Evidence of a causal fatigue failure process in musculoskeletal tissues

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This paper details evidence of a potentially causal fatigue failure process in the development of musculoskeletal disorders (MSDs). Evidence includes data from epidemiology studies, animal studies, and studies of eccentric exercise in humans. Up until the current time, the implications of an underlying fatigue failure process related to MSD development have generally not been considered in the ergonomics literature, nor in ergonomics risk assessment tools. If indeed MSDs are the result of a fatigue failure process, many important implications must 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. It is the author’s 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 our quest to reduce the pain and disability of MSDs.

Practitioner Summary: Evidence suggests that the effect of repetition is highly dependent on the forces experienced by the worker. The higher the force, the greater the effect of repetition will be in the development of musculoskeletal disorders.

Keywords: FORCE, REPETITION, FATIGUE FAILURE, MUSCULOSKELETAL DISORDERS, MUSCULOSKELETAL DISORDER ETIOLOGY

1. Introduction

Musculoskeletal disorders (MSDs) are widespread in the United States and throughout the world, and are associated with substantial financial and societal costs. MSDs are the second greatest cause of disability globally, having increased 45% worldwide according to the 2010 Global Burden of Disease Study (Horton, 2010). In 2011, MSDs accounted for 33% of workplace injuries and illnesses in the U.S. and a median of 11 days absence from work (Bureau of Labor Statistics, 2012). MSDs constitute a major proportion of all compensable work-related diseases in many countries, including the United States. In 2004, the estimated direct cost of treatment for MSDs was estimated at $510 billion, equivalent to 4.6% of the gross domestic product (GDP). Indirect costs were estimated to add $339 billion more, resulting in total cost for MSDs of $849 billion, or 7.7% percent of the GDP (AAOS, 2008).

Epidemiological studies have revealed several physical risk factors for work-related MSDs common to both upper extremity and low back pain (LBP). These include exposure to high force demands, repetitive exertions, adoption of non-neutral postures and exposure to whole-body or hand-arm vibration. Guo et al. (1995) estimated that 65% of LBP cases in the United States are attributable to the physical demands of work. Worldwide, 37% of LBP has been attributed to occupational risk factors and were estimated to cause 818,000 DALYs (disability adjusted life years) lost annually from LBP (Punnett et al. 2005).

The majority of epidemiology studies and systematic reviews have implicitly assumed that MSD risk factors function independently (i.e., no interactions) (NIOSH, 1997; NRC-IOM, 2001), an assumption common to MSD risk assessment tools as well (Waters et al., 1993; McAtamney et al., 1993; Latko et al., 1997). However, recent evidence suggests: (1) MSD risk factors may not be independent, (2) interactions between MSD risk factors may be due to an underlying a fatigue failure process in musculoskeletal tissue, and (3) inclusion of interactions between risk factors may lead to improved MSD risk assessment tools. The current paper details results of a systematic review of the MSD epidemiology literature and other recent evidence that suggests that MSDs may be the result of a fatigue failure process. Implications of these findings will be then considered.
2. Background

It has long been recognized that all materials can fail through either application of a one-time application of a large force (at the so-called “ultimate stress” [US] of the material), or through repeated application of loads at some percentage of the material’s US. The process of fatigue failure in a material begins with a small micro-failure in the material incurring the stress, usually on or near the surface and near a surface discontinuity or scratch. This area of micro-failure leads to a stress concentration in the area of the micro-failure, and with repeated loadings, the area of initial damage starts to expand. The rate of the expansion is a function of the load(s) imposed and the number of repetitions experienced. As more cycles accumulate, the area of damage grows until finally the remaining portion can no longer carry the load, and the material fails.

Biological tissues are also materials, and would be expected to incur damage in accordance with same principles, though with some important differences. A relatively limited number of fatigue failure studies have been performed on cadaver biological materials and these have demonstrated that human tissues do demonstrate fatigue failure processes in vitro. For example, a comprehensive study that examined the effects of force levels and repetition on the failure of spinal motion segments in a neutral posture was described by Brinckmann et al. (1988), which clearly demonstrated the fatigue failure process. Gallagher et al. (2005, 2007) also examined fatigue failure in lumbar motion segments; however, these test incorporated the effects of different motion segment flexion angles and load rates as well.

Tests on in vitro human tendons have also demonstrated the process of fatigue failure. For example, Schechtman and Bader (1997) examined fatigue failure of 90 extensor digitorum longus (EDL) tendons and tested them to fatigue at percentages of ultimate tensile strength (UTS) from 10% to 90%. The results are consistent with the spinal motion segment data in that tendons subjected to low percentages of UTS last many thousands of cycles, while those subjected to high levels of force relative to UTS fail much more rapidly, in accordance with fatigue failure theory.

It is difficult to imagine that biological tissues in vivo would be somehow immune from the process of fatigue failure given sufficient loading and repetition. However, biological tissues do have a unique characteristic not shared by most other materials – the ability of self-repair. The repair process in biological tissues, however, is accomplished at a rather deliberate pace. Thus, it would not be surprising that the process of damage accrual in biological tissues could surpass the rate of the tissue repair.

While it appears reasonable to imagine that a process of fatigue failure might be a causal mechanism in the development of damage to musculoskeletal tissues (and subsequent pain and disability), scant attention has been paid to this possibility in the literature. If a fatigue failure process is involved with the development of MSDs, several important implications ensue (as discussed below). Many of these implications challenge current models and thought regarding MSD development, not to mention prevention and control measures. The purposes of this paper are: (a) to examine recent evidence that suggests the presence of a fatigue failure process in musculoskeletal tissues, and (b) to discuss the implications that follow should a fatigue failure process be responsible for MSD development.

3. Evidence of a Fatigue Failure Process in Musculoskeletal Tissues

Several lines of evidence have recently emerged to suggest that a fatigue failure process may be associated with the development of MSDs, and may be a causal mechanism in their progression. While studies have clearly demonstrated that biological tissues experience fatigue failure in vitro, the following sections summarize evidence that suggest that fatigue failure may also be present in vivo.

3.1 Evidence of a force-repetition interaction with respect to MSD risk

It has long been recognized that forceful exertions, repetitive motion, non-neutral body postures, and exposure to vibration are important physical risk factors for MSDs. Of particular interest to the present
discussion are the risk factors of force and repetition. Should a fatigue failure process be involved with the expression of MSD risk, one would anticipate that an interaction would be observed between the risk factors of force and repetition. Such an interaction would be due to the shape of the fatigue failure (or ‘S-N’ curve). As shown in Figure 1, the S-N curve is a decreasing exponential curve, where the number of cycles to failure is related to the load on the material (expressed as a percentage of the material’s ultimate strength). If a material is repetitively loaded at 80% of its US, it will still eventually fail, but this may take 100 cycles. Loading at 50% of US may cause failure in 1000 cycles, etc. For some materials there exists a so-called “endurance limit” (usually around 30% US) where materials can be loaded for a great number of cycles without failure (Ashby, 2010). Thus, increased repetition for low force tasks would be expected to result in a modest increase in risk, as the number of cycles to failure would be large, and the effect of each repetition in terms of damage accrual would be very small. However, the impact of repetition is much greater when forces are high. Thus, high repetition in combination with high force would be expected to result in a dramatic increase in risk. Therefore, increases from low to high repetition for low force tasks would be expected to result in a modest increase in MSD risk. However, the impact of repetition is much greater when forces are high. Thus, high repetition in combination with high force would be expected to result in a dramatic increase in risk. Therefore, increases from low to high repetition for low force tasks would be expected to result in a modest increase in MSD risk.

A recent systematic review of occupational-related MSD epidemiology evaluated studies that either tested for an interaction (Gallagher and Heberger, 2013). A study was selected for inclusion in this review if the exposed and control working populations were well-defined, the exposure was explicitly and operationally defined with respect to force and repetition, and the study allowed an appraisal of whether evidence of an interaction between force and repetition might be present. The latter criterion included analysis of plots of odds ratios (ORs), risk ratios (RRs) or prevalence rate ratios (PRRs) from contingency tables, or a statistical analysis (for example, logistic regression) in which an interaction between force and repetition was explicitly tested by the authors. Outcomes included either one or more well-defined musculoskeletal disorders assessed via explicit and clinically relevant criteria as well as outcomes consisting of self-reported pain/discomfort. It is important to emphasize that studies that considered force and/or repetition solely as main effects without assessing a force x repetition interaction were not included in this review.

The search led to 501 citations from which relevant studies were selected for the review. Titles and abstracts were examined to evaluate potential relevance of these papers, with 457 citations excluded as irrelevant. The remaining 44 papers that examined force and repetition as potential risk factors were reviewed and assessed to determine whether the data contained in the paper might provide information regarding a force-repetition interaction. Of these, 12 studies were identified that evaluated combinations of force and repetition in a manner that allowed for assessment of an interaction. Ten of the twelve studies were found to provide evidence of interaction between the risk factors of force and repetition.

Figure 2 provides plots of data from seven cross-sectional studies that permitted assessment of MSD risk broken down into four quadrants of risk: low force, low repetition (LFLR); low force, high repetition (LFHR); high force, low repetition (HFLR), and high force, high repetition (HFHR). As can be seen, a consistent pattern of interaction was observed over a wide range of disorders, supporting the hypothesized fatigue failure relationship. MSDs demonstrating this pattern include carpal tunnel syndrome, tendinitis, epicondylitis, hand pain and low back disorders (Gallagher and Heberger, 2013). This systematic review was recently awarded the 2013 International Ergonomics Association/Liberty Mutual Medal for Occupational Safety and Ergonomics.
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 (LFLR), low-force, high-repetition (LFHR), high-force, low-repetition (HFLR) or high-force, high-repetition (HFHR) exertions (Barbe et al., 2013). After exposure to these regimens for a twelve-week period, tissue pathology and serum cytokine data were obtained from the rats. Tissue pathology results for tendon damage, cartilage damage and bone volume all demonstrated significant force-repetition interactions of the pattern consistent with an underlying fatigue failure process. Furthermore, many serum cytokines exhibited the same pattern of force-repetition interaction, including TNF-alpha, Interleukin Ia, Interleukin Ib, and Macrophage Inflammatory Protein 2. Inflammation and histopathology are often congruent and the magnitude of an inflammatory response to tissue insult or overuse appears indicative of the extent of injury in the tissues (Carp et al. 2007), thus these cytokine results also support the presence of an underlying fatigue failure process in the development of tissue damage and MSDs.

3.3 Evidence from Study of Muscle Damage and Inflammation due to Eccentric Exercise

In an effort to investigate whether a fatigue failure process might be evaluated in human tissues in vivo, investigators examined the effects of force and repetition during eccentric exercise of the biceps (Gallagher et al., 2014). Eccentric exercise is known to lead to sarcomere “popping” (i.e., muscle fiber damage), which is repaired over the course of 1-2 weeks. Subjects who experience such eccentric bouts of exercise will experience a short-term inflammatory response (peaking 2-4 days post-exercise) that is healed over the period of 7-14 days, and will gain a training benefit that lasts up to 6 months.

Twenty-four subjects (18 males and 6 females) were recruited to participate in this study. Subjects were randomly assigned to one of four force-repetition categories. 6 subjects were assigned to each of the
following groups: low force, low repetition (LFLR), low force, high repetition (LFHR), high force, low repetition (HFLR) or high force, high repetition (HFHR). Subjects were remunerated for their participation, and all procedures were reviewed and approved by the Auburn University Institutional Review Board (IRB).

Subjects were assigned to one of the four force-repetition conditions (6 subjects per condition) and had a baseline MRI taken prior to the performance of the required exercise on day 0. Other baseline measures taken included relaxed elbow angle of the subject non-dominant arm, isometric strength with the non-dominant arm at a 90-degree angle. Isometric strength is one of the best measures of the state of recovery of muscle after eccentric exercise. Relaxed elbow angle is an indicator of the state of muscle damage and is thought to be indicative of the influx of calcium from the damaged sarcoplasmic reticulum, and appears to be indicative of the amount of damage sustained by the affected muscle due to eccentric contractions. A second MRI was obtained 2 days post exercise, and contrast-to-noise (CNR) ratios comparing the affected muscles (biceps and brachialis) to unaffected muscle (triceps). The higher the CNR, the greater the edema in the affected elbow flexor group.

The interaction between force and repetition and relaxed elbow angle is thought to be due to an influx of calcium from the damaged sarcoplasmic reticulum, and appears to be indicative of the amount of damage sustained by the affected muscle due to eccentric contractions. Isometric strength is considered one of the best measures of the state of muscle damage and recovery, and also showed a force-repetition interaction on day 2 post-exercise. Both of these findings illustrated the pattern of force-repetition interaction expected should an underlying fatigue failure pattern be present. The CNR analysis from the MRI images showed the general pattern anticipated, but significant between subjects variability was present and did not result in a significant force-repetition interaction from being detected.

Figure 3. Resting elbow angle results for Days 1, 2, and 4 post-exercise.

Figure 4. MRI Contrast to Noise Ratio result
4. Discussion

Several avenues of inquiry suggest that musculoskeletal tissues may become damaged as the result of a fatigue failure process. These include in vitro studies using cadaver tissues, epidemiology studies of MSD risk, results from animal models, and studies of muscle tissue damage and inflammation after eccentric exercise. To date, neither epidemiological studies nor ergonomics risk assessment tools have incorporated fatigue. If this is indeed the case, several major implications related to assessment of MSD risk and methods of prevention for these disorders must be considered. Some of these are discussed below.

4.1 New understanding of MSD physical risk factors

MSD risk factors have often been treated as acting independently with respect to MSD risk. However, evidence seems to suggest an interaction exists between force and repetition with respect to MSD risk. This suggests that these two risk factors should not be treated as independent, but have a dependent relationship in that the effect of repetition is highly dependent on the forces experienced by tissues. Neither risk factor can be considered separately -- their effect on MSD risk must be considered in tandem.

The role of a third MSD risk factor may also be considered in this context -- that of posture. One aspect of this risk factor is that adoption of awkward or non-neutral postures often leads to increased force requirements and increased stresses on musculoskeletal tissues. According to the force x repetition paradigm discussed above, any increased force demands that may result from the use of awkward or non-neutral postures would also be expected to lead to a more rapid escalation of MSD risk. It is quite possible that one major reason posture emerges as a risk factor for MSDs is simply due to the increased tissue loads that result from adoption of awkward or non-neutral postures. Finally, it should also be recognized that vibration exposure is a combination of force and repetition. It may also be worth evaluating whether vibration exposure be considered from a fatigue failure context, as well.

4.2 Improved estimates of cumulative loading

Fatigue failure theory provides established techniques for assessing cumulative damage due to exposure to highly variable combinations of force and repetition. For example, the following cumulative damage model for fatigue life was proposed by Palmgren (1924) and Miner (1945):

$$ c = \sum_{i} \frac{n_i}{N_i} + \frac{n_2}{N_2} + \cdots + \frac{n_k}{N_k} $$

where c is a constant (often set at 1, but which can vary), ni... equal the number of exposure cycles experienced at force levels at which Ni ... cycles would result in fatigue failure. When the right hand sum is equal to one, the material would be expected to fail. Previous attempts at developing cumulative loading metrics for LBP (Norman et al., 1998), especially the total “area under the loading curve” models, are ungrounded from a fatigue failure theory perspective.

4.3 Effects of individual characteristics on risk

An important precept of fatigue failure theory is that the effect of a given load must be indexed to the US of the exposed tissue. It is important to recognize that each individual’s tissue strength will be unique, and that these strengths can show huge variability. 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 load 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 for more difficult jobs). From a fatigue failure perspective, it must be said that it may make sense in some circumstances to employ such an approach to reduce MSD risk. For example, if a
job incurs a spinal load of 3 kN and an older male doing the job has a spine US of 6 kN, it is likely that significant damage to spinal tissues will eventually accrue. If a younger male with a 12 kN spine US is brought in to do the job, any spinal damage would be expected to develop much more slowly, if at all.

We are certainly not saying that the approach above is to be preferred -- ergonomic design of the workplace (to eliminate the lift or reduce the spinal load) is clearly a superior approach. However, in circumstances where it is difficult or cost prohibitive to implement an ergonomics fix (or while these are being implemented), having workers with stronger tissues perform the more physically demanding jobs does make some sense from a fatigue failure perspective.

4.4 The battle for 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 make sure 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 activity 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. Clearly, maintaining a modest degree of damage is critical to maintenance of tissue homeostasis.

Healing of tissues requires periods of unloading (rest) 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, it would seem 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.

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 is also evident in the development of MSDs. Up until the current time, the implications of an underlying (and potentially causal) fatigue failure process related to MSD development have generally not been considered in prior MSD epidemiology studies, MSD risk assessment tools, or MSD prevention strategies. If this evidence is correct, there are many important implications that need to be considered based on fatigue failure theory. 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. It is the author’s 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 our quest to reduce the pain and disability associated with musculoskeletal disorders.

References


