not always practical and in addition to generalized aches and pains, somatic symptoms and cognitive disturbance (memory problems and diminished mental acuity) may predominate.

Atypical sensory processing in the CNS and dysfunction of skeletal muscle nociception are now considered important in the understanding of the condition (Gracely et al, 2002). Because so many symptoms are non-specific (lethargy, myalgia, insomnia) in the early stages, fibromyalgia syndrome is difficult to diagnose. Symptoms can mimic various disorders, for example, viral infections, poly-myalgia, rheumatoid arthritis or chronic fatigue syndrome. Therefore, delay or errors in diagnosis can prove costly and frustrating for patients because of debilitation and loss of income.

What mechanisms are involved?

The main pathophysiological hypothesis 'central pain sensitization' or 'central sensitivity syndrome' considers fibromyalgia to be a disorder of the CNS resulting in a heightened experience of pain, or pain amplification, in other words, a disturbance of nociceptive processing (Yunus, 2007).

Sensory fibres are broadly composed of two types: thin myelinated A delta fibres which mediate first or fast pain (sharp and localized), and unmyelinated C fibres involved in second or slow pain (dull, intense, and diffuse), the latter being the type of pain associated with chronic medical conditions. Studies of pain in fibromyalgia therefore centre round the application of pressure to specific tender points thus eliciting impulses from C fibres.

Three major functional neuroimaging techniques allow the visualization and measurement of neuronal activity in the brain: positron emission computed tomography, single photon emission computed tomography and functional magnetic resonance imaging. The latter two techniques indicate differences between patients with and those without fibromyalgia syndrome. Both positron emission computed tomography and single photon emission computed tomography measure regional cerebral blood flow by the application of very small amounts of short-lived radioactively labelled tracer molecules given intravenously or inhaled. Functional magnetic resonance does not involve the use of radioactivity. Single photon emission computed tomography imaging has shown reduced blood flow to the thalamus, caudate nucleus and pons, i.e. areas involved the processing of pain.

Decreased thalamic blood flow has been shown in several studies (Cook et al, 2007). Patients seem to have an increased sensitivity to sensory stimuli that are not normally painful (allodynia) and an exaggerated response to painful stimuli (hyperalgesia). In other words, minor sensory stimuli that ordinarily would not cause pain in most individuals induce disabling, sometimes severe pain in patients with fibromyalgia (Williams and Gracely, 2006). Normally, 4 kg/cm^2 pressure (using an algometer) does not cause pain in a person without fibromyalgia. In normal individuals 4 kg/cm^2 is approximately the pressure needed to blanch the skin at the top of one's thumb. Patients with fibromyalgia wince with pain or suddenly withdraw when the tender point is palpated at a lower pain threshold when this pressure is applied.

Fibromyalgia patients differ from healthy persons in regional cerebral blood flow distribution in several brain structures involved in pain processing and modulation, both at rest and during experimental pain induction. These variations may contribute to or account for the abnormal pain sensitivity and maladaptive pain behaviours that characterize many patients with fibromyalgia (Mountz et al, 1995; Bradley et al, 2000). There is grow-

ing evidence that the anterior cingulate cortex is involved in processing the affective, unpleasant aspects of pain (Gracely et al, 2002).

Sixty-eight haemodynamic studies of experimental pain in normal subjects, 30 in clinical pain conditions, and 30 using neuroelectrical methods met selection criteria and were used in a meta-analysis. Another 24 articles were identified where brain neurochemistry of pain was examined. The meta-analysis highlighted important methodological differences in identifying the brain network underlying acute pain perception. The brain network for acute pain perception in normal subjects was at least partially distinct from that seen in chronic pain condition. Chronic pain engaged brain regions critical for cognitive or emotional assessments, implying that this component of pain could distinguish between chronic and acute pain. The authors concluded that the nociceptive system is now recognized as a sensory system in its own right, from primary afferents to multiple brain areas, and that pain experience is strongly modulated by interactions of ascending and descending pathways (Apkarian et al, 2005).

The pain of fibromyalgia may be aggravated by emotional stress. Corticosteroid hormones are released in high amounts after stress. The hormones bind to high affinity mineralocorticoid receptors – particularly plentiful in limbic regions – as well as to lower affinity glucocorticoid receptors which are more widespread. Shortly after a stressful event, corticosteroids (in concert with specific monoamines and neuropeptides) have the potential to increase cellular excitability in areas of the hippocampus which is sensitive to stress and is affected by disorders such as fibromyalgia with its associated chronic pain. However, to complicate matters, in some patients fibromyalgia is associated with a decreased cortisol response to stress. Stress thus functions generally as an initiator, inhibitor or perpetuator of functional alterations in the corticotrophin-releasing hormone neuron, with associated effects on the hypothalamic–pituitary axis and other neuroendocrine axes.

Substance P, a polypeptide containing 11 amino acid residues, is found in high concentrations in the spinal cord, limbic system, hypothalamus and nigrostriatal system. It is also involved in the transmission of pain impulses from peripheral receptors to the CNS. Discovered in 1931, it belongs to the tachykinin family and is considered to be important in pain pathways transmission in the dorsal horn of the spinal cord. Theoretically at least, inhibitors of substance P could provide pain relief in fibromyalgia (Russell et al, 1994; Russell, 2002). Substance P and NK1 (neurokinin) are highly concentrated in the most superficial regions of the dorsal horn (substantia gelatinosa), the first relay station of primary afferent signals where information to the brain is integrated. Nerve growth factor, which belongs to the family of neurotrophins, is involved in the synthesis of proteins associated with neuronal development. Nerve growth factor may indirectly exert its effect through enhancing glutaminergic transmission and could account for sustained central sensitization in fibromyalgia syndrome (Russell et al, 1998; Russell, 1999).

Levels of the neurotransmitter serotonin have been found to be low in some studies in patients with fibromyalgia syndrome. Serotonin is present in highest concentration in blood platelets and in the gastrointestinal tract. It regulates mood, non-rapid eye movement sleep, pain and the immune system. In the brain it is present in the midline raphe nuclei which project to the hypothalamus, limbic system, neocortex, cerebellum and spinal cord (Barrett et al, 2010). However, although serum levels of serotonin in patients with fibromyalgia syndrome are lower than in some patients with rheumatoid arthritis and healthy controls, the variation is too broad and therefore measurement of serotonin in the serum is not a useful tool for the diagnosis of fibromyalgia (Jaschko et al, 2007).

Human DNA contains nearly 10 million sites where individuals differ by a single nucleotide base. These sites are called single nucleotide polymorphisms. When sets of single nucleotide polymorphisms localized on the same chromosome are inherited together in blocks, the pattern of single nucleotide polymorphisms in each block is termed a haplotype (Kennelly and Rodwell, 2006). The single nucleotide polymorphism haplotypes in the catecholamine-O-methyltransferase and β2-adrenergic receptor genes have been linked to increased pain perception, which may account for the CNS being somehow supersensitive to many different sensory stimuli.

Enhanced glutaminergic neurotransmission resulting from higher concentrations of glutamine within the posterior insula may play a role in the pathophysiology of fibromyalgia syndrome and other central pain augmentation syndromes since glutamate is a major cortical excitatory neurotransmitter that functions in pain neurotransmission (Harris et al, 2009).

Evidence for abnormal sensitization mechanisms in fibromyalgia includes enhanced temporal summation of delayed pain in response to repeated heat taps and repeated muscle taps, as well as prolonged and enhanced painful after-sensations in fibromyalgia patients but not control subjects. Magnitudes of enhanced after-sensations are predictive of fibromyalgia patients' ongoing clinical pain. Such alterations of pain mechanisms may lead to long-term neuroplastic changes that exceed the antinociceptive capabilities of affected individuals, resulting in ever-increasing pain sensitivity and dysfunction (Price and Staud, 2005).

A study by Harris and colleagues (2007) used μ-opioid receptor positron emission tomography in fibromyalgia patients and in matched healthy controls. Patients with fibromyalgia syndrome display reduced μ-opioid receptor binding potential within several regions known to play a role in pain modulation, including the nucleus accumbens, the amygdala and the dorsal cingulate. The

findings indicated that altered endogenous opioid analgesic activity occurs in fibromyalgia, which may explain why exogenous opiates appear to have reduced efficacy in patients with fibromyalgia syndrome.

Although the numbers of patients involved in neuroimaging studies is small, evidence is gradually accumulating which may help to increase our understanding of supraspinal mechanisms associated with fibromyalgia (Gracely and Ambrose, 2011). Because cingulate and prefrontal cortices are particularly implicated in pain modulation (inhibition and facilitation of pain), structural changes in these systems could contribute to the chronic pain associated with fibromyalgia (Kuchinad et al, 2007).

What types of treatment help?

The non-specific nature of the symptoms means that many patients will be self-medicating with paracetamol or ibuprofen before they seek medical attention, usually with other over-the-counter analgesics, oral or topical, and various vitamins and minerals. Pharmacological agents known to be effective in reducing pain in fibro-myalgia act by either increasing levels of inhibitory neurotransmitters or decreasing levels of excitatory neurotransmitters, in turn altering levels of substance P.

In the USA, pregabalin was the first drug to be approved by the Food and Drug Administration for the treatment of fibromyalgia and has been shown to improve pain, sleep and quality of life, although it is ineffective against depression. The main inhibitory mediator in the brain, gamma amino-butyric acid (GABA), is formed from glutamate (excitatory) by the enzyme glutamate decarboxylase. Pregabalin increases neuronal GABA levels by producing a dose-dependent increase in glutamate decarboxylase activity. Adverse effects of pregabalin are frequent and sometimes troublesome: they include drowsiness, dizziness, nausea and weight gain. Gabapentin causes dizziness, somnolence, peripheral oedema and gait disturbance. Pregabalin and gabapentin (both used for epilepsy) appear to be more effective than placebo in reducing mean pain scores but have only been tested in short-term trials. In one trial 44% of patients in the pregabalin group said they felt better after 13 weeks *vs* 35% of patients in the placebo group. However, adverse effects are frequent and sometimes troublesome (drowsiness, dizziness, nausea, weight gain). In clinical trials, 19–33% of patients stopped treatment because of adverse effects after 13 weeks, depending on the dose of pregabalin (Arnold et al, 2007).

In three large randomized placebo-controlled trials duloxetine was associated with significant pain improvement in patients suffering from fibromyalgia and similar results were reported for milnacipran (Lee et al, 2011).

A meta-analysis of 21 clinical trials was undertaken to estimate treatment differences *vs* placebo, separately, for duloxetine, fluoxetine, gabapentin, milnacipran, pramipexole, pregabalin, either of two tricyclic antidepressants, and tramadol plus paracetamol. When compared with placebo, statistically significant improvement of 30% and 50% were observed with duloxetine, milnacipran 200 mg/day, pregabalin 300 or 450 mg/day, and tramadol plus paracetamol. The meta-analysis showed a statistically increased risk of discontinuation because of adverse events for milnacipran and pregabalin (Roskell et al, 2011).

Antidepressants may improve fibromyalgia symptoms by reducing pain, stabilizing mood and improving sleep. Disturbed sleep may be both a causative factor as well as a symptom of fibromyalgia syndrome. If abnormal sleep precedes the development of fibromyalgia the effect of antidepressants may be primarily associated with improved sleep. However, the efficacy of tricyclic anti-depressants is difficult to quantify. Their limited superiority over placebo lasts no more than a few months. A meta-analysis of ten randomized double-blinded, placebo-controlled studies revealed only poor to moderate evidence for a beneficial effect at low doses of amitriptyline (25 mg daily) over 6–8 weeks. Higher doses or longer duration of amitriptyline prescribing did not make a great deal of difference (Nishishinya et al, 2008).

The efficacy of selective serotonin-reuptake inhibitors, for example, fluoxetine, paroxetine and citalopram, is also not conclusive. More promising results have been demonstrated with serotonin-noradrenaline reuptake inhibitors such as duloxetine. Both 5-HT (serotonin) and noradrenaline exert analgesic effects via descending pain pathways (Fava et al, 2004). Pain is a prominent feature of depression and vice versa and the alleviation of one modifies the other (Bair et al, 2003; Dunne, 2011). The latter reduces fatigue and duloxetine improves mood. The recognition of fibromyalgia as a syndrome with trials that support pharmacological treatment offers validation and encouragement to patients who have suffered with fibromyalgia.

Other drugs used in this condition include milnacipran and cyclobenzaprine (a muscle relaxant structurally related to tricyclic antidepressants). Milnacipran and cyclobenzaprine are not available in the UK. Tramadol (a serotonin-noradrenaline reuptake inhibitor) is also a weak μ-receptor opioid agonist that has been used to control the pain but its adverse effects are those of opiates in general, mainly nausea and dependence.

Assessments of non-drug treatments in this setting are generally mediocre. Aerobic exercises benefit some patients, especially when combined with biofeedback, patient education and cognitive therapy. Treatments such as graded exercises, yoga, dietary advice, balneotherapy (heated pool bathing), homeopathy, massage, acupuncture, patient education, group therapy and cognitive behaviour therapy have been suggested and tried, although few of the non-pharmacological approaches have been demonstrated to have clear-cut benefits in

randomized controlled trials. Support groups may help some patients (Arnold, 2006; Nihalani et al, 2006; Carville et al, 2008).

In practice, when a patient presents with symptoms compatible with fibromyalgia, the first step is to rule out a treatable condition. Quality of life may be improved by first acknowledging that the pain is real, and possibly by providing psychological, medical, social and occupational support. The limited efficacy of available drugs and their potential adverse effects should be discussed with the patient (*Table 2*).

Conclusions

Fibromyalgia is a musculoskeletal disorder characterized by chronic pain, hyperalgesia and allodynia. It is now considered to be, in part, a disorder of central pain processing. There is objective evidence of augmented pain processing in many hyperalgesic states, including fibromyalgia (Gracely et al, 2002). Although many patients have characteristic tender points, the vast majority describe diffuse pain that is not necessarily more pronounced when specific areas are palpated. Central sensitization manifests as pain hypersensitivity, particularly allodynia, and hyperalgesia (Woolf, 2011). It is believed that central sensitization occurs in part through the action of glutamate on the N-methyl-D-aspartate (NMDA) receptor, resulting in an increase in intracellular calcium and kinase activation, leading to hyperalgesia and allodynia (Lee et al, 2011).

Many patients also describe migraine headaches, shooting pains in the extremities and restless legs. Some report alternating constipation and diarrhoea, usually labelled as irritable bowel syndrome; others do not have gastrointestinal symptoms. Because of the difficulty in diagnosing the condition it may take many years from the time the patient first reports symptoms to the time fibromyalgia syndrome is formally diagnosed. Response to standard analgesics is erratic and more promising results have emerged with drugs such as the serotonin-noradrenaline reuptake inhibitors duloxetine and milnacipran, and the anticonvulsants gabapentin and pregabalin, either used alone or in combination, or with other agents such as amitriptyline. There is only modest evidence to support use of selective serotonin-reuptake inhibitors or tramadol. All have been the subject of good trials and meta-analyses. In addition, neuroimaging studies have made a significant scientific impact in the study of central pain and our understanding of nociceptive processing in the CNS has grown considerably over the past 20 years.

Fibromyalgia is not a distinct condition with a single pathophysiological mechanism. More likely it is a symptom complex characteristic of the heightened perception of pain associated with a number of different precipitating factors. The aetiology and pathophysiology are in general not known, although this is true for many medical disorders. Hence, treatment using a multidisciplinary approach should be based on each patient's case history. The condition remains undiagnosed in the majority of patients and those who are seen tend to be assessed mainly in primary care with more severe cases seen in rheumatology clinics.

Treatment needs to be holistic and multidisciplinary, focussing on both physical pain management and psychological dysfunction. The multidisciplinary approach, although not quantifiable, may help by imparting a sense of empathy and support for patients. Most patients with fibromyalgia syndrome continue to have chronic pain and fatigue and symptoms persist for many years although some show improvement (Fitzcharles et al, 2003; Walitt et al, 2011). Younger patients, those with recent onset of symptoms and patients with less sleep disturbance have a better prognosis. Fibromyalgia is not a progressive disease and although remissions are rare, they do occur, especially in primary care settings (Nampiaparampil and Schmerling, 2004). Long-term studies with fibromyalgia syndrome patients in different settings are needed to define prognostic factors. Development and validation of outcome measures for

Table 2. Interventions for managing fibromyalgia

Standard analgesics	
Muscle relaxants	
Tramadol short term only	
Transcutaneous electrical nerve stimulation machine	
Selective serotonin-reuptake inhibitors, serotonin–noradrenaline reuptake inhibitors	
Low dose amitriptyline	
Gabapentin, pregabalin	
Graded aerobic exercise regimen to include	Individualized to patient
	Set specified targets that increase weekly
	Encourage small amounts often
	Encourage continuation despite pain
	Retrain to avoid operant behaviour
Other	Cognitive therapy to aid coping strategies
	Meditational yoga
	Behavioural therapy

KEY POINTS

- Fibromyalgia is a chronic musculoskeletal disorder which very often goes undiagnosed.
- Tender points are not always present.
- It may take years before the diagnosis is made.
- Patients may be stigmatized as malingerers because of the diffuse nature of the symptoms.
- Fibromyalgia should be considered a disturbance of nociceptive processing.
- Treatment is holistic and multidisciplinary.

fibromyalgia syndrome are needed to provide standardization for clinical trials. More specific CNS targeted and effective treatments may improve prognosis in the future. The recognition of fibromyalgia as a syndrome with trials that support pharmacological and non-pharmacological treatment offers encouragement to patients who suffer from this and other conditions which involve central pain amplification. **BJHM**

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