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Musculoskeletal disorders as a fatigue failure process: evidence, implications and research needs

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ABSTRACT

Mounting evidence suggests that musculoskeletal disorders (MSDs) may be the result of a fatigue failure process in musculoskeletal tissues. Evaluations of MSD risk in epidemiological studies and current MSD risk assessment tools, however, have not yet incorporated important principles of fatigue failure analysis in their appraisals of MSD risk. This article examines the evidence suggesting that fatigue failure may play an important role in the aetiology of MSDs, assesses important implications with respect to MSD risk assessment and discusses research needs that may be required to advance the scientific community's ability to more effectively prevent the development of MSDs.

Practitioner Summary: Evidence suggests that musculoskeletal disorders (MSDs) may result from a fatigue failure process. This article proposes a unifying framework that aims to explain why exposure to physical risk factors contributes to the development of work-related MSDs. Implications of that framework are discussed.

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Musculoskeletal disorders; fatigue failure; cumulative trauma; rest; risk assessment

1. Introduction

Musculoskeletal disorders (MSDs) are widespread throughout the world, and are associated with enormous financial and societal costs. MSDs are the second-greatest cause of disability globally, having increased 45% since 1999 (Horton 2010). They account for roughly one-third of all workplace injuries and illnesses in the United States annually (BLS 2015). In 2004, the estimated direct cost of treatment for MSDs in the United States was estimated at $510 billion, equivalent to 4.6% of the gross domestic product (GDP) (AAOS 2008). Indirect costs were estimated to add $339 billion more, for a total cost for MSDs of $849 billion, or 7.7% of the GDP (AAOS 2008).

Our understanding of the aetiology of MSDs has advanced considerably over the past few decades. Importantly, epidemiological studies have identified several physical risk factors for work-related MSDs common to both upper extremity disorders and low back pain (LBP) (Punnett et al. 2005). These include exposure to tasks requiring: (1) high-force exertions, (2) highly repetitive tasks, (3) adoption of non-neutral postures and (4) exposure to whole-body or hand-arm vibration (NIOSH 1997; NRC-IOM 2001; Punnett et al. 2005). However, lacking in previous analyses of these risk factors has been the development of an underlying theoretical framework that could explain how and why these risk factors are associated with the development of MSDs.

Recently, however, a systematic review of the literature identified a consistent statistical interaction between the risk factors of force and repetition with respect to risk of a wide variety of MSDs including low back disorders (LBDs), carpal tunnel syndrome (CTS), lateral epicondylitis, shoulder pain and many others (Gallagher and Heberger 2013). The authors noted that the pattern of interaction observed in the reviewed studies was indicative of the presence of a fatigue failure process in musculoskeletal tissues and may provide a unifying framework to explain the effects of all of the physical MSD risk factors noted above. If MSDs are indeed the result of a fatigue failure process, numerous important implications arise with respect to how risk of MSDs should be assessed and how prevention efforts should be designed. This paper describes the evidence that suggests MSDs may be the result of a fatigue failure process, explores important implications in terms of exposure and risk assessment and discusses recommendations for future research.

2. Background

It has long been recognised that materials experience failure through either: (1) application of a one-cycle high-magnitude stress (at the so-called 'ultimate stress' [US] of the material), or (2) repeated application of loads

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at some percentage of the material's US (Peterson 1950). The American Society for Testing and Materials (ASTM) has defined the latter failure mode, known as fatigue failure, as:

> … the process of progressive localized permanent structural change occurring in a material subjected to conditions that produce fluctuating stresses and strains at some point (or points) and that may culminate in cracks or complete fracture after a sufficient number of fluctuations. (ASTM 2000)

The rate of damage propagation in a material is a function of several loading characteristics and the number of cycles experienced at various loads. The relationship between applied stress and the number of cycles to failure is exponential in nature and is typically described in an *S–N* diagram, which describes the manner in which the number of cycles to failure (*N*) varies with respect to a constant cyclic stress (*S*). An example *S–N* diagram is provided in Figure 1. As can be seen in this figure, higher levels of loading will result in failure in fewer cycles and lower levels of loading will last an exponentially larger number of cycles. In fact, millions of cycles may be necessary to create failure in low load situations, and for many materials there exists a fatigue (or endurance) limit (usually around 30% of the material's US) where failure will not occur no matter the number of cycles experienced in fully reversed loading conditions (Ashby, Shercliff, and Cebon 2010).

The traditional domain of fatigue failure analysis has been in evaluation of components and/or engineered structures such as bridges, aircraft and automobile parts, and nuclear pressure vessels. However, biological tissues are also materials, and would be expected to incur damage in accordance with the same principles, though with some important differences due to the fact that these materials reside in a complex physiological environment.

While it has been generally recognised by the field that MSDs result from a progression of cumulative damage (as the term 'cumulative trauma disorders' implies), application of fatigue failure principles has not been apparent in the design of current MSD risk assessment tools or recent

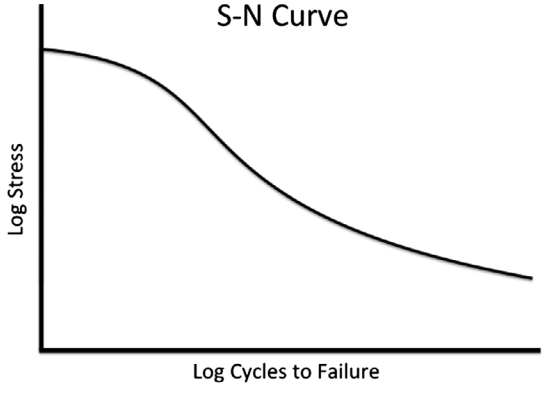

Figure 1. Example of an *S–N* diagram, relating the level of stress (*S*) to the number of cycles to failure (*N*).

epidemiological studies. Nor have the foremost reviews of the MSD literature evaluated risk in accordance with the tenets of fatigue failure (e.g. NIOSH 1997; NRC-IOM 2001). However, as described below, evidence from a variety of sources strongly suggests that fatigue failure is occurring in musculoskeletal tissues, and may be an important etiological mechanism in the development of MSDs.

3. Evidence of a fatigue failure process in musculoskeletal tissues

Several lines of evidence support the notion that MSDs might be the results of a fatigue failure process in musculoskeletal tissues. These include *in vitro* testing of musculoskeletal tissues, animal studies of tissue loading and the epidemiological studies mentioned above.

In vitro studies have been performed on tendons (Schechtman and Bader 1997; Wang, Ker, and Alexander 1995), ligaments (Lipps, Ashton-Miller, and Wojtys 2014; Lipps, Wojtys, and Ashton-Miller 2013; Thornton, Schwab, and Oxland 2007), cartilage (Bellucci and Seedhom 2001) and spinal motion segments, both in compression (Brinckmann, Biggemann, and Hilweg 1988), shear (Cyron and Hutton 1978), and combined compression and shear loading (Gallagher et al. 2005, 2007). Irrespective of the material studied, all studies have demonstrated an exponential relationship between the stress applied and the number of cycles to material failure. In this respect, musculoskeletal tissues are shown to be no different from other (non-biological) materials.

Additional support for the fatigue failure hypothesis of MSD causation can be found in data from a rat model where Sprague-Dawley rats were exposed to one of the following conditions: low-force, low-repetition, low-force, high-repetition, high-force, low-repetition or high-force, high-repetition exertions (Barbe et al. 2013). Tissue pathology results for tendon damage, cartilage damage and bone volume and cytokine responses to applied loading, all demonstrated statistically significant force–repetition interactions of the pattern consistent with an underlying fatigue failure process. Furthermore, Andarawis-Puri and Flatow (2011) showed in an *in vivo* mouse model that fatigue-loaded tendons demonstrated a structural damage progression that started with fibre kinking for low level fatigue loading, to development of a widened interfibre space in tendons with moderate fatigue loading, to a severe matrix disruption with high-level fatigue loading. These results provide evidence that fatigue failure is not just a response observed in *in vitro* studies – musculoskeletal tissues also experience fatigue failure *in vivo*.

Finally, as mentioned previously, epidemiological studies that have examined a force–repetition interaction have shown a pattern of risk consistent with a fatigue failure

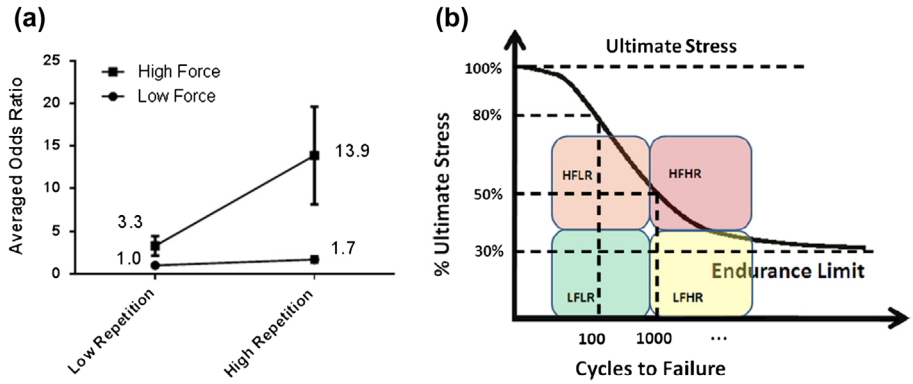

Figure 2. (a) Averaged Odds Ratios for seven studies examining quadrants of risk for force and repetition (Gallagher and Heberger 2013), and (b) fatigue failure curve.
Note: The pattern of risk observed in (a) would be anticipated if MSD development was the results of a fatigue failure process (b).

process (Figure 2). MSDs demonstrating this pattern include CTS, tendinitis, epicondylitis, hand pain and LBDs (Gallagher and Heberger 2013). Recent findings of a large prospective epidemiological study indicating that 'forceful repetition' was the loading variable most associated with development of CTS comports with fatigue failure theory and provides additional support for our model (Harris-Adamson et al. 2015). The additional information provided by these epidemiological studies is that human tissues also appear to be experiencing the same fatigue failure process during the development of MSDs. Given the available evidence, it would seem prudent to consider the implications of fatigue failure theory in terms of MSD risk assessment and prevention efforts, which are discussed below.

4. Implications of MSDs as a fatigue failure process

Despite mounting evidence that fatigue failure may be important in MSD aetiology, there are currently no examples to the authors' knowledge that any ergonomics risk assessment tools have used fatigue failure principles as a basis for ascertaining MSD risk. If MSDs are indeed the result of a fatigue failure process, several fundamental implications related to assessment of risk and methods of prevention for these disorders must be considered. The following sections discuss both general implications and important analysis principles that should be considered when assessing MSD risk from a fatigue failure perspective.

4.1. A unifying framework for MSD risk factors

MSD risk factors have traditionally been assumed to function in a statistically independent manner *vis a vis* MSD risk. For example, several comprehensive reviews of the literature (e.g. NIOSH 1997; NRC-IOM 2001) did not evaluate the potential for an interaction of force and repetition. However, both *in vitro* and *in vivo* evidence strongly suggests that a consistent statistical interaction exists between force and repetition with respect to MSD risk. This suggests that these two risk factors cannot be treated independently, but instead have an important dependency wherein *the impact of repetition is highly dependent on the forces imposed on the tissues*. If fatigue failure were indeed etiologically significant in MSDs (and a force–repetition interaction exists), examining the main effects of force and repetition would provide unreliable estimates of risk, as main effects are uninterpretable in the presence of an interaction (Meyer 1991). The implication is that force and repetition must be considered in tandem, not in isolation, when assessing MSD risk.

A fatigue process in musculoskeletal tissues clearly would alter the manner in which we would consider the risk factors of force and repetition, but what about the other risk factors for MSDs? For example, consider the adoption of non-neutral postures, another important physical risk factor for MSDs. It should be recognised that adoption of awkward or non-neutral postures often leads to imposition of increased stress on musculoskeletal tissues (in some form or fashion). According to the force × repetition interaction paradigm discussed previously, any increased force demand that may result from the use of non-neutral postures would also be expected to lead to a more rapid escalation of MSD risk. For example, compared to an upright posture, bending the trunk forward into full flexion can triple the stress experienced by the lumbar spine (Nachemson 1976). Studies have demonstrated a dose–response relationship as non-neutral trunk postures becomes more extreme (Punnett et al. 1991), following an expected increase in spinal forces as more extreme neutral postures are adopted. Similarly, working with a deviated wrist posture may increase frictional forces on tissues of the tendons that may also lead to tissue frictional fatigue and, ultimately, CTS (Armstrong and Chaffin 1979).

Adoption of non-neutral postures may have an important role with respect to increasing the mean stress on musculoskeletal tissues, which has an important impact on the fatigue life of tissues, as discussed below. Clearly, awkward postures can have other impacts such as impeding blood flow (Chaffin, Andersson, and Martin 1999) or increasing ligament laxity (Solomonow et al. 2003), which may affect tissue health and/or injury potential. However, a major reason posture emerges as a risk factor for MSDs may simply be due to the increased tissue loads that result from adoption of awkward or non-neutral postures, and the effects of these increased loads in the fatigue failure paradigm.

Finally, it should be recognised that vibration exposure is a combination of force and repetition. When engineers evaluate the effects of vibration on the life of a particular component, they often utilise the techniques of fatigue failure analysis (Sarkani and Lutes 2004). These techniques include cycle counting using the rainflow algorithm (Matsuishi and Endo 1968) and summation of damage incurred by the vibration using the Palmgren–Miner (Miner 1945; Palmgren 1924) technique, both traditional tools of fatigue failure analysis. Thus, it may also be worth evaluating effects of vibration exposure on musculoskeletal tissues from a fatigue failure context as well.

4.2. Validated methods for assessing risk of cumulative damage

The ability to quantify cumulative damage related to repetitive loading of musculoskeletal tissues has long been a holy grail of the ergonomics community. Fortunately, fatigue failure theory has validated methods to predict damage accumulation associated with the variable loading regimens typically experienced by musculoskeletal tissues in occupational (and non-occupational) settings.

The variable amplitude loading typically experienced by musculoskeletal tissues is often termed 'spectrum' loading in the fatigue literature, and the term 'cumulative damage' refers to fatigue effects of non-uniform repeated loading events (Stephens et al. 2001). The most commonly used method of assessing or predicting damage resulting from spectrum loading is the linear cumulative damage rule for fatigue life from spectrum loading was proposed by Palmgren (1924) and Miner (1945):

$$c = \sum_{i}^{k} \frac{n_1}{N_1} + \frac{n_2}{N_2} + \cdots + \frac{n_k}{N_k} \quad (1)$$

where c is a constant (often set at 1, but which can vary), $n_i \ldots$ equal the number of exposure cycles experienced at force levels at which $N_i \ldots$ cycles would result in fatigue failure. When the right-hand sum is equal to one, the material would be expected to fail. However, for different materials the value of c has been shown to vary above and below this number.

A rudimentary example of the Palmgren–Miner technique is provided below. In this illustration, the need to examine both force and repetition in combination should become apparent. Suppose that a worker performs a task that stresses a tendon at 15 cycles at 60% of ultimate tensile stress (UTS), 100 cycles at 50% UTS and 700 cycles at 40% UTS. Suppose also that the cycles to failure for 60, 50 and 40% UTS are 1000, 10,000, and 100,000 cycles, respectively. The Palmgren–Miner technique would calculate the cumulative damage (Dt) by summing the quotients of the number of cycles experienced at each stress level divided by their respective cycles to failure. The result of the calculation (seen in Figure 3) is 0.032, suggesting that this load would create damage of approximately 3% of the material's fatigue life.

Notice that if one were to focus on the risk factor of repetition in isolation, as has often been done in the past, it would appear that the 700 repetitions at 40% UTS would be the condition of primary concern. However, when examined in relation to the number of cycles to failure at each % UTS, it can be seen from the Palmgren–Miner equation that the 15 cycles at 60% UTS actually result in more than twice the cumulative damage compared to 700 cycles at 40% UTS. This example should illustrate clearly that the impact of repetition changes dramatically as a function of the stress imposed on tissues, and that examining repetition in isolation may lead to improper conclusions regarding the nature of MSD risk experienced by a worker.

The Palmgren–Miner rule often provides a useful approximation of the accumulation of fatigue damage in a material; however, it must be understood that it is an approximation. Numerous factors can influence the development of fatigue failure and these factors can influence the fatigue failure process in a manner not captured by the simple linear relationship expressed above. For example, localised stress concentrations in a material may lead to microstructural failure that causes a portion of the material to become unable to support a load, leading to

% Ult. Strength	Cycles to Failure	Cycles experienced
60%	1000	15
50%	10000	100
40%	100000	700

$$D_{(t)} = \frac{15}{1000} + \frac{100}{10000} + \frac{700}{100000}$$

$$= 0.015 + 0.01 + 0.007 = 0.032$$

Figure 3. Example of cumulative damage calculation using the Palmgren–Miner rule.

a decrease in fatigue life. On the other hand, there may be situations where changes in molecular orientation may actually slow down the fatigue failure process (Stephens et al. 2001). Such factors are not taken into account by the Palmgren–Miner rule, but can have large influences on fatigue life (Roylance 2001). Despite these limitations, the Palmgren–Miner rule remains a useful method with which to estimate cumulative damage in variable loading conditions and may be helpful in ascertaining MSD risk.

Other methods of evaluating cumulative loading metrics for LBP have included measures such as the area under the loading curve (Norman et al. 1998), which makes intuitive sense. Such techniques, however, do not address many important issues that are important in the development of cumulative damage from a fatigue failure perspective (Stephens et al. 2001). The following section discusses some of the issues related to cumulative damage estimation based on loading situations experienced by musculoskeletal tissues.

4.3. The critical roles of stress range and mean stress on cumulative damage

Loading cycles on musculoskeletal tissues can vary in many ways, one of which is the amount of time spent in the loaded phase versus the unloaded phase of a cycle (otherwise known as the duty cycle). To examine the effect of duty cycle, a few basic techniques of fatigue failure analysis must be covered. To begin, consider a standard method of performing loading in fatigue failure studies, specifically the condition known as completely reversed loading using a sinusoidal loading pattern. Completely reversed loading represents a loading condition where an object is subjected to alternating tensile and compressive stresses and where the mean stress is 0. Figure 4(a) illustrates such a loading pattern. As can be seen in the figure, several characteristics of the loading pattern can be defined. σ_a represents the average of the maximum minus the minimum load of the cycle, σ_m represents the mean loading associated with the cycle, which in the case of fully reversed loading is equal to 0.

The standard *S–N* curve for a material is developed assuming a fully reversed loading cycle (i.e. where $\sigma_m = 0$). However, if σ_m is not equal to 0, certain specific loading conditions are known as either repeated stress or fluctuating stress (Figures 4(b) and (c)). Repeated stress is defined as a loading pattern where the minimum stress is zero and cycles to some positive (tensile) or negative (compressive) value. This loading pattern is representative of the type of loading experienced by tendons or ligaments. Fluctuating stress is when the minimum stress is non-zero and cycles to a stress of larger absolute magnitude. An example of this would be the loading pattern experienced by a worker repeatedly lifting bags off of a conveyor. The worker begins by standing upright (nothing in the hands) with a load of approximately 500 N on the spine then repeatedly lifts

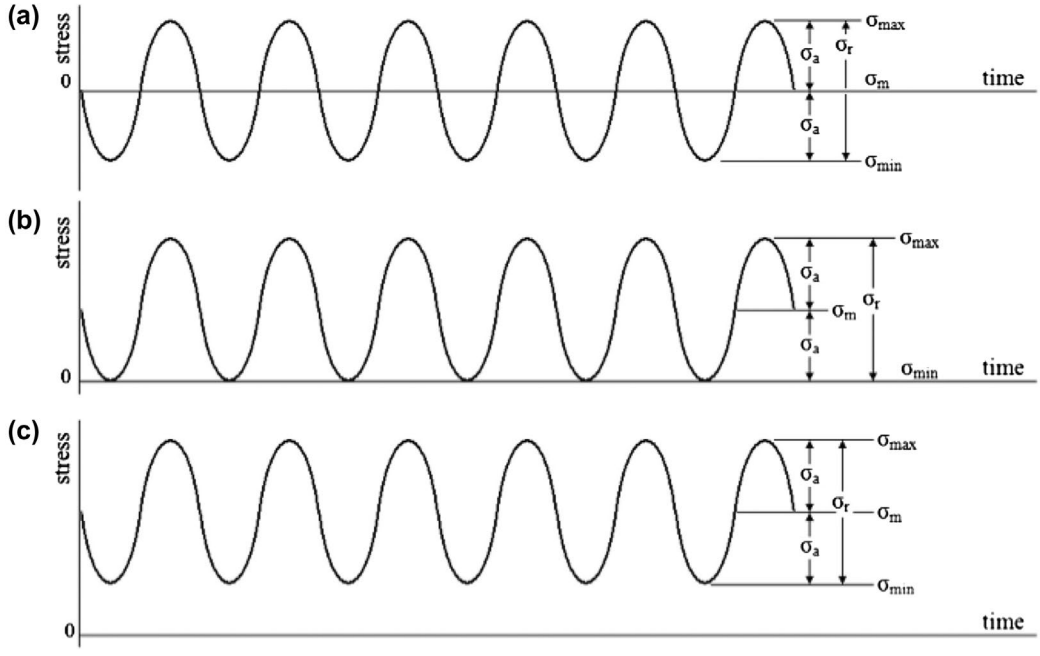

Figure 4. Examples of a (a) fully reversed sinusoidal loading, (b) repeated stress, and (c) fluctuating stress, where σ_a = stress amplitude, σ_r = stress range, σ_{max} = maximum stress, σ_{min} = minimum stress and σ_m = mean stress.
Note: Deflections below zero represent compressive loading, while deflections above zero represent tensile loading (Figure from http://www.engineeringarchives.com/les_machdes_cyclicloading.html).

bags off of the conveyor increasing the compressive load on the spine (say, to 3000 N), which returns to 500 N when the load is released. In this case, the spine is always experiencing compression which cycles from some non-zero number to a larger magnitude compressive stress (i.e. the stress on the spine is never reduced to zero). Both repeated and fluctuating stresses will result in a non-zero mean stress on the tissues, which may shift the fatigue failure curve down, meaning that fewer loading cycles would be needed reach failure compared to a fully reversed loading condition (Figure 5).

Fatigue failure theory has methods for calculating safety factors and expected cycles to failure for materials subjected to repeated or fluctuating stress. These techniques are the Goodman line (Goodman 1899) and the Gerber (1874) criterion, with the Goodman criterion serving as the more conservative of the two. Actual experimental data on fatigue life tend to reside between these two lines. For both criteria, every point on the line corresponds to failure in 10^6 cycles. Thus, combinations of stress amplitude and mean stress that reside beneath the lines would be said to have 'infinite life' and points above the curves would have finite life.

In materials engineering applications, these design techniques often will be used to design materials or parts for 10^6 cycles to failure (considered to be 'infinite life'). In other cases, however, engineers may design for finite life ($<10^6$ cycles to failure). In such cases, it must be estimated how many cycles would be expected until failure when infinite life conditions are exceeded, given a certain stress amplitude (σ_a) and mean stress (σ_m). Under the completely reversed loading situation, the following equation would be used:

$$N = \left(\frac{\sigma_a}{a}\right)^{\frac{1}{b}} \tag{2}$$

where N represents cycles to failure, σ_a is the stress amplitude and a and b are:

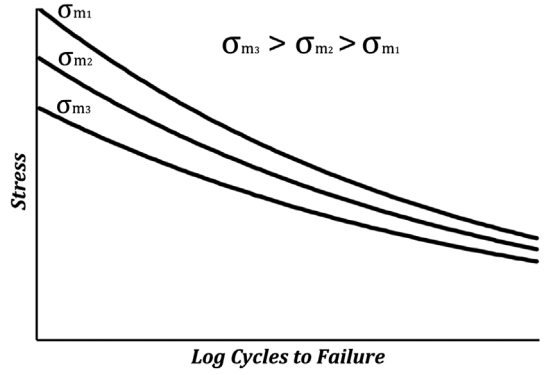

Figure 5. The influence of mean stress on *S–N* curves. As mean stress increases, cycles to failure will decrease at a give level of stress.

$$a = \frac{(f \cdot S_{ut})^2}{S_e} \tag{3}$$

$$b = -\frac{1}{3} log\left(\frac{f \cdot S_{ut}}{S_e}\right) \tag{4}$$

where f is the fatigue strength fraction (approximation of the fatigue strength at 10^3 cycles), S_{ut} is the ultimate tensile strength and S_e is the Stress at the Endurance Limit.

However, in the fluctuating stress situation, we cannot use σ_a in Equation (2) above as this only pertains to the completely reversed loading. In the case of fluctuating stress, we must instead calculate σ_{rev} that represents an equivalent value for completely reversed stress under repeated or fluctuating stress, and will replace σ_a in Equation (2). Thus, for fluctuating stress conditions (using the Goodman design criterion) our equation for N cycles to failure becomes:

$$N = \left(\frac{\sigma_{rev}}{a}\right)^{\frac{1}{b}} \tag{5}$$

where σ_{rev} is:

$$\sigma_{rev} = \frac{\sigma_a}{1 - \frac{\sigma_m}{S_{ut}}} \tag{6}$$

and for the Gerber relation σ_{rev} is:

$$\sigma_{rev} = \frac{\sigma_a}{1 - \left(\frac{\sigma_m}{S_{ut}}\right)^2} \tag{7}$$

The influence of mean stress in this relationship has relevance to the issue of duty cycle in occupational tasks. Figure 6 below shows an example of the influence of mean stress that will be used to calculate expected cycles to failure for each instance. Figure 6(a) illustrates loading with a 40% duty cycle, while Figure 6(b) represents a duty cycle of 70%. The mean stress (σ_m) for the former condition would be 13.93 MPa, while the latter has a mean stress of 25.87 MPa.

There are several methods of predicting cycles to failure given the loading amplitude and mean stress. Two of the most popular are the Goodman equation and the Gerber equation. Of the two, the Goodman criterion tends to result in relatively conservative estimates of fatigue life and the Gerber curve results in a more generous fatigue life prediction. Test data tend to fall between the two predictions (Stephens et al. 2001).

Calculation of the expected cycles to failure according to the Goodman equation suggests a fatigue life of 5700 cycles to failure for the 40% duty cycle condition and 1423

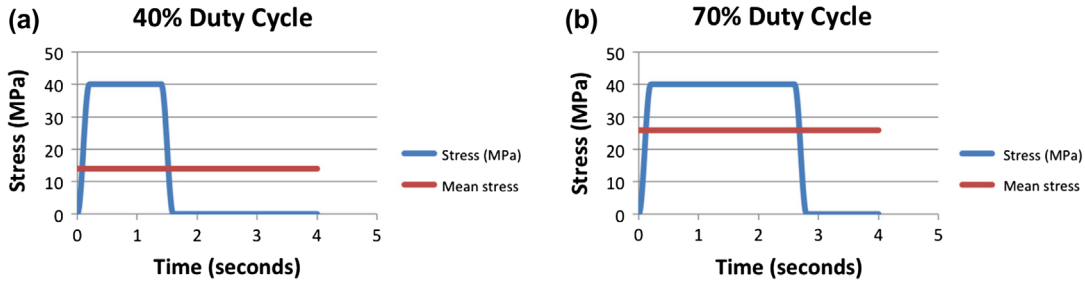

Figure 6. Comparison of the mean stress in (a) a 40% duty cycle (13.93 MPa) versus (b) a 70% duty cycle (25.9 MPa).

cycles to failure for the 70% duty cycle condition. Using the Gerber criterion, the 40 and 70% duty cycle conditions are predicted to last 19,300 and 12,150 cycles, respectively.

4.4. Various types of rest and musculoskeletal health

When considering the impact of rest on MSDs, a distinction may be made between short-term rest (short cyclic loading 'gaps' in the midst of a sequence of repetitive tissue loading) and long-duration rest (tissue unloading) experienced over more extended periods during which significant tissue loading is sparse. With respect to short-term loading gaps, it is likely that the effect on tissue health may be *primarily the influence that the rest period has on the* ***mean stress*** *experienced by tissues during the loading process*. As demonstrated previously, short duty cycles result in a greater fatigue life compared to longer duty cycles due to the lower mean tissue stress. However, remodelling and repair of tissue damage is a time-consuming process taking weeks, months or years, and short-term loading gaps (say, a few seconds in length) are unlikely to provide the opportunity for meaningful tissue healing (Sharma and Maffulli 2005). Tissue unloading lasting extended periods would seem more conducive to repair and remodelling of tissues. Thus, increased rest both in loaded and non-loaded states may be protective against MSDs, but in different manners. Short-term loading (stress) gaps in the midst of frequent tissue loading would decrease the mean stress experienced during loading and increase fatigue life, while long-term stress relief would facilitate tissue remodelling and repair. It should be noted that short-term breaks may be beneficial in terms of other sorts of musculoskeletal function (for example, reducing development of muscle fatigue), but the actual healing and regeneration of tissues during short periods of rest would be minimal at best.

4.5. Counting cycles in variable amplitude loading

Musculoskeletal loading patterns in occupational settings tend to exhibit substantial variability (Mathiassen 2006; Mathiassen, Möller, and Forsman 2003). One commonly used technique to evaluate highly variable loading patterns in the context of a fatigue failure process is known as 'rainflow analysis' (Matsuishi and Endo 1968). The 'rainflow' term refers to an analogy of rain dripping off of the roof of a pagoda. This analysis technique takes a complex set of varying stress exposures and breaks it down into a series of stress reversals. Once these stress reversals are obtained, one can apply the Goodman and/or Gerber relationships and the Palmgren–Miner technique to estimate the amount of cumulative damage in the material of interest. An example of the rainflow analysis technique is provided below. It is important to note that this technique assumes all loads are independent from one another and that there are no sequence effects.

The example in Figure 7(a) presents a stress-loading curve as might be experienced by a tendon during work. Figure 7(b) provides a rainflow analysis of the curve presented in Figure 7(a). The black line represents the variable stress loading experienced by the material, and the blue lines represent the half cycles. The horizontal lengths of the blue lines are dictated by whether you encounter either: (1) a valley lower than or equal to the one at which you started, or (2) a peak greater than or equal to the one at which you started. As can be seen with some of the lines in Figure 7(b), stress reversals may be defined not by the first peak or valley encountered, but subsequent peaks or valleys as the 'rain' drips off of different levels of the pagoda 'roof' (if one were to imagine the figure rotated 90 degrees clockwise). In such circumstances, notice that there are short lines that account for the part of the loading not involved with the line dripping off multiple pagoda roof levels. In this manner, every part of the loading signal is accounted for in the rainflow analysis (Downing and Socie 1982). Table 1 presents the breakdown of stress reversals resulting from this example and calculates predicted cycles to failure (N) and damage per cycle ($1/N$) using the Goodman criterion. For these analyses, the fatigue strength fraction (f) (i.e. S_f/S_{ut} at 10^3 cycles) was assumed to be 0.42 and the S_e (S_f at 10^6 cycles) was estimated at 10% S_{ut} based on data from Schechtman and Bader (1997) and Thornton, Schwab, and Oxland (2007).

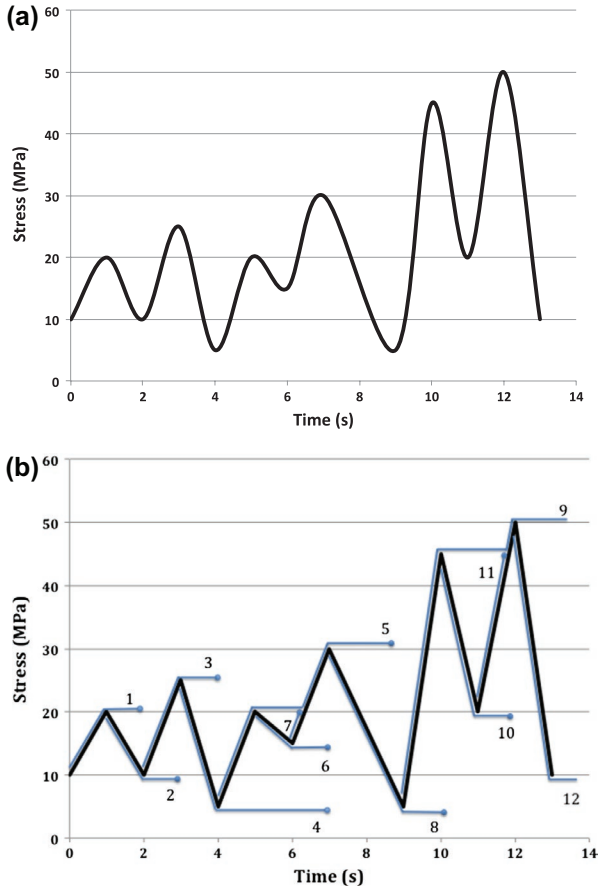

Figure 7. (a) Example of loading curve as might be experienced by a tendon. (b) Rainflow analysis defining half cycles for the loading sequence in (a).

Inspection of Table 1 provides several insights in terms of the damage associated with different portions of the loading sequence shown in Figure 7. One important insight from this analysis is the importance of the stress range in the development of material damage. As can be seen from this table, the two half cycles resulting in the vast majority of damage (86%) from this loading sequence are the ones possessing the greatest stress range. In fact, stress range can have a bigger impact on fatigue damage in variable amplitude loading than measures such as maximum stress.

This finding has significant consequences in terms of assessing risk of MSDs in occupational settings. Obviously, it would seem important to evaluate the service load histories of musculoskeletal tissues when exposed to occupational (or non-occupational) stressors, as are commonly performed for bridges, aircraft wings and the like. Materials engineers have the benefit of being able to mount strain gages to critical components that need to be analysed for failure risk or design purposes. For the biomechanist, things are not so simple, especially when *in vivo* loads need to be ascertained. Instead, load histories will usually have to be estimated using biomechanical analysis and modelling techniques. Using biomechanical modelling techniques, estimates of the important variables of fatigue failure analysis can be reasonably estimated for musculoskeletal tissues, for example, the stress range and the mean stress. A technique sometimes used to quantify a service load history (in this instance, perhaps one workday of exposure) is to summarise the results of a rainflow analysis as in Table 2. As can be seen in this table, (half) cycles are broken down into their stress range/mean stress components and tabulated. If one can also estimate the US, fatigue strength fraction and endurance limit of the material, all of the necessary variables are available to estimate the accrual of cumulative damage.

In an ideal world, we would be able to assess the totality of loading on an individual. However, in the real world, it may be necessary to estimate a worker's cumulative loading on the basis of careful work sampling. This would not only include the main tasks performed, but inclusion of infrequent tasks as well. Methods such as Predetermined Time & Motion might be used to derive a statistically representative daily cumulative load. If job rotation were performed, each task would have to be analysed and cumulative loads from each task summed to determine the cumulative daily load.

Table 1. Results of rainflow analysis of loading cycles from Figure 7.

Reversal #	Starting Stress (MPa)	Ending Stress (MPa)	Stress Range (MPa)	Mean Stress (MPa)	Predicted *N* (Goodman)	Damage per cycle (1/N)	% of total damage
1	10	20	10	15	12860623	0.000000053	0.03
2	20	10	10	15	12860623	0.000000053	0.03
3	10	25	15	17.5	1582133	0.000000398	0.19
4	25	5	20	15	457361	0.000001478	0.71
5	5	30	25	17.5	135325	0.000004657	2.25
6	20	15	5	17.5	313226248	0.000000002	0.00
7	15	20	5	17.5	313226248	0.000000002	0.00
8	30	5	25	17.5	135325	0.000004657	2.25
9	5	50	45	27.5	4291	0.000110456	53.44
10	45	20	25	32.5	51509	0.000007965	3.85
11	20	45	25	32.5	51509	0.000007965	3.85
12	50	10	40	30	6388	0.000069026	33.39
Total						0.000206712	100.0

Table 2. Hypothetical example of the number of cycles at various stress range/mean stress combinations from a loading spectrum (subjected to rainflow analysis) as might be experienced in an occupational workday.

	Mean stress (MPa)														
Stress range (MPa)	0	2.5	5	7.5	10	12.5	15	17.5	20	22.5	25	27.5	30	32.5	35
5		539	370	201	152	94	80			42					
10			163	312	49	215	42				25				
15				148	95	427	233	142	37	13		17			
20					12	127	64	99	109	40	31				
25							12	72	49	63	25		19	12	
30								17		15	7	13			5
35												9	13		
40												6			
45													3		
50															

4.6. Individual characteristics and risk

An important precept of fatigue failure theory is that the effect of a given load *is indexed to the US of the exposed tissue*. It is important to recognise that each individual's tissue US will be unique, and variability between individuals may be immense. Given the same load and rate of repetition, different tissue strengths can lead to vastly different rates of damage. For example, a spinal load of 3 kN will cause more damage per cycle to a spine whose US is 6 kN than one of 12 kN. Of course, each individual's unique tissue strength profile will be heavily influenced by factors such as age, gender and anthropometry.

A common tactic of industry for physically demanding jobs is that of worker placement (e.g. getting younger, stronger individuals to work more physically demanding jobs). Designing such that 75% of females and 90% of males have the capability to perform a job should be protective of workers; however, it bears consideration that it may be overprotective for individuals with higher tissue strengths. These individuals may be able to operate quite safely at a higher absolute level of loading that the population-based design criteria would suggest. In this respect, it may be said that design according to population guidelines as above may lead to an unnecessarily strict constraint and a loss of work capacity for industry.

Design according to individual tolerances is not without peril, however, and would need to be very carefully managed. Even individuals with high tissue strength can be overloaded, and develop cumulative damage. However, if MSDs are the result of a fatigue failure process, individualised 'safe loads' may be possible and may make sense as a method of controlling MSDs without being unnecessarily restrictive. Of course, that is not to say that the approach above is to be preferred – ergonomic design of the workplace to eliminate the lift or otherwise reduce the spinal load is clearly a superior approach. However, in circumstances where it is difficult or cost prohibitive to implement an ergonomics fix, having workers with stronger tissues perform the more physically demanding jobs does make some sense from a fatigue failure perspective.

Moreover, the large differences in tissue strength strongly suggest that recommendations for controlling the incidence of MSDs should take age and gender issues into account. As individuals age, the US of musculoskeletal tissues will experience significant weakening and acceptable loads for repetitive activities should decrease correspondingly. It must also be recognised that large differences in tissue strengths are present between the genders, and acceptable loads for repetitive activities are going to differ substantially between males and females. A third individual characteristic that might have influence in terms of acceptable loads is anthropometry. Larger individuals will generally exhibit larger tissue size and strength, which would also significantly influence acceptable loads for repetitive tasks. Again, muscle strength may be a good surrogate measure for tissue strength, and may be useful to monitor from a design standpoint, i.e. designing jobs at some percentage of a maximum voluntary contraction (% MVC) may reduce fatigue failure development.

4.7. Maintenance of tissue homeostasis

In biological systems, both tissue damage and tissue repair processes are continually in progress. The key to prevention of MSDs is to try to ensure that the amount of damage accrued in tissues does not exceed the capacity of the repair mechanisms to heal. The unfortunate truth is that tissue damage can develop relatively rapidly, while the repair process is time-consuming process that can take weeks, months or years. Even when the repair process is complete, many types of tissues (such as tendons, ligaments and cartilage) never regain their original strength and/or tissue quality. Clearly, maintaining a modest degree of damage is critical to maintenance of tissue homeostasis.

Nash (1966) put forth a generalised model of fatigue failure for self-healing biological materials, which can be expressed as follows:

$$D(t) = D_D(t) + D_A(t) + D_S(t) - H(t) \quad (8)$$

where $D(t)$ represents total tissue damage over a time frame, $D_D(t)$ is damage due to disease, $D_A(t)$ is damage due to aging, $D_s(t)$ is damage due to imposed stresses on tissues and $H(t)$ represents healing over the time frame of interest. If one is considering a time frame where disease is not present and the effect of aging is not significant, then this equation can be simplified:

$$D(t) = D_S(t) - H(t) \quad (9)$$

where $D(t)$ represents total tissue damage over a time frame, $D_s(t)$ is damage due to imposed stresses on tissues and $H(t)$ represents healing over the time frame of interest. The term $D_s(t)$ can be estimated using the Palmgren–Miner rule, as described above. To do this one would have to know or estimate the ultimate strength of the tissue in question and be able to quantify the stress experienced by the tissue. One would then simply have to know the healing rate of the stressed tissue over time to quantify the total amount of cumulative damage accrual in the tissue.

Healing of tissues requires periods of unloading (rest) and some controlled loading so that damage accumulation can cease and repair mechanisms can have the time necessary to heal the tissue. But how much rest is needed? This is a question that does not yet have a clear answer. However, the model described above would suggest that the amount of rest necessary for healing would have to be related to the amount of damage incurred in some (as yet undetermined) manner. It might be possible, however, to examine the relationship of cumulative tissue loads (developed using fatigue failure techniques) with respect to the amount of rest available to determine whether certain ratios of cumulative loading to rest result in lower MSD rates, while others lead to increased risk.

Poorly vascularised tissues would be expected to be more susceptible to fatigue loading compared to highly vascularised tissues, due to the reduced availability of the biochemical and nutritional elements required for healing. It is worth noting that most of the tissues associated with MSDs are generally poorly perfused and slower to heal, likely permitting increased damage accumulation as the tissue labours to heal.

4.8. Research needs

If a fatigue failure process is involved with the development of MSDs, there may be great opportunity to improve our understanding of the aetiology of these disorders, to better assess risk and to develop more effective interventions. Doing so will require a significant investment in research to acquire the knowledge and techniques necessary to drive this effort forward. The research implications are substantial, and a few of these are considered below. In general, there are three main areas where research is needed: (1) improved characterisation of the US and fatigue life of musculoskeletal tissues; (2) accurate determination of stresses experienced at the tissue level; and (3) improved characterisation of the dynamic properties of the musculoskeletal system, specifically tissue healing, remodelling and atrophy.

In an ideal world, the risk of cumulative tissue damage for an individual could be accurately predicted, given knowledge of the strength of the tissues being stressed and the magnitude, distribution and frequency of loading on these tissues. First, we would have knowledge of the US (*in vivo*) of the tissue being stressed, and would have precise knowledge of the distribution of tissue strain due to repetitive loading experienced by the tissue. Further, we would have accurate knowledge of the healing rate and capabilities of the involved tissue for the individual in question, and would understand the proper balance in terms of activity and rest for healing to be optimised. We would understand how adoption of different postures would change the stress distribution in the tissues and areas of stress concentration. We would understand the effects of ageing and relevant disease processes on these tissues. The impact of prior tissue damage would be understood. The understanding of how psychological stresses impact tissue loading and healing would also be fully comprehended.

It may be possible that technology eventually will provide methods to better understand some of these issues, though for some aspects, it may be in a rather distant future. However, we are currently missing some rather basic information necessary to evaluate the fatigue failure process *in vivo*. The following sections describe some of the areas where research is needed to better understand fatigue failure processes in the human body, which will hopefully lead not only to better design of jobs, but better overall musculoskeletal health through life.

4.8.1. Improved characterisation of musculoskeletal tissue properties

Data on fatigue failure of musculoskeletal tissues remain relatively sparse, and a much greater exploration of the responses of musculoskeletal tissues is warranted. As an example, there is scant evidence evaluating long-cycle fatigue (>10,000 loading cycles) in spinal motion segments. An improved understanding of long-cycle responses would be important in developing the *S–N* curves that define these tissue responses. Effects of load rate, variable loading amplitudes, damage nucleation and propagation, and fatigue of aging tissues are not sufficient. Viscoelastic responses are still not well understood, particularly the effects of variable load rates during a loading process. Furthermore, developing an improved understanding

of load sharing in tissues would be helpful, and how and where stress concentrations develop and how these are affected by changes in posture.

Statistical variability is an important issue with respect to fatigue testing, and using an appropriate sample size is a critical aspect of developing *S–N* curves. The study by Schechtman and Bader (1997) is instructive as a model of how the relationship between loading and cycles to failure is necessary for constructing an *S–N* curve. As these authors demonstrate, it may necessary to measure the fatigue life of 10–20 specimens at each of 10 or so load levels to define the *S–N* curve properly. Obviously, development of a full *S–N* curve is tedious; however, understanding the fatigue responses of musculoskeletal tissues involved with MSDs is critical to our understanding and to MSD prevention efforts. For many tissues involved with specific MSDs, we have little to no data at all. In ligaments, for example, we have only found only two studies of fatigue failure – one in the human anterior cruciate ligament (Lipps, Wojtys, and Ashton-Miller 2013) and one in the rabbit medial collateral ligament (Thornton, Schwab, and Oxland 2007). Further research in this area is necessary.

Furthermore, it should be recognised that damage to viscoelastic tissues can result from both fatigue failure and creep loading. It has been demonstrated that the former will lead to more rapid tissue damage than the latter (Thornton, Schwab, and Oxland 2007); however, it should be recognised that damage is likely the result of the combination of creep and fatigue loading. The nature of the relationship between these two loading modalities in terms of damage accrual is unknown at the current time, and deserves attention in future research studies.

4.8.2. *Estimating tissue strength* in vivo

Understanding tissue strength is a critical piece of information in assessing MSD risk. Fortunately, there are many technologies that may be very helpful to estimate tissue strengths *in vivo*. An example is dual-energy X-ray absorptiometry, which can provide information on bone densitometry that may be extremely helpful in understanding the risk of vertebral end-plate fractures in the spine. Bone mineral content has been shown to be highly correlated with the ultimate strength (Biggemann, Hilweg, and Brinckmann 1988) and fatigue life (Gallagher et al. 2007) of spinal motion segments *in vitro*, a relationship that is surely present *in vivo* as well. This may be helpful when comparing demands of the job to worker capacity and establishing risk. Other useful imaging techniques include MRI and ultrasound that can help establish the dimensions and estimated strength of tissues important in the determination of stress.

Other methods may also be useful in aiding our understanding of tissue strength. For example, isometric muscle strength appears to be one of the best metrics of recovery from injury (Prasartwuth, Taylor, and Gandevia 2005). Stronger muscle strength implies stronger tissues throughout the system – muscles, tendons and bone. Changes in muscle strength throughout life undoubtedly reflect changes in the integrity of musculoskeletal tissues as a whole. As a result, muscle strength may be a reasonable method with which to estimate tissue strength of individuals, and it may be possible to prevent fatigue failure in tissues.

4.8.3. *Understanding dynamic properties of the musculoskeletal system*

The unique physiological setting of fatigue failure for musculoskeletal tissues *in vivo* complicates an already complex process. Musculoskeletal tissues are highly dynamic, and can respond relatively quickly to changing demands. The ability of biological tissues to self-heal is a unique aspect of the fatigue failure process in humans that needs to be better understood with respect to its role in MSD risk. In particular, the relationship of rest necessary to heal various amounts of cumulative damage must be better studied. There is a baseline rate of tissue healing (not well quantified presently) that occurs every day and which is apparently able to keep pace with minor damage that occurs when loading is not excessively forceful and repetitive. When loading on tissues leads to a substantial increase in cumulative damage, however, the healing process accelerates. This acceleration, however, varies dramatically between tissues that are highly perfused and those with poor levels of perfusion. Highly perfused tissues such as muscle and bone can heal relatively quickly when a minor amount of cumulative damage is experienced. However, low metabolism tissues such as tendon, ligament and cartilage do not heal as rapidly. Mechanical loading that results in tendon overuse injury can initiate a repair process but, after failed initial repair, non-resolving chronic attempted repair appears to lead to a 'smouldering' fibrogenesis (Thornton and Hart 2011).

4.8.4. *Beneficial versus detrimental tissue loading*

Musculoskeletal tissues must experience stress to maintain healthy function. This is abundantly clear from the experience of astronauts living in microgravity. Studies have demonstrated that astronauts experience up to a 20% loss of muscle mass on spaceflights lasting five to 11 days, and may lose up to 2% of their bone density per month if bone and muscle are not purposefully stressed (NASA 2001, 2015). Although no other working population is subjected to the dramatic environmental conditions of space, atrophy of tissues will also occur in normal gravity if individuals are not active (though at a less rapid pace).

It is also clear that a limited number of high-stress exertions, combined with sufficient rest, can lead to significant gains in strength of tissues, including muscle, tendons and ligaments. For example, Arampatzis, Karamanidis, and Albracht (2007) showed increased Achilles tendon stiffness during a 14-week exercise protocol involving strain of 4.5%, but not for exercise involving strain of 3%, though exercise frequency and volume were equal. Kongsgaard et al. (2007) also demonstrated increased tendon stiffness (in the patellar tendon) with high-resistance load, but not for a light resistance regimen. These data suggest that a certain loading magnitude threshold must be exceeded to elicit an anabolic tissue response. However, the difference between conditions of high-magnitude stress that lead to anabolic responses and those leading to catabolic tissue changes appears not to be tremendously different (Heinemeier and Kjaer 2011). Understanding these thresholds is an important research issue and poorly understood presently. It would be very useful to increase our understanding of conditions leading to optimal musculoskeletal tissue health compared to those that lead to progressive accumulation of damage.

Furthermore, we need to better understand the negative and positive impacts of loading during the tissue repair process. When tissue becomes damaged, the damaged region becomes an area of stress concentration in the tissue and, therefore, vulnerable to additional fatigue damage even in the presence of lower magnitude loads (Gallagher and Heberger 2013). However, it has been shown that controlled loading during the healing process (for example, in tendons) can help to improve the synthesis and alignment of collagen fibres, leading to an improved repair outcome (Kellett 1986). Thus, tissue loading can be both a hindrance and a benefit in the tissue repair process. The timing and magnitude of loading that should be experienced in the repair process to (1) decrease damage and/or (2) facilitate healing are poorly known presently but important to the preservation of optimum musculoskeletal tissue health.

4.8.5. Risk assessment in epidemiological studies

Past epidemiological studies have not examined MSD risk in a manner congruent with the precepts of fatigue failure. If MSDs are indeed the result of a fatigue failure process, important modifications would be needed with respect to how physical MSD risk factors are assessed. For example, it will be important to evaluate repetition as a function of force level experienced by participants, due to the highly variable impact of repetition at different force levels. Current tools used to assess force and repetition do not appear to appropriately weight the impact of repetition as force levels vary. Nor have important aspects such as the mean stress experienced by tissues been evaluated. Furthermore, as mentioned above, fatigue failure theory would indicate that a key element of risk assessment is evaluation of the load experienced by an individual relative to their tissue strength, which may be highly influenced by age, gender and anthropometry.

The development of new technologies holds great promise in helping to better quantify the physical exposures of work and may prove extremely beneficial in terms of evaluating MSD risk from a fatigue failure perspective. Wireless wearable motion sensors, for example, are innovative, unobtrusive devices that may be combined with force-sensing technologies (e.g. pressure sensing insoles or gloves, force plates) to obtain biomechanical loading estimates for joints of interest (Faber et al. 2016; Kim and Nussbaum 2014). Wireless electromyography systems, pressure mapping systems and other miniature force and torque measurement products may also be useful in this regard. Furthermore, new video-based technologies and advanced digital human modelling capabilities have shown considerable promise in assessing the data necessary for fatigue failure-based analysis (Chaffin 2005; Chen et al. 2015).

Despite recent advancements, additional research is needed to further improve and evaluate these emerging technologies, particularly for use in dynamic work environments. While several wireless wearable motion sensor systems have been observed to exhibit good accuracy and stability in both field and laboratory settings (e.g. Bauer et al. 2015; Kim and Nussbaum 2013; Schall et al. 2015), the accuracy of these devices has been known to degrade when work activities involve complex, dynamic motions (Brodie, Walmsley, and Page 2008; Godwin, Agnew, and Stevenson 2009) or when measurements are taken in the presence of magnetically distorted fields (Schiefer et al. 2014). Sensor fusion algorithms such as Kalman filters represent one approach to improving the accuracy of motion sensor devices under variable conditions (Bergamini et al. 2014; Ligorio and Sabatini 2015). However, systematic evaluations of the effects of dynamic motion and magnetic distortion (and their interaction) on the accuracy of these technologies are still necessary to further improve estimates of workplace exposure (e.g. Pasciuto et al. 2015). Moreover, evaluation of these technologies for use on complex body segments (such as the wrist) are needed to more effectively study prevalent musculoskeletal conditions that may be a result of a fatigue failure process such as CTS.

"Efficient estimation of the physical demands of work remains somewhat limited by the need for multiple sensors" (Schall, Fethke, and Chen 2016, 107). The creation of additional technologies capable of simultaneously capturing several components of work would allow workers to move more naturally, thereby improving estimates of workplace exposure while further increasing the

cost-efficiency of direct measurement (Trask et al. 2014). Moreover, the development of standardised, non-proprietary metrics and procedures for using these new technologies is needed (e.g. Faber et al. 2013; Palermo et al. 2014). Conversion algorithms intended to relate or synthesise workload estimates from various studies may also be useful for efficiently evaluating MSD risk and relating it to fatigue failure theory.

5. Summary

All materials (including biomaterials) have been demonstrated to incur damage via the process of fatigue failure. Recent evidence strongly suggests that a fatigue failure process may be etiologically significant in the development of MSDs. However, as of this writing, the implications of an underlying (and potentially causal) fatigue failure process in MSD development have generally not been considered in prior epidemiological studies, MSD risk assessment tools or MSD prevention strategies.

If this evidence is correct, there are many important implications that need to be considered. These include understanding important interactions between MSD risk factors, the ability to develop improved cumulative loading estimates on tissues, the importance of individual characteristics and MSD risk and perhaps improved understanding of the relationship between tissue damage and healing. The authors hope that the concept that MSDs may be caused (at least in part) by a process of fatigue failure may provide fertile ground for research in the quest to reduce the pain and disability associated with these burdensome health conditions.

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