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FATIGUE IN MUSCULOSKELETAL CONDITIONS

Sarah Hewlett **arc** Professor of Rheumatology and Nursing, Hon Consultant Nurse, University of the West of England, Bristol

Joanna Nicklin Nursing Research Fellow, University of the West of England, Bristol

Gareth J Treharne Lecturer in Psychology, University of Otago, Dunedin, New Zealand/ Hon Psychology Research Fellow, Department of Rheumatology, Dudley Group of Hospitals NHS Trust

- **Fatigue is as common and severe as pain in musculoskeletal conditions**
- **Validated measures of fatigue exist, with limitations**
- **Fatigue has a multicausal pathway, with various components contributing different amounts in different patients at different times**
- **Predictors of fatigue may include inflammation, pain, disability, coping, mood and beliefs about illness**
- **Evidence for interventions to ameliorate fatigue is not abundant, but includes some support for medications, exercise, education and cognitive-behavioural therapy**
- **Until evidence accumulates, clinicians should discuss fatigue with patients, address potential and perceived causes and support self-management strategies**
- **Research needs to address mechanisms, measurement and management**

INTRODUCTION

Fatigue is a frequent and distressing problem for many patients across all musculoskeletal conditions. It is often as severe and important as pain, yet there are few evidenced-based interventions available. The patient perspective on priorities for different symptoms has been a catalyst for the adoption of fatigue as a recommended measure in all clinical trials in rheumatoid arthritis (RA).[1] This review covers the meaning, mechanisms, measurement and management of fatigue, and suggests (with caveats) practical approaches for the clinician.

THE MEANING OF FATIGUE IN MUSCULOSKELETAL CONDITIONS

Four qualitative studies have specifically explored fatigue in RA and fibromyalgia syndrome (FMS), while qualitative studies in other musculoskeletal conditions, although not focused on fatigue, suggest similar experiences. In total 76 RA patients were interviewed about fatigue, from the UK, USA and the Netherlands, and 25 women with FMS from Sweden, covering a range of demographic and disease variables.[2-5] These four studies yielded similar concepts and thus provide strong collective evidence on the nature, consequences and management of and attitudes towards musculoskeletal fatigue.

The nature of fatigue

For people with musculoskeletal conditions who are experiencing fatigue, it occurs on most days and varies in intensity and frequency, ranging from heaviness through weariness and on to exhaustion. Occasionally, sudden and dramatic overwhelming 'wipe-out' comes on without warning, which has catastrophic consequences as people are forced to stop and lie down. Patients clearly differentiate between the 'normal' tiredness they experienced before RA and RA exhaustion. Fatigue is considered equal to or worse than pain and is deemed unearned (and thus unfair and unpredictable) and unresolving. In all of these qualitative studies patients described not only physical fatigue but also cognitive fatigue, manifesting as an inability to think clearly, concentrate, or be motivated to do anything.

The consequences of fatigue affect every part of musculoskeletal patients' lives, with far-reaching effects on physical function, everyday tasks, work and leisure activities. Fatigue threatens traditional roles as patients struggle to maintain childcare, housework, social engagements and close relationships. Fatigue is the factor that most limits staying in paid employment, and causes patients to sacrifice enjoyable leisure activities in order to save energy for perceived 'essential' activities such as chores. The emotional consequences of fatigue are graphically described by patients as frustration, irritability, resentment and tearfulness.

Self-management of fatigue occurs through behavioural means (resting, pacing, planning, using appliances), cognitive means (distraction, prioritising, re-normalising life) and social means (seeking emotional and practical support). Despite these attempts, musculoskeletal patients view their fatigue as unmanageable and unresolving. They feel unsupported by health professionals, and report that clinicians rarely ask about fatigue – thus patients believe clinicians are not interested in fatigue and so fail to raise it themselves. However, when patients did raise the problem of fatigue they perceived it was dismissed or they were offered generic advice that was unhelpful.

Fatigue in other long-term conditions (LTCs) has very similar physical and cognitive features, functional and emotional consequences and self-management strategies as in musculoskeletal conditions, but with some key differences.[6,7] Multiple sclerosis (MS) fatigue is accompanied by neurological symptoms (nausea, dizziness, burning), which might indicate differences in disease-specific fatigue mechanisms.[6] People with MS believe that fatigue *exacerbates* disease activity,[6] whereas people with RA perceive fatigue as a *consequence of* disease activity.[2] Cancer fatigue is seen by patients as predictable and linked to chemotherapy, and thus the onset of fatigue outside chemotherapy may cause fear of disease progression.[7] Across all the studies, patients reported using self-management through trial and error (largely unsuccessful), while professional support was notable by its apparent absence.[2-7]

Normal tiredness is clearly differentiated from the features of fatigue related to an LTC by people in these studies. Fatigue in healthy working adults comprises similar physical and cognitive components, but is less profound, has a predictable cause (activity or stress), and is temporary and easily resolved through rest, while fatigue in LTCs is frequent, severe, unpredictable and unresolving.[8] FMS is predominantly muscular pain plus fatigue and is diagnosed through tender point counts, differentiating it from chronic fatigue syndrome (CFS), which is predominantly fatigue plus pain – defined as medically unexplained fatigue of >6 months that is unrelated to exertion, not resolved by rest, and includes extreme activity reduction and ≥4 of 8 other symptoms (e.g. lymphadenopathy).[9] This review covers fatigue in musculoskeletal conditions, not CFS.

Fatigue level and importance

Quantitative studies consistently show, often in large cohorts, that significant fatigue is common in RA (42–69%), osteoarthritis (OA) (41%), systemic lupus erythematosus (SLE) (90%), primary Sjögren's syndrome (PSS) (68%) and FMS (76%).[10-13] Fatigue is often as severe as pain (e.g. in OA both pain and fatigue scoring 1.6 out of 3) and can be more severe than pain (e.g. in RA fatigue 1.6 out of 3, pain 1.4).[10] Fatigue differentiates between different levels of overall quality of life in RA, impacts on quality of life (in combination with pain and depression) and predicts deterioration in quality of life, and patients find it as difficult to cope with as pain.[10,14,15] Therefore it is not surprising that patients place a high importance on fatigue.[10,16,17]

Future research into the meaning of fatigue

While there are good qualitative studies exploring fatigue in RA and FMS, there are few in other musculoskeletal conditions. Qualitative exploration of the physical and cognitive features of fatigue using mixed groups of people with various musculoskeletal conditions and LTCs might reveal different features that could indicate different fatigue mechanisms. Quantitative studies on the variations of fatigue during the day and the patterns of fatigue over the seasons may also help elucidate mechanisms and self-management solutions.

CAUSES AND PREDICTORS OF FATIGUE *(see Table 1)*

Disease activity/severity

Inflammatory markers of disease activity/severity tend to be weakly related to fatigue in RA and SLE in cross-sectional studies.[18] However, two longitudinal studies of people with SLE suggest that greater disease activity predicts higher fatigue after 1 year.[19,20] When people with RA commence disease-modifying anti-rheumatic drugs (DMARDs) or biologic therapy, the improvements in fatigue they report after 3–6 months are directly related to a reduction of composite disease activity and pain.[21] In contrast, one longitudinal study of people with RA found that lower inflammation (erythrocyte sedimentation rate – ESR) predicted higher fatigue after 1 year.[22] This is a relative effect around the sample's mean ESR, which can be high when sampling consecutive outpatients who can access emergency appointments during flares of their disease. On balance, the evidence suggests fatigue can be present regardless of disease activity/severity. However, many musculoskeletal conditions have different routine measures of disease activity/severity so it is not possible to generalise across conditions. Patient-reported disease activity/severity may differ from clinicians' assessments[18] and it is important to discuss patients' concerns.

Demographics

Sex differences in fatigue are rarely evident in musculoskeletal conditions. Women with RA may report higher fatigue than men with RA but this has only been supported by two of the many cross-sectional studies[23,24] and no sex differences in the longitudinal course of fatigue have been found. However, many observational studies of people with musculoskeletal conditions recruit mainly women for convenience; future studies must include more men with musculoskeletal conditions to test conclusively whether their fatigue trajectory differs from women's. Evidence for a relationship between fatigue and time since diagnosis with a musculoskeletal condition is inconsistent. Fatigue has sometimes been found to be higher in people who have been diagnosed with RA for a longer time[25,26] and sometimes higher among those with more recent RA onset.[23] People with RA of any duration should therefore be included in interventions aimed at avoiding the onset of fatigue or bolstering coping with existing fatigue. Age and ethnicity have not been reported to relate to fatigue in musculoskeletal conditions.

Musculoskeletal pain, functional disability and practical support

On days when people with FMS, juvenile rheumatic diseases (JRDs), OA or RA have increased pain their fatigue is higher and this effect spills over to a maintained increase in fatigue the subsequent day.[27-30] Higher fatigue after 1 year is predicted by having less perceived help at home[31] and greater functional disability among people with RA.[31,32]

Poor mood, stress and sleep disruption

Mood disorders are common among people with musculoskeletal conditions[33] and they have a complex association with fatigue. Greater trait anxiety (the propensity to experience anxiety, rather than current clinical state) has been found to predict fatigue after 1 year among people with RA.[31] Furthermore, fatigue is higher among people with RA who have a lifetime history of mood disorder (i.e. current or previous clinical depression or generalised anxiety). As a result, their fatigue trajectories tend to be stable but elevated over 7 years as compared to people with RA with no previous mood disorder, whose fatigue trajectories start lower but tend to increase over time.[33] When people with RA report greater distress (i.e. depressed mood) at annual assessment, fatigue is increased, although this increase is less pronounced for those who have greater aggregate distress across all assessments.[33] Similarly, women with SLE who report increases in stress and depression between baseline and an interim 9-month assessment experience higher fatigue after another 6 months.[34] Poorer mood on a daily basis (i.e. decreases in positive affect and increases in negative affect) also relates to increased daily fatigue for people with FMS, JRDs, OA and RA,[28-30] as does greater daily stress for children with JRDs.[28,29] This pattern suggests that those people with musculoskeletal conditions who have generally lower distress have lower fatigue but are most susceptible to increased fatigue at times when they are experiencing distress. Nights of poorer sleep also relate to higher daily fatigue among people with RA or FMS.[27,35] The pattern of fatigue across the day in RA and SLE is reported to be a J-shaped curve with levels decreasing across the morning and then building up to a peak in the late evening.[35,36] This has implications for timing the assessment of fatigue in research and clinical practice. It would be optimal to ask patients to complete a structured log of their fatigue for a few days or weeks before their appointment.

Illness perceptions, symptom-control, self-efficacy and coping

Two longitudinal studies have explicitly tested Leventhal's Common-Sense Model (CSM) of beliefs about illness applied to fatigue among people with RA. Higher fatigue after 1 year is consistently predicted by perceptions that RA has severe consequences.[22,37] Lower self-efficacy (perceived personal control) over pain or mood/fatigue has been found to predict higher fatigue after 2 years in a further longitudinal study.[38] Although the CSM predicts that coping

TABLE 1. Summary of observational studies providing evidence for significant predictors of fatigue among people with musculoskeletal conditions.

First author	Year published	Sample (location, population, size, sex)	Approach (design, period of follow-up)	Assessment of fatigue	Processes identified as predicting higher fatigue (concept, measure)	Limitations	Commendable points
Brekke[38]	2001	Norway RA=815 (21% men)	Longitudinal 2 years	- VAS	- Self-efficacy for pain (ASES) - Self-efficacy for mood/fatigue (ASES)	- Conducted in a language in which concepts may have differing meanings - Predictors were not analysed concurrently	- Notably large sample
Dobkin[34]	2001	Canada SLE=120 (0% men)	Longitudinal 15 months	- SF36 vitality	- Decreases in stress (HS) and depression (SCL-90-R) between baseline and an interim assessment	- Data were analysed as a secondary study to a randomised trial of psycho-therapy	- Acknowledges that vitality is a proxy concept for fatigue - Used multiple assessments to examine change
Gilboe[19]	2001	Norway SLE=87 (10% men)	Longitudinal 2 years	- VAS	- Deterioration in disease activity (SLEDAI)	- Conducted in a language in which concepts may have differing meanings	- Patterns of change were comparable to a matched sample of 65 people with RA
Fifield[33]	2001	USA RA=415 (17% men)	Longitudinal 7 years	- 101-point NRS	- History of mood disorder (clinical interview) - Increases in distress scores (CES-D) - Lower aggregate distress scores (across all assess-ments)	- Mental health conditions other than depression and anxiety were not assessed - The trajectory models may not translate to clinical significance	- Notably large sample - The growth-curve modelling makes good use of the annual assessments
Mancuso[31]	2006	USA RA=91 (baseline 16% men; final proportion not reported: maximum possible 22% men)	Longitudinal 13.8 months	- FSS	- Higher trait anxiety (STAI) - Greater functional disability (HAQ) - Less perceived help at home (DSSSS)	- All participants were employed, which limits generalisability but provides useful specific evidence	- The effect of trait anxiety was also observed in an illness-free control group, providing support for generalisability
Pollard[21]	2006	UK RA+anti-TNF=30 (7% men) RA+DMARDs=54 (25% men)	Longitudinal 6 months and 3 months (res-pectively)	- VAS	- Lower improvement in disease activity (DAS) - Lower improvement in pain (VAS)	- Changes in psychological factors were not included	- The pragmatic nature of the study suggests it corres-ponds with patients seen in routine practice
Repping-Wuts[32]	2007	Netherlands RA=123 (32% men)	Longitudinal 1 year	- CIS	- Lower general health (VAS) - Greater functional disability (HAQ)	- Conducted in a language in which concepts may have differing meanings	- Used specific cut-offs for fatigue which may have clinical significance

Scharloo[37]	1999	Netherlands RA=71 (25% men)	Longitudinal 1 year	- VAS	- Perceiving their RA to have more severe consequences (IPQ) - Greater use of avoidant coping (UCL)	- Conducted in a language in which concepts may have differing meanings	- Applied a specific model of beliefs about illness
Tayer[20]	2001	USA SLE=81 (9% men)	Longitudinal 3 months	- FSS - Adapted MAF	- Worse disease status (SLAM)	- The follow-up period may have been too short	- Mood was tested as a mediator but not significant
Treharne[22]	2008	UK RA=114 (26% men)	Longitudinal 1 year	- VAS	- Lower inflammation (ESR) - Perceiving their RA to have more severe consequences (IPQ)	- Consecutive recruitment from secondary care may have led to oversampling periods of flare at baseline	- Applied a specific model of beliefs about illness
Nicassio[27]	2002	USA FMS=63 (substudy sample not reported on: maximum possible 14% men)	Daily 6 sequential days (once a day)	- VAS - Adapted MAF (cross-sectional)	- Increased pain (VAS) the previous day - Worsened sleep quality (3 questions) the preceding night	- Data were analysed as a secondary study to a randomised trial of psychotherapy	- The mediational model tested indicated that poor sleep explains the association between pain and fatigue
Schanberg[28]	2000	USA JRDs=12 (aged 7–15 years; 17% boys)	Daily 7 days (once a day)	- VAS	- Poorer mood (FAS) on the same day	- Small sample of a heterogeneous disease entity	- Valid measures for the young age group
Schanberg[29]	2005	USA JRDs=51 (aged 8–17 years; 35% boys)	Daily 2 months (once a day)	- VAS	- Poorer mood (FAS) on the same day - Greater stress (DEI) on the same day	- Wide age range spans several stages of development and education	- Valid measures for the young age group - Longer diary period enhances validity
Stone[35]	1997	USA RA=35 (29% men)	Daily 7 days (7 times a day)	- 7-point NRS	- Worsened sleep quality (3 questions) the preceding night	- Psychological moderators of daily associations were not significant	- The assessment of fatigue and pain at many points throughout the day indicates a diurnal pattern
Zautra[30]	2007	USA FMS=90, OA=76, RA=89 (0% men)	Daily 32 days (once a day)	- 101-point NRS	- Increased pain (NRS) on the same day or the previous day - Poorer mood (PANAS) on the same day	- Mixed sample of distinct diagnoses	- Effects were consistent across diagnoses, providing some support for generalisability - Longer diary period enhances validity

ASES Arthritis Self-Efficacy Scale; CES-D Center for Epidemiologic Studies Depression scale; CIS Checklist Individual Strength; DAS Disease Activity Score; DEI Daily Events Inventory; DMARD disease-modifying anti-rheumatic drug; DSSSS Duke Social Support and Stress Scale; ESR erythrocyte sedimentation rate; FAS Facial Affective Scale; FMS fibromyalgia syndrome; FSS Fatigue Severity Scale; HAQ Health Assessment Questionnaire; HS Hassles Scale; IPQ Illness Perception Questionnaire; JRDs juvenile rheumatic diseases; MAF Multidimensional Assessment of Fatigue; NRS numerical rating scale; OA osteoarthritis; PANAS Positive and Negative Affect Schedule; RA rheumatoid arthritis; SCL-90-R Symptom Checklist 90-Revised; SF36 Medical Outcomes Studies 36-item Short-Form questionnaire; SLE systemic lupus erythematosus; SLAM Systemic Lupus Activity Measure; SLEDAI SLE Disease Activity Index; STAI State-Trait Anxiety Inventory; TNF tumour necrosis factor; UCL Utrecht Coping List; VAS visual analogue scale

mechanisms mediate the effect of perceptions on health outcomes, only one of the previous studies has identified a relationship between avoidant coping and fatigue after 1 year,[37] and the effect of perceptions of consequences remained significant along with that of coping style. Further evidence is required on this issue, particularly for conditions other than RA.

Future research into the mechanisms of fatigue

There are several variables that are not covered in this review because only cross-sectional evidence exists for their link to fatigue in musculoskeletal conditions (e.g. headache, napping in the day and obesity). These variables require targeted longitudinal and daily observation. Further patient perspective workshops at the international consensus group OMERACT (Outcome Measurements in Rheumatology Clinical Trials) could usefully provide important additions to this researcher-generated list of potential predictors of fatigue.

MEASUREMENT OF FATIGUE

In the absence of good physical, behavioural or biological markers of fatigue, accurate assessment hinges on valid self-report measures. Reviews of fatigue scales have been conducted in SLE, arthritis and RA.[12,39,40]

Generic single-item fatigue scales

Ordinal scales (e.g. none, mild, moderate, severe) differentiate between RA patients with and without inflammation, show fatigue fluctuations during the day, and correlate with other symptoms, although sensitivity data are not evident in the literature.[35,40] Numerical rating scales (NRS) (e.g. 0–100) show daily variation (RA, OA, FMS) and reliability and correlate with other fatigue scales.[30] Visual analogue scales (VAS; 10 cm horizontal line with two descriptive anchors) were shown to be robust and sensitive for pain, but validation for fatigue VAS is based on accumulative RA data rather than specific validation studies. While accumulative data show fatigue VAS to have reasonable construct validity in RA, and to perform as well as longer fatigue questionnaires, reliability and sensitivity data are inconsistent.[40,41] In both PSS and SLE, fatigue VAS correlate significantly with the Chalder Fatigue Scale, and differentiate between patients and controls (the Chalder Fatigue Scale did not differentiate).[42] However, a review showed that out of 26 VAS identified as used for RA fatigue only three were identical, which limits comparison between studies; therefore a standardised RA fatigue VAS is currently being validated.[40,43]

Generic multi-item fatigue scales

Given that fatigue is present in many LTCs, generic scales might capture musculoskeletal fatigue and facilitate comparison across conditions. The Medical Outcomes Studies 36-item Short-Form questionnaire (SF36) includes a 4-item vitality subscale (pep, energy, worn out, tired),[44] which differentiates between healthy controls and people with PSS or ankylosing spondylitis (AS).[42,45] While many RA studies support validation and sensitivity to change for the SF36 vitality subscale in RA, in other studies the SF36 shows people with RA as having more vitality than people without illness, has inconsistent correlation with inflammatory markers, and does not easily distinguish between depression and RA fatigue.[40] Conceptually, the absence of vitality may not be a measure of fatigue, as it is possible to be neither full of pep yet not fatigued (i.e. neutral). The SF36 vitality subscale would benefit from further validation in RA and other rheumatic diseases.[40] The Multidimensional Fatigue Inventory (MFI) comprises 5 fatigue subscales (general, physical, activity, motivation, mental), was developed in Dutch cancer and CFS patients, and has been used in RA, AS, FMS and PSS.[46-49] Some items may potentially be confounded by disability or inflammatory activity (e.g. 'Physically I feel only able to do a little'), and the MFI did not differentiate between people with RA and healthy controls on 2 of the 5 subscales.[40] The Functional Assessment of Chronic Illness Therapy scale was developed for USA cancer patients and has a 13-item fatigue subscale (FACIT-F), validated in RA and psoriatic arthritis (PsA).[50,51] It shows good internal consistency, convergent validity with disease activity, and (in RA) sensitivity to change. However, some items may be irrelevant in arthritis (e.g. being too tired to eat) or confounded by disability (e.g. needing help to perform activities).

Disease-specific scales

Disease-specific scales might address the concern that generic scales may measure irrelevant, confounding or insufficient items. The Fibromyalgia Impact Questionnaire (FIQ)[52] comprises 8 subscales, one of which is fatigue. This VAS subscale was not validated against a gold standard fatigue scale, but shows reliability over 1 week and has been used in many FMS studies. The Multidimensional Assessment of Fatigue (MAF) scale is RA-specific and was developed from a USA cancer fatigue scale.[53] It has 16 questions measuring 4 physical fatigue dimensions (fatigue severity, distress, impact and timing) and yields a global score. There is good evidence of construct validity, discrimination between patients and controls, internal consistency and sensitivity to change.[39,40] However, it lacks cognitive items and (anecdotally) the questionnaire layout leads patients to answer the questions in terms of disability rather than fatigue. It is possible

that different dimensions of fatigue might respond differently to an intervention, and therefore a new RA-specific fatigue scale with a range of subscales, including cognition, is being developed and validated in the UK.[54] The Fatigue and Discomfort Questionnaire, developed with UK patients with PSS, includes a Profile of Fatigue (ProF), a stand-alone scale with 16 items comprising a somatic fatigue domain (needing rest, poor starting, low stamina, weak muscles) and a mental fatigue domain (poor memory, mental fatigue).[13] A study comparing the ProF with the generic MFI showed that both scales demonstrated good internal consistency, and were strongly related, but that the ProF has a stronger internal structure.[48] Fifteen fatigue instruments were reviewed in SLE and the Fatigue Severity Scale (FSS) was recommended.[12] This USA-originated scale comprises 9 items on fatigue impact, differentiates people with SLE from controls, shows internal reliability, construct validity and sensitivity to change, and has also been used in FMS.[39] While some of the assessment scales used in AS and OA contain fatigue items, they have not been validated for producing identifiable fatigue scores, although there is some evidence for an AS fatigue item.[45] In summary, while there is some evidence for the validity of some fatigue scales in musculoskeletal conditions, scales should be selected with care.

The smallest change in fatigue that someone with SLE or RA might notice (minimal clinically important difference – MCID) has been explored. On a scale of 0–100, evidence suggests that a difference of 7–14 points is recognisable by people with SLE as being a significant change, and 10 points in people with RA.[55,56]

Future research into the measurement of fatigue

Measures with valid subscales are needed to explore different facets of fatigue, as these might be separately changed by different interventions (e.g. a behavioural intervention might not change fatigue severity but may well ameliorate its impact). Standardised fatigue VAS and NRS should be formally compared as the trend for transforming VAS into boxes, numbers or circles for ease of on-line computer-based studies, or for scanning data into spreadsheets, may alter the psychometric properties of the VAS.

MANAGEMENT OF FATIGUE: EVIDENCE FROM RANDOMISED CONTROLLED TRIALS

Medication

DMARDs and biologic agents, used both individually and in various combinations, can improve fatigue in inflammatory musculoskeletal conditions, as is reported in many randomised controlled trials (RCTs), Cochrane reviews and overviews,[57] although the mechanism may be through association with changes in pain rather than inflammation.[21] A systematic review shows antidepressants may reduce fatigue in FMS.[58] However, fatigue commonly occurs without inflammation or depression and therefore RCT evidence for non-pharmacological interventions was explored. Relatively few RCTs could be identified.

Exercise

Graded exercise therapy improved fatigue in people with SLE immediately post-intervention compared to relaxation or usual care (n=93, SF36 vitality 51 vs 41 and 34, p=0.015) and was maintained at 3 months.[59] Home aerobic training for people with RA showed only a trend toward fatigue improvement[60] but group exercise in people with self-reported arthritis (8 weeks of 2 x 1-hour sessions) showed an improvement in fatigue post-intervention compared to controls (n=346, VAS 35.4 vs 43.7, p=0.01), which was maintained at 6 months.[61] A Cochrane review of exercise in FMS found 16 studies in which fatigue was measured, and concluded that effects on fatigue were unknown (moderate quality evidence).[62]

Education or self-management programmes

A 2003 Cochrane review of RA education programmes did not examine effects on fatigue, but an RCT of the Arthritis Self-Management Programme in patients with a GP diagnosis of 'arthritis' reported a trend to fatigue reduction at 4 months, which reached significance at 12 months, compared to control (n=554, VAS 0–10 −0.44 vs +0.05, p=0.02).[63]

Psychological interventions

A systematic review of psychological interventions in RA up to 2001 analysed 25 RCTs but none addressed fatigue. Cognitive-behavioural therapy (CBT) addresses the links between thoughts or beliefs, feelings and behaviours, and uses individualised goal-setting and cognitive restructuring to help patients make desired changes in behaviour. In people with early RA who were experiencing psychological distress, CBT resulted in a significant improvement in fatigue post-intervention, which was maintained at 6 months (n=59, effect sizes 0.55, 0.48).[64] Although CBT resulted in an improvement in fatigue in people with SLE, this was not significantly greater than symptom monitoring or usual care.[65] A systematic review of 13 RCTs of mind-body therapies in FMS found a single trial of hypnotherapy, with inconclusive evidence of effects on fatigue.[66] Written emotional disclosure (about traumatic events, deep thoughts and feelings, or benefit-finding) reduced fatigue at 3–4 months compared to factual writing or usual care in people

with RA or SLE (n=75, VAS 40.9 and 57.8 vs 75.8)[67] and in people with FMS (n=92, SF36 –13.7 vs –3.7, p=0.05),[68] although this effect was lost by 10 months in FMS. A psychological intervention combining self-efficacy, social support, problem-solving and repeated counselling for people with SLE and their partners reduced fatigue at 12 months (n=122, 10-point scale 5.1 vs 6.3, p=0.02).[69] A combination of CBT with education and exercise in FMS resulted in an improvement in fatigue at 4 months (n=183, 10-point scale –0.61 vs +0.09, p=0.02).[70]

Other therapies

A large study of acupuncture versus three different types of sham acupuncture (n=100, 24 treatments) showed no effect on fatigue in FMS.[71] While homoeopathy improved pain and quality of life in FMS patients compared to placebo, it did not change fatigue (n=62),[72] and the positive effects of spa therapy on FMS fatigue compared to usual care were lost after 2 weeks (n=30).[73]

In summary, evidence for non-pharmacological interventions is constrained by the small number of RCTs (some of which have small sample sizes or are not of high quality), the use of unvalidated scales (often VAS), and the fact that they are often not primarily aimed at or powered for fatigue. There is some evidence for exercise, education, CBT and emotional disclosure in the short to medium term.

Future research into the management of fatigue

Future research needs to address whether, rather than changing the severity of fatigue per se, we might be able to change beliefs about coping with fatigue, or change ability to participate in socialising despite continuing fatigue, and thus reduce the impact of persistent fatigue. Suggestions that interventions work for particular sub-groups should be pursued (e.g. early disease, distressed patients).[64] Where there are complex intervention approaches, evidence on the contribution of different components (e.g. goal-setting, energy conservation, cognitive restructuring) would be helpful. Studies should have fatigue as their primary outcome, be well designed, robust, and adequately powered, and should address interventions that can be easily translated into clinical practice (e.g. few rheumatology departments have a clinical or health psychologist within their team). In addition, long-term follow-up and the use of booster sessions should be explored.

CONCEPTS OF FATIGUE IN MUSCULOSKELETAL CONDITIONS

There is no universally-accepted definition of fatigue in either health or illness, but conceptual and theoretical frameworks for fatigue in cancer and MS are being developed to help classify fatigue so as to enhance measurement and intervention.[74,75] A framework for fatigue in musculoskeletal conditions should be able to incorporate classifications of fatigue (e.g. physical, emotional, cognitive, motivational), define incremental fatigue states (e.g. tiredness, weariness, exhaustion), account for different manifestations (e.g. gradual onset, acute wipe-out), identify potential drivers (e.g. biological, psychological, social), allow for cyclical states (e.g. fatigue leading to depression, which fuels further fatigue) and sit within a theoretical framework to exemplify opportunities for intervention (e.g. biopsychosocial or cognitive-behavioural frameworks). A conceptual and theoretical framework is currently being developed for fatigue in musculoskeletal conditions (by the Fatigue in RA Group (FRAG); contact *sarah.hewlett@uwe.ac.uk*).

APPLICATION OF THESE FINDINGS TO CLINICAL PRACTICE

Mood changes and illness perceptions have the most observational evidence of an association with fatigue in musculoskeletal conditions. These issues could be applied as 'yellow flags' for identifying individuals who are at risk of the onset of fatigue, or are developing persistent fatigue despite pharmacological management (e.g. the use of DMARDs to control disease activity).

With the caveat that *existing evidence for interventions is limited*, clinicians might consider the following approaches to such patients:

- discussing fatigue with patients, which may help them to feel their symptom and associated distress are validated
- checking for and treating anaemia, thyroid dysfunction, diabetes or depression if appropriate
- providing literature that explains fatigue (e.g. the **arc** patient leaflet 'Fatigue and Arthritis', *www.arc.org.uk/arthinfo/patpubs/6269/6269.asp*)
- developing fatigue self-management strategies within existing education programmes
- identifying a team member to specialise in fatigue (and refer patient to them)
- utilising a fatigue diagram to explore patient's perceived areas for intervention (untested, Figure 1)
- considering use of daily diaries to identify behaviours such as 'boom and bust' or excessive rest, accompanied by supported, individualised goal-setting to change behaviour.

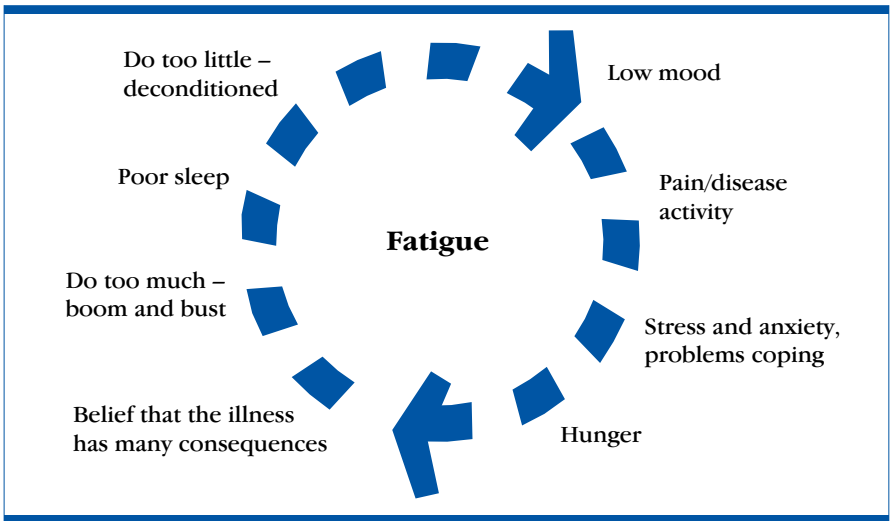

FIGURE 1. Exploring patient perceptions of the causes of fatigue in clinic.

CONCLUSION

The current interest in fatigue in musculoskeletal conditions is a testament to the voice of the patient perspective in outcome measurement. Further research is needed into the meaning, mechanisms, measurement and management of fatigue. While debate continues about whether fatigue is specific to inflammatory arthritis or is simply the fatigue of an LTC, patients still have to manage this difficult symptom. Research is continuing internationally, with a long-term aim of developing an evidence-based treatment algorithm.

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