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Examining the Interaction of Force and Repetition on Musculoskeletal Disorder Risk: A Systematic Literature Review

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Abstract

Objective—Our aims were (a) to perform a systematic literature review of epidemiological studies that examined the interaction of force and repetition with respect to musculoskeletal disorder (MSD) risk, (b) to assess the relationship of force and repetition in fatigue failure studies of musculoskeletal tissues, and (c) to synthesize these findings.

Background—Many epidemiological studies have examined the effects of force and repetition on MSD risk; however, relatively few have examined the interaction between these risk factors.

Method—In a literature search, we identified 12 studies that allowed evaluation of a force–repetition interaction with respect to MSD risk. Identified studies were subjected to a methodological quality assessment and critical review. We evaluated laboratory studies of fatigue failure to examine tissue failure responses to force and repetition.

Results—Of the 12 epidemiological studies that tested a Force \times Repetition interaction, 10 reported evidence of interaction. Based on these results, the suggestion is made that force and repetition may be interdependent in terms of their influence on MSD risk. Fatigue failure studies of musculoskeletal tissues show a pattern of failure that mirrors the MSD risk observed in epidemiological studies.

Conclusions—Evidence suggests that there may be interdependence between force and repetition with respect to MSD risk. Repetition seems to result in modest increases in risk for low–force tasks but rapid increases in risk for high–force tasks. This interaction may be representative of a fatigue failure process in affected tissues.

Keywords

systematic review; force; repetition; musculoskeletal disorders; risk factors; fatigue failure; epidemiology

INTRODUCTION

Musculoskeletal disorders (MSDs) represent one of the leading causes of lost workdays in industry and are associated with major economic costs (American Academy of Orthopaedic Surgeons [AAOS], 2008). In 2004, 16.3 million strains and/or sprains were treated in the U.S. health care system, and the estimated cost of treating all musculoskeletal injuries was \$127.4 billion (AAOS, 2008). MSDs have been shown to be more severe than the average nonfatal workplace injury or illness, to require longer recovery times, and to be responsible for millions of lost workdays every year (AAOS, 2008).

Several risk factors are known to be associated with MSDs. Among the most commonly accepted physical risk factors are exposure to tasks involving high force demands, tasks involving high rates of repetition, tasks involving awkward postures, and tasks of long duration (Bernard, 1997; Hoogendoorn, Poppel, Bongers, Koes, & Bouter 1999). It must also be recognized that other risk factors, including physiological or psychosocial factors, comorbid diseases, and personal factors, have been shown to play a role in the expression of MSDs (National Research Council & Institute of Medicine, 2001). However, in the current article, we seek to scrutinize more closely the physical risk factors of force and repetition in the development of MSDs.

Force and repetition have often been assumed to function as independent factors with respect to MSD risk. This tacit assumption can be found in many epidemiological studies and reviews, in ergonomics exposure assessment tools, and in guidelines developed to reduce the risk of MSDs. Nevertheless, it is always important to verify such assumptions. As discussed in this article, there is evidence to suggest that force and repetition interact and that the combination of both factors may be necessary to accurately ascertain MSD risk (risk being defined as the number of individuals experiencing an MSD divided by the number exposed to particular divided by the number risk factor[s]). Furthermore, the nature of the interaction observed in several epidemiological studies matches what would be anticipated if exposed tissues were to become injured as the result of a fatigue failure process. In this article, we describe results of a systematic literature review of studies that have examined a Force \times Repetition interaction on MSD risk, describe a potential mechanism underlying the observed results, and explore implications for research, exposure assessment methods, and recommendations for reducing MSD risk.

LITERATURE REVIEW: EPIDEMIOLOGY

Identification of Relevant Studies

A literature search was performed to identify studies that evaluated an interaction between force demands and repetition with respect to MSD risk. We identified relevant studies using the following strategies:

1. A search of the PUBMED database was formed. The search strategy specified that papers have *epidemiological study* or *epidemiology* and *occupational* or *work-related low back pain* or *low back disorders* in the title or abstract. Limits were that documents were journal articles on humans and were published between January 1, 1980, and May 3, 2011. In addition to the low back (as in the aforementioned

example), searches were performed for other MSDs or common MSD symptomatology (i.e., joint pain), including carpal tunnel syndrome, hand-wrist tendonitis, elbow pain, shoulder and neck pain, and knee pain.

2. Studies contained in the National Institute for Occupational Safety and Health (NIOSH) critical review *Musculoskeletal Disorders and Workplace Factors* (Bernard, 1997) were reviewed.
3. Bibliographies of relevant articles were reviewed.

A more detailed review was undertaken if studies met the following criteria: (a) They were published in English, (b) they addressed any of the MSDs or symptoms detailed previously, (c) they were conducted in one or more working populations, (d) the study group had exposure to varying levels of repetition and/or force, (e) the study design was case control, was cross-sectional, or used a longitudinal cohort or randomized controlled trial.

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 MSDs assessed via explicit and clinically relevant criteria as well as outcomes consisting of self-reported pain or discomfort. It is important to emphasize that studies that considered force and/or repetition solely as main effects without assessing a Force × Repetition interaction were not included in this review.

The search led to 501 citations from which relevant studies were selected for the review. We examined titles and abstracts to evaluate potential relevance of these papers, with 457 citations excluded as irrelevant. We reviewed and assessed the remaining 44 papers that examined force and repetition as potential risk factors to determine whether the data contained in the papers 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. A methodological quality assessment of these papers was performed by two raters (SG and JRH) using criteria from Huisstede et al. (2006); Lievense, Bierma-Zeinstra, Verhagen, Verhaar, and Koes (2001); van Tulder, Furlan, Bombardier, and Bouter (2003); and the Dutch Cochrane Centre as described by van Rijn, Huisstede, Koes, and Burdorf (2009). Criteria for the methodological assessment are contained in Table 1, and results of the assessment are contained in Table 2. Initial agreement of the two raters was 79.2% (152 of 192 items). Initial disagreements were resolved in a consensus meeting of the raters. Average quality ratings of studies demonstrating positive versus negative findings were found to be non-significant, $t(9) = -0.36$, $p = .73$. Table 2 presents the consensus ratings of these studies.

Assessment of Epidemiological Studies Examining an Interaction of Force and Repetition on MSD Risk

Of the 12 studies that met the inclusion criteria, 10 provided evidence of interaction between the MSD risk factors of force and repetition. Figures 1a through 1g provide 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). It should be noted that the findings of two of the studies listed were analyzed post hoc (J. F. Thomsen, personal communication, November 18, 2011; Thomsen et al., 2007; Zurada, Karwowski, & Marras, 1997). We analyzed data from these two studies by performing median splits of the existing data sets, allowing data to be separated into the four quadrants listed previously.

Several observations regarding the relationship of force and repetition can be made from these figures. One consistent feature is that the slope of the low-force and high-force lines exhibit very different tendencies. Low-force activities were often associated with a mild to moderate increase in risk (Armstrong et al., 1987; Haahr & Andersen, 2003; Silverstein, Fine, & Armstrong, 1987; Zurada et al., 1997); however, occasionally no change or slight decreases in risk were observed with LFHR tasks (Frost et al., 2002; Nathan, Meadows, & Doyle, 1988; J. F. Thomsen, personal communication, November 18, 2011; Thomsen et al., 2007). As opposed to the variable (positive or negative) slopes observed with low-force tasks, the slope for high-force tasks was always positive and the slope greater (often substantially greater) than for low-force tasks.

A common finding in many of the studies was that the HFHR condition was the only condition found to be significantly different from the LFLR referent (Armstrong et al., 1987; Haahr & Andersen, 2003; Nathan et al., 1988; Silverstein et al., 1987). To compare with the previously cited studies, we ran a stepwise logistic regression analysis on the data from one study that originally used a “nonrepetitive” group as a referent so as to use the LFLR group as a referent (Frost et al., 2002). When the LFLR group was used as a referent, this study also showed that the HFHR group was the only group that was significantly different from the LFLR group.

For the Frost et al. (2002) study, the HFHR odds ratio against LFLR was 1.90 (95% confidence interval [CI] [1.05, 3.43]). In another study involving a nonrepetitive referent (J. F. Thomsen, personal communication, November 18, 2011; Thomsen et al., 2007), LFLR (OR = 1.6, 95% CI [1.1, 2.3]), HFLR (OR = 1.9, 95% CI [1.2, 3.0]), and HFHR (OR = 2.4, 95% CI [1.6, 3.7]) conditions were significantly different from the nonrepetitive referent (sufficient data were not available to examine LFLR as a referent). The analysis of data from the Marras et al. (1993) study data presented in Zurada et al. (1997) was accomplished by the performance of a median split on both frequency and peak moment (used as a force surrogate measure). Results of logistic regression of this data indicate that compared with the LFLR referent, both HFLR (OR = 9.54, 95% CI [3.16, 28.78]) and HFHR (OR = 42.62, 95% CI [11.02, 164.77]) were significantly different.

Given the patterns of interaction observed in the seven studies listed, it was of interest to evaluate contrasts of “simple effects” for these studies. We performed contrasts to examine

differences in the proportions of MSD risk attributed to increased force in low-repetition and high-repetition conditions separately, using a directional hypothesis ($HF > LF$) in six of the studies, as the necessary data were not available for the seventh. Fisher's exact test was used when samples available for the test were less than 500, whereas z tests were employed for sample sizes greater than that number. A Bonferroni adjustment was employed for the two contrasts tested within each study. As shown in Table 3, significant differences in MSD risk were observed between low force and high force for low repetition in just two studies (Haahr & Anderson, 2003; Zurada et al., 1997). On the other hand, significant differences in MSD risk between low force and high force for high-repetition tasks were observed in five of the six studies. Difference scores between high force and low force were consistently higher for high-repetition tasks compared with low-repetition tasks in these studies.

Other studies examining a Force \times Repetition interaction did so using regression approaches. Using logistic regression, Shiri, Viikari-Juntura, Varonen, and Heliovaara (2006) found a significant Force \times Repetition interaction for possible or definite lateral epicondylitis (although not for medial epicondylitis), and Chiang et al. (1993) found a marginally significant association between force and repetition for physician-observed shoulder girdle pain in a logistic regression model. In addition, Chiang et al.'s study found that crude ORs were significant for HFHR versus LFLR task comparisons in physician-observed carpal tunnel syndrome, shoulder girdle pain, and elbow pain. Menzel, Brooks, Bernard, and Nelson (2004) used linear regression to assess frequency and severity of musculoskeletal discomfort and found a significant Force \times Repetition interaction for frequency and severity of knee discomfort, and a Force \times Repetition factor was included in a significant regression analysis for frequency and severity of wrist discomfort as well. These authors stated that the same factors were significant in logistic regression analyses (not reported in the article).

Of the two studies that did not identify an interaction, both contained methodological issues that might reduce the chance of observing an interaction even if one were present. Babski-Reeves and Crumpton-Young (2003) did not observe a wide range of force and repetition in their study; the tasks studied were generally all HFHR in nature, as the authors themselves attest. Although the authors did test for an interaction, the uniformity of force and repetition exposure for the activities studied (fish-processing tasks) practically assured that any test for interaction would be unsuccessful. Furthermore, both negative studies (Babski-Reeves & Crumpton-Young, 2003; Nathan, Keniston, Myers, & Meadows, 1992) make the incorrect assumption that each hand from an individual is statistically independent. It should be noted that one of the positive studies also makes this assumption (Nathan et al., 1988).

The findings of Nathan et al. (1992) differ dramatically from all other studies in that the HFHR condition was found have the same risk as the LFLR condition. The methodology of the Nathan et al. study came under critique in the review by Bernard (1997). One reason for the drop in prevalence in the HFHR group not addressed by the authors was the dramatic dropout rate of HFHR cases in the follow-up (Bernard, 1997). Furthermore, the categorization of participants from the Nathan et al. (1988) study seems to have changed in the later presentation (Nathan et al., 1992). Both tables should have been identical; however, it appears that numbers shifted between hand-use categories (Bernard, 1997). Finally, the statistical analysis of Nathan et al. (1992) was questioned by Bernard, who found statistical

differences between higher force and repetition categories using standard statistical tests, whereas none were detected in the analysis performed by Nathan et al. (1992).

It must be noted that most of the studies examining Force \times Repetition interactions were cross-sectional in nature; only two prospective studies were found (Nathan et al., 1992; J. F. Thomsen, personal communication, November 18, 2011; Thomsen et al., 2007). One high-quality prospective study (J. F. Thomsen, personal communication, November 18, 2011; Thomsen et al., 2007) reported an interactive pattern for hand pain at baseline (as reported earlier), and although HFHR tasks in the incident portion were significantly greater than the referent, the pattern of risk for the quadrants of force and repetition was not indicative of an interaction for hand pain (LFLR, OR = 1.2, 95% CI [0.8, 1.7]; LFHR, OR = 1.9, 95% CI [1.2, 2.9]; HFLR, OR = 1.4, 95% CI [0.9, 2.0]; HFHR, OR = 2.1, 95% CI [1.5, 2.9]). As discussed previously, methodological issues with the Nathan et al. (1992) prospective study limit the ability to interpret results with confidence.

Overall, Force \times Repetition interactions were observed for MSDs across a wide range of joint disorders and symptoms, including low-back disorders, carpal tunnel syndrome, hand-wrist tendinitis, wrist discomfort, lateral epicondylitis, shoulder tendinitis, shoulder discomfort, and knee discomfort. Although interactions were often not explicitly tested by the authors, it appears from the majority of these studies that repetition has a different influence on risk, dependent on the level of force exposure. These findings would seem to be sufficient to suggest that future epidemiological studies should routinely examine a Force \times Repetition interaction. Since it is known that main effects are incorrectly estimated in the presence of an interaction (Meyer, 1991; Petersen, 1985; Underhill, 1997), examining the main effects of force and repetition alone would seem insufficient, given these results. Knowledge of both factors, working in tandem, may be required to accurately assess MSD risk.

The prospect that force and repetition interact in the development of MSD risk would have significant implications in terms of the etiology of MSDs, not to mention the development of recommendations and guidelines aimed at reducing these disorders. Specifically, guidelines should be sensitive to the large increase in MSD risk when high-force tasks are performed repetitively. On the other hand, if tasks are very low force in nature, high rates of repetition may not incur a large increase in MSD risk and may be more acceptable. As discussed next, the pattern of MSD risk related to force and repetition in epidemiological studies corresponds to what would be expected if tissues of the human body experienced damage in the same manner as other materials—and in the way they evidence failure in laboratory studies—through the process of fatigue failure.

EFFECT OF FORCE AND REPETITION IN FATIGUE FAILURE STUDIES OF BIOLOGICAL TISSUES

A limited number of fatigue failure studies have been performed on biological materials that can be specifically related to a potential Force \times Repetition interaction; however, two studies in particular (one testing human spinal motion segments and the other testing human tendons) are useful. A comprehensive study that examined the effects of force levels and

repetition (i.e., loading cycles) on failure of spinal motion segment endplates was described by Brinckmann, Biggemann, and Helweg (1988). These authors sectioned cadaveric lumbar spines into multiple motion segments and tested the ultimate compressive strength (UCS) of a randomly selected motion segment from a spine. They did so to estimate the compressive strength of adjacent segments (a correction factor was applied to estimate the UCS of adjacent segments). These adjacent motion segments were then repeatedly loaded at a certain percentage of the predicted UCS and the number of cycles until failure of the motion segment was recorded.

Figure 2 presents data from the Brinckmann et al. (1988) study. The divergence in the lines between force levels (percentages of predicted UCS for the segments) and the number of repetitions to failure suggests that the amount of force imposed leads to a differential response in terms of the number of cycles to failure of spinal tissues. Congruent with findings of the epidemiological data discussed earlier, when spinal motion segments were subjected to relatively low-force loadings (<40% UCS), a small proportion of specimens experienced failure, even after thousands of cycles of repeated loading. In contrast, specimens exposed to higher loads (>40% UCS) led to a higher proportion of specimens failing overall, and these specimens experienced many more failures at low cycle counts. Similar responses were observed in studies that measured fatigue failure of lumbar motion segments with loads associated with lifting in varying levels of flexion (Gallagher, Marras, Litsky, & Burr, 2005; Gallagher, Marras, Litsky, Burr, Matkovic, & Landoll 2007).

Tests on human tendons exhibit similar results. Schechtman and Bader (1997) examined fatigue failure of 90 extensor digitorum longus (EDL) tendons from human legs and tested them to fatigue at percentages of ultimate tensile strength (UTS) from 10% to 90%. Figure 3 presents the results of the data from 30% to 90% UTS up to 5,000 cycles. The results are consistent with the Brinckmann et al. (1988) data in that tendons subjected to low percentages of UTS last many thousands of cycles, whereas those subjected to high levels of force relative to UTS fail much more rapidly. Schechtman and Bader presented the following model that describes the relationship between normalized stress level and the number of cycles to failure, having an $R^2 = .88$:

$$S=93.98-13.13\log(N), \quad (1)$$

where S is the normalized stress (expressed as % UTS) and N is the number of cycles to failure.

These results indicate that the rate of damage experienced by tendons (as with spinal motion segments) is highly dependent on the level of loading. Low levels of loading resulted in a modest increase in failure with high rates of repetition, and high levels of loading result in much more rapid failure with repetition. The findings of both studies suggest that low-force loading of tissues can be well tolerated for many thousands of cycles, whereas exposure to repetitive high-force loading tends to cause damage to some specimens quite quickly and to most, if not all, specimens eventually.

An important point needs to be made when comparing results of epidemiological studies of MSD risk to results of in vitro studies of tissue failure. In many in vitro tissue studies, the

end result of fatigue failure is ultimate destruction of the tissue (for example, complete rupture of a tendon). MSDs are usually not characterized by complete rupture of a tissue but are instead characterized by a lower-magnitude, localized tissue damage sufficient to trigger an inflammatory response. The point to bear in mind is that fatigue failure is a process of progressive and localized structural damage that occurs when a material is subjected to repeated loading and unloading. The process begins with exposure of healthy tissues to sufficient levels of loading and repetition that leads to development of microscopic fissures in affected tissues. Continued loading of the tissue will cause these microscopic fissures to expand. The rate of this expansion depends on both the magnitude of the load and the number of loading cycles. The damage that accumulates during this process need not approach that required for complete tissue failure to result in an MSD. What fatigue failure studies demonstrate is that even this subultimate failure damage can accumulate rapidly when loads are high and will accumulate more slowly (or not at all) when loads are more modest.

It should also be noted that some fatigue failure studies on human tissues have not employed ultimate destruction of tissues as endpoints. The study by Brinckmann et al. (1988) and those by Gallagher et al. (2005, 2007), for example, used fracture of the vertebral endplate as an endpoint for their study. Fractured endplates are a common finding in spines of living persons and are believed to play an important role in disc degeneration and internal disc disruption (Adams, Bogduk, Burton, & Dolan, 2006). These findings indicate that in vitro fatigue failure studies can reproduce damage to tissues observed in vivo and that the pace of damage is dependent on the load incurred, as predicted by fatigue failure theory.

The Fatigue Failure Curve Suggests a Force × Repetition Interaction for Damage to Tissues

The pattern of Force × Repetition interactions observed in the epidemiological data (see Figure 1) matches what would be anticipated should musculoskeletal tissue damage result from a fatigue failure process. Figure 4 presents a typical fatigue failure (or S-N) curve with superimposed quadrants of force and repetition exposure (high and low for both). According to fatigue failure theory, the ultimate stress of a material is the amount of force that results in failure with just one loading cycle. However, as illustrated in the hypothetical example provided in Figure 4, if a material is repeatedly loaded at 80% of its ultimate stress, it will also fail but may take perhaps 100 cycles to do so. If loaded at 50% ultimate stress, the material may require 1,000 cycles to fail. Interestingly, for many materials, there exists an endurance (or fatigue) limit at which repeated loading will *not* lead to failure (or at which the material will last an extraordinarily large number of cycles). This limit often occurs at approximately 30% of a material's ultimate stress. When materials are loaded at less than 30% of their ultimate stress, fatigue damage would be expected to be relatively minor.

If one considers the epidemiological evidence of MSD risk for various levels of force and repetition in the context of the fatigue failure model, one finds a good correspondence to the epidemiological results discussed previously. For purposes of this illustration, we will consider exposure to lower than 40% ultimate stress to be low force and greater than this value to be high force. Fewer repetitions than 800 will be considered low repetition, and

more than 800 repetitions will be considered high repetition. Note that these values are arbitrary, and it must be understood that the exact parameters of the fatigue failure curve for many biological materials is not well established, although the general shapes of S-N curves are similar. The purpose of this example is simply to illustrate conceptually how different force and repetition combinations would relate to a fatigue failure curve.

As illustrated in Figure 4, LFLR exertions reside well beneath the fatigue failure curve and would not be expected to lead to tissue damage. LFHR tasks would be expected to incur only a slight increase in risk, or sometimes no increase in risk, dependent on the exact level of stress imposed on the tissue and on the number of cycles.

The HFLR quadrant is intriguing and suggests that it may be safe to perform tasks that require high force for a limited number of cycles. However, the number of repetitions that can be safely performed would be greatly reduced compared with low-force tasks and would be critically dependent on the percentage of ultimate stress imposed on the tissue. It should be noted that exertions in this quadrant may actually lead to a training effect that can *improve* the strength of muscles, ligaments, and tendons. Athletes seeking to develop increased muscle strength, for example, typically perform multiple sets of 10 to 15 high-force exertions involving the muscles targeted for improvement. Importantly, strength-training regimens usually involve periods of rest in between training days, allowing the body to recover and adaptively remodel musculoskeletal tissues. However, although tissue-strengthening benefits can be derived from limited high-force exertions in this quadrant, it is critically important to realize that such gains might be quickly reversed if too many loading cycles are imposed.

When considering the HFLR quadrant further, it might be worthwhile to consider how exertions in this region might serve as a “setup” for the development of MSDs. The problem that might arise is that individuals may be deceived by their ability to perform a respectable number of high-force exertions without becoming injured. An expectation might understandably develop that one could continue to perform such exertions indefinitely without adverse effects. Unfortunately, continued exposure to high-force activities might at some point initiate the process of fatigue failure in exposed tissues.

The final quadrant is HFHR. On the basis of the fatigue failure framework, and for reasons discussed previously, frequent exposure to tasks requiring high forces would be expected to result in rapid tissue damage and a sizeable increase in MSD risk. Indications from epidemiologic studies suggest a rapid escalation in risk is indeed evident for HFHR tasks.

As alluded to previously, biological tissues differ from other materials in that biological tissues have the ability to repair and remodel. As discussed next, a fatigue failure injury will result only if the fatigue process proceeds at a rate faster than that of the remodeling or repair process (Schechtman & Bader, 1997). Unfortunately, there is a limit to the speed with which the body can repair tissue, and it should not be surprising if the deliberate pace of repair were to become overwhelmed in the face of continued exposure to physically demanding tasks.

Fatigue Failure With Variable Exposures to Force and Repetition

The epidemiologic data and the framework discussed earlier presuppose categories (LFLR, LFHR, HFLR, and HFHR) that can be clearly defined and allow for some estimate of effect. However, mixed exposures to force and repetition are far more prevalent in the workplace. Fortunately, research in materials science may provide a framework to approximate the likelihood of fatigue failure in situations in which exposure to force and repetition levels is variable. For example, a cumulative damage model for metallic structures was proposed by Palmgren (1924) and later experimentally validated by Miner (1945), as follows:

$$c = \sum_{i=1}^j \frac{n_i}{N_i} = \sum \frac{n_1}{N_1} + \frac{n_2}{N_2} + \frac{n_3}{N_3} + \cdots + \frac{n_j}{N_j}, \quad (2)$$

where c is a constant (whose value is usually set at 1 but can range above or below this value) and n_i equals the number of exposure cycles experienced at force levels at which N_i cycles would result in fatigue failure. When the sum of the right-hand side of the equation is equal to 1, the material would be expected to fail because of fatigue loading caused by the mixed force and repetition exposures. Nash (1966) extended this cumulative damage model to biological tissues as presented in the following:

$$D(t) = D_S(t) + D_A(t) + D_D(t) - H(t), \quad (3)$$

where $D(t)$ is the total tissue damage at time t , $D_S(t)$ is the tissue damage associated with mechanical loading as described by the Palmgren-Miner model (Equation 2), $D_A(t)$ represents damage associated with aging, $D_D(t)$ represents damage from disease, and $H(t)$ represents the damage repaired by healing or remodeling. If loading occurs to an otherwise healthy individual across a relatively short time span, the equation can be simplified (Schechtman & Bader 1997):

$$D(t) = \sum_{i=1}^j \left\{ \frac{n_i}{N_i} \right\} - H(t), \quad (4)$$

where $D(t)$ is the cumulative damage index, which ranges from 0 to 1 (0 = undamaged state prior to loading, 1 = failure attributed to fatigue); the term $\sum_{i=1}^j \left\{ \frac{n_i}{N_i} \right\}$ represents stress-related damage per the Palmgren-Miner model, and $H(t)$ represents healing that occurs across the time frame studied. Unfortunately, there is rather scant information regarding the healing rate of human tissues. However, studies that have examined the rate of increase in strength for tendons and ligaments during remobilization after a period of stress shielding suggest that a healing rate (increase in strength) of approximately 1% per day can be realized (Hayashi, 1996; Noyes, 1977; Woo et al., 1987). If one were to accept such a rate for healing, fatigue damage experienced because of repeated loading would be expected to accumulate in a tissue, such as a tendon or ligament, if the damage reduced tissue strength at a rate greater than 1% per day.

An interesting feature of the fatigue failure curve that might prove useful to the ergonomist is that the relationship between stress and the rate of damage to tissues is logarithmic in

nature. This relationship means that relatively small reductions in the level of imposed stress may result in large increases in the number of cycles to failure for a tissue (and thus a much slower rate of damage accumulation). In Table 4, for instance, reducing the stress from 45% to 40% UTS increases the human EDL fatigue life from 6,000 cycles to 13,000 cycles. Even more substantial gains in allowable loading cycles would be realized if the % UTS were decreased further. It should be noted that relatively small decreases in stress may not just expand fatigue life of exposed tissues; it may importantly permit a greater opportunity for the healing process to take place in the affected tissues. Again, it should be emphasized that values in Table 4 represent median cycles to tendon rupture for an isolated EDL tendon (more than needed to result in an MSD). However, even if one considers lesser insults to tissue, the development of fatigue damage could be substantially reduced if the loading on the tissue is decreased moderately, especially as one gets closer to the endurance limit.

DISCUSSION

Force and repetition have long been recognized as two key risk factors influencing the development of MSDs; however, these risk factors have generally been assumed to act independently. This assumption seems to have been implicit in the development of the vast majority of ergonomic tools as well as in several critical reviews of the MSD epidemiology literature. However, the current systematic review indicates that studies examining interaction between these factors have generally supported the notion that these factors interact with respect to MSD risk. Not only does there seem to be a dependency, but the pattern of the interaction is strikingly similar in many studies. To be fair, some recognition that force and repetition might interact may have been intuited by developers of certain ergonomics tools that multiply the effects of these risk factors in their models (e.g., Moore & Garg, 1995; Waters et al., 1993). However, in the development of the tools themselves, reference is never made to the interaction of force and repetition as a basis for the development of the multipliers chosen.

As mentioned previously, increased repetition for low-force tasks appears to result in somewhat variable estimates in MSD risk. A moderate increase in risk was the most common response; however, LFHR tasks sometimes exhibited no increase or a slight decrease in risk. It is possible that the variation in slope for low-force tasks may be because some low-force tasks reside above the tissue endurance limit, whereas other low-force tasks remain below this level. Other factors, such as the amount of rest available, may also play a role, as rest may permit some healing to occur. However, it should be recognized that humans often perform highly repetitive tasks (such as walking) for long periods without experiencing significant injury. It has been suggested that during normal activity, a tendon in vivo is subjected to less than 25% of its ultimate stress (Carlstedt & Nordin, 1980), which would be lower than the endurance limit and would presumably allow tissues to resist damage and/or allow for healing of minor injuries. However, it seems apparent that many occupational tasks raise force levels well above the endurance limit. If such tasks are repeated frequently enough, damage to the exposed tissues are sure to develop. The higher the magnitude of forces experienced, the more rapid the process of tissue deterioration.

The consistency of the interaction pattern observed in this review would seem to suggest that epidemiological studies should consider an interaction term between force and repetition when the influence of these factors on MSD risk is being studied. As mentioned previously, if an interaction between variables is significant, the influence of main effects cannot be accurately estimated (Meyer, 1991; Petersen, 1985; Underhill, 1997). Thus, studies that examine only the main effects of force and repetition without considering an interaction may present results that may be misleading in terms of the influence of either or both factors.

Should one be surprised at the interactive nature of force and repetition demonstrated in epidemiology studies? Perhaps not, if one recognizes how materials (including biomaterials) accumulate damage during repeated loading at different levels of force. The fatigue failure process would seem to be extremely relevant to the ergonomist interested in disorders resulting from exposure to force and repetition. The epidemiologic literature and fatigue failure studies of bio-materials seem to suggest similar interactions of force and repetition in the development of tissue damage. Interestingly, a recent laboratory study indicated that tissue oxygenation (measured via near-infrared spectroscopy) was affected by a Force \times Repetition interaction, with HFHR tasks leading to decreased oxygenation in the anterior deltoid during a weightlifting task (Ferguson, Allread, Le, Rose, & Marras, 2001).

The role of a third MSD risk factor may also be relevant in the context of this discussion—that of posture. One aspect of this risk factor is that changes in posture, in particular, adoption of awkward or non-neutral postures, often lead to increased force requirements and thereby increased stresses on musculoskeletal tissues. According to the fatigue failure paradigm discussed earlier, 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.

Typically, changes in posture result in increased compressive (spine) or tensile (tendon or ligament) forces on tissues. However, when one looks at the effects of awkward wrist postures, a different variety of force may come into play. As Armstrong and Chaffin (1979) demonstrated, increasingly deviated postures of the wrist result in corresponding increases in force placed on adjacent wrist structures (flexor retinaculum, carpal bones, etc.). The increased forces placed on these structures would lead to frictional stresses when the tendons slide against these structures, which may thereby become damaged as the result of a fatigue failure process. Of course, changes in posture can also result in changes in blood flow, ligament laxity, and other physiological changes that may influence MSD development. However, the increased forces that result from adoption of non-neutral or awkward postures may provide at least a partial explanation as to why non-neutral or awkward postures are frequently associated with higher MSD risk.

The Palmgren-Miner framework described earlier may eventually permit improved methods of risk assessment for occupational tasks that result in variable occupational loading regimens. This situation is currently difficult to assess with most available ergonomic tools. Such a method would require data on the distribution of forces in detailed biomechanical models as well as additional data on the fatigue life of human tissues of interest. It may

someday be possible to incorporate the remodeling and healing process for living tissue in an MSD risk assessment and, eventually, the effects of aging and disease. Furthermore, animal studies have recently demonstrated that force and repetition have important roles to play in the healing process of tissues. Specifically, it appears that injured tissues exposed to continued high-force or high-repetition activities are slower to heal, and continued exposure may lead to a vicious cycle of reinjury, chronic or systemic inflammation, fibrosis, and tissue breakdown (Barbe & Barr, 2006). In contrast, injured tissues exposed to low force and low rates of repetition appear to heal more quickly and completely (Backmann, Boquist, Friden, Lorentzon, & Toolanen, 1990; Barr, Barbe, & Clark, 2004; Stauber & Willems, 2002).

Figure 5 presents a conceptual model of the effects of force and repetition on the development of (and recovery from) MSDs. This conceptual model summarizes the findings of studies presented in this article on the role of force and repetition on MSD development and recovery. In this model, musculoskeletal tissues maintain homeostasis, mostly when the tissues experience LFLR conditions and often (although not always) for LFHR conditions. When tissues experience high-force exertions, a low number of repetitions may be tolerated well and could even make tissues stronger, as long as repetitions are limited and sufficient rest is allowed. HFHR tasks are a clear recipe for injury development.

When a tissue is injured, it enters a phase of increased susceptibility to reinjury, experiencing an inflammatory response as the body attempts to repair the tissue. Studies suggest that low force can be tolerated during the repair process, but highly repetitive low-force exposure appears to lengthen the time necessary for the tissue to heal. In many animal studies, exposing the injured (and vulnerable) tissue to higher force demands seems to lead to exacerbation of the injury, a chronic inflammatory state, and the development of fibrosis, pain, and loss of function.

Some limitations of the findings here must be noted. One is that the epidemiological studies cited are largely cross-sectional in nature, and although most of these studies have suggested a force-interaction association, more well-designed prospective studies are needed to confirm these findings. Most of the studies vary widely in terms of definition of high and low force and what constitutes high versus low repetition, and consistent definitions of what constitutes high versus low for both measures might help to clarify the relationship. Recent papers have examined this issue and may provide important guidance for future research in this area (Bao, Howard, Spielholz, & Silverstein, 2006; Bao, Spielholz, Howard, & Silverstein, 2006). Exposure assessment for force in some studies was in the form of questionnaires rather than the preferred quantitative assessment. Furthermore, it should be noted that examination of the force-repetition relationship may be best evaluated by studies evaluating all four quadrants of risk, as comparisons of interaction involving just HFHR versus LFLR (as in some studies analyzed by logistic regression) may not provide sufficient information regarding the nature of the interaction (J. F. Thomsen, personal communication, November 18, 2011). Clearly, additional research will be necessary to more fully understand the relationship of force and repetition and their effect on MSDs.

As suggested previously, and assuming that the relationships discussed earlier are confirmed, recommendations aimed at the prevention of MSDs might benefit from incorporation of the concept of a force-repetition interaction. Recommendations based on a fatigue failure model may differ somewhat from current recommendations, in that high repetition in itself is not necessarily negative (if exposed to very low forces) and that exposure to high-force exertions is not necessarily negative (as long as repetition is sufficiently limited). Exposure to the latter condition might even lead to a beneficial training effect for the worker (i.e., strengthening muscles, tendons, and ligaments) if sufficient rest is made available for tissue remodeling between exposures. However, the number of high-force exertions would have to be strictly limited so that any potential training benefit does not transition into a fatigue injury. Understanding the nature of this transition may be an important topic for future research. Of course, exposure to a combination of high force and high repetition would be expected to result in rapid tissue damage and a high MSD risk, and such tasks demand the immediate attention of the ergonomist.

Researchers are often relieved when no interactions are found in their data analysis, and understandably so. Interactions complicate the data analysis process as well as data interpretation. Nevertheless, interactions among variables occur commonly, and researchers must discard main effects explanations when they do. In the current article, evidence is presented that repetition does not have an equivalent impact on MSD risk for high-force as opposed to low-force tasks. These epidemiologic findings mirror the experience of tissue failure during repetitive loading of human tissue specimens at low versus high force levels. The suggestion is made that the reason for the Force \times Repetition interaction is that tissues loaded repetitively at low levels have a higher fatigue life (lower rate of damage), whereas those loaded at higher levels have a greatly reduced fatigue life (higher rate of damage), in accordance with fatigue failure theory. Clearly, this proposition requires a great deal of further study, and the relationships of the factors involved require more clarification. However, the concept that MSDs may be affected by a Force \times Repetition interaction may provide fertile ground for research in the quest to reduce the pain and disability associated with these disorders.

CONCLUSIONS

Based on this review, the following conclusions are drawn:

1. Epidemiological studies evaluating presence of a Force \times Repetition interaction generally have reported evidence to support an interactive effect between these two factors. Typically, increased repetition led to modest increases in MSD risk with low-force exertions but rapid increases in MSD risk with high-force exertions.
2. Evidence from fatigue failure studies on biological tissues suggests a similar interaction between force and repetition, with low-force loadings resulting in a low rate of tissue damage and high-force loadings resulting in a more rapid progression of damage.
3. Models of fatigue failure exist for variable exposure to force and repetition levels as well as for self-healing structures, which may be of use in assessing MSD risk.

4. Ergonomic guidelines and recommendations benefit from incorporating an interactive effect of force and repetition on MSD risk as well as a fatigue failure approach to assessing risk.

Acknowledgments

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Biographies

Sean Gallagher performed research from 1984 to 2011 to reduce musculoskeletal injury risk in the mining industry, initially with the U.S. Bureau of Mines and subsequently with the National Institute for Occupational Safety and Health. A major focus of his research has been to quantify the physical demands associated with work in the underground coal mine environment and the biomechanical and physiological effects of working in restricted work spaces. He accepted a faculty position at Auburn University that started in January 2012. He received his PhD in industrial and systems engineering at The Ohio State University in 2003.

John R. Heberger has been working at the National Institute for Occupational Safety and Health in the Student Career Experience Program since 2010. He has a bachelor of arts in economics from St. John Fisher College and a master of arts in economics from the University at Buffalo, the State University of New York. He is currently finishing his thesis for a master of science degree in epidemiology at the University at Buffalo.

KEY POINTS

- Of 12 studies that investigated the interaction between force and repetition, 10 provided evidence of an interaction between these variables and risk for musculoskeletal disorders (MSDs).
- Increased repetition in low-force tasks results in a modest MSD risk response (ranging from slight decrease to moderate increase); however, high-force tasks resulted in a consistent and substantial increase in MSD risk.
- In vitro fatigue failure studies on human tissues exhibit a Force × Repetition interaction with respect to tissue damage in a pattern comparable to that observed in epidemiology studies.
- Ergonomic guidelines and recommendations may benefit from incorporating a force-repetition interaction to assessing MSD risk. This interaction may be the result of a fatigue failure process experienced by musculoskeletal tissues.

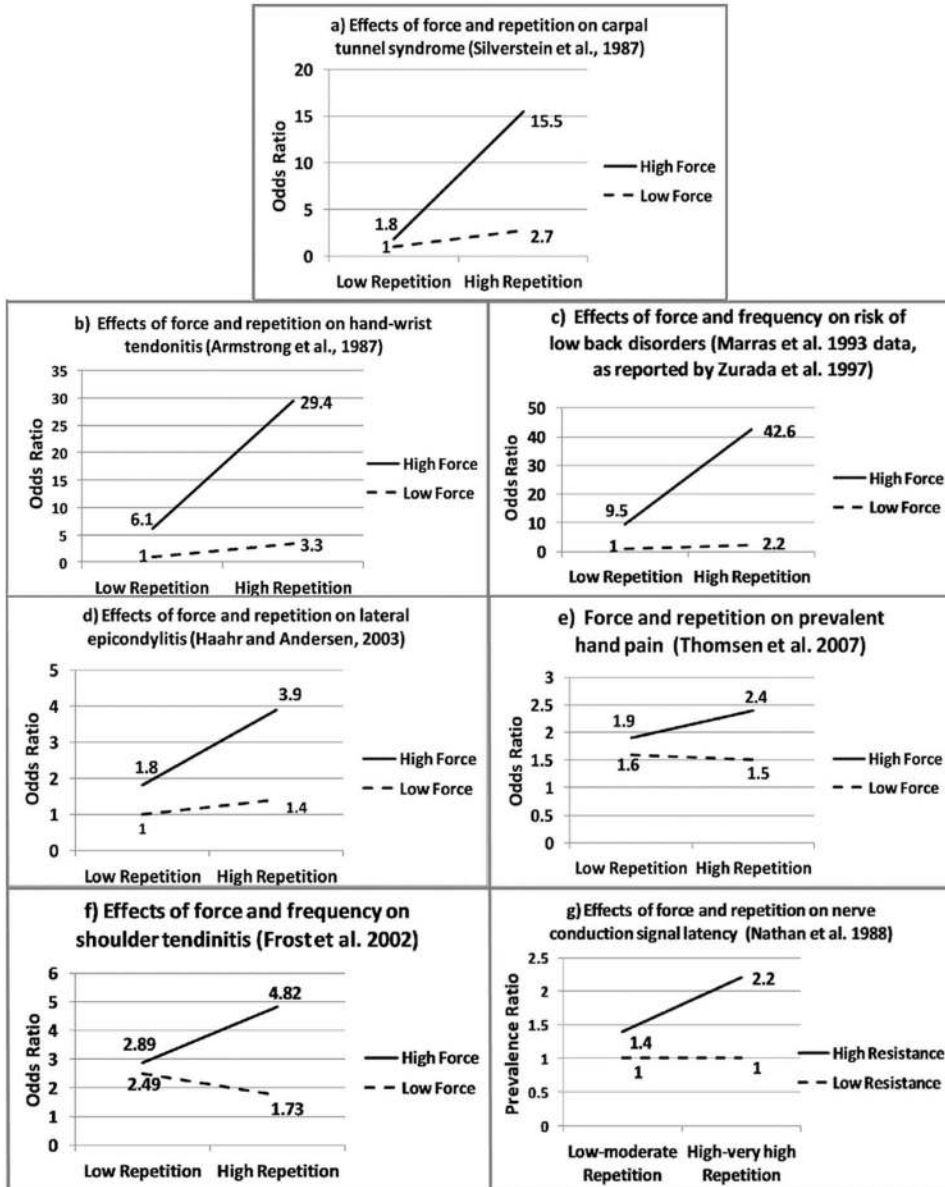


Figure 1. Results of seven cross-sectional epidemiological studies allowing 2 × 2 analysis of force and repetition and that exhibit a Force × Repetition interaction: (a) Silverstein, Fine, and Armstrong (1987); (b) Armstrong, Fine, Goldstein, Lifshitz, and Silverstein (1987); (c) Marras et al. (1993; data reported in Zurada, Karwowski, & Marras, 1997); (d) Haahr and Andersen (2003); (e) Thomsen et al. (2007; additional data analysis provided by J. F. Thomsen, personal communication, November 18, 2011); (f) Frost et al. (2002); (g) Nathan, Meadows, and Doyle (1988).

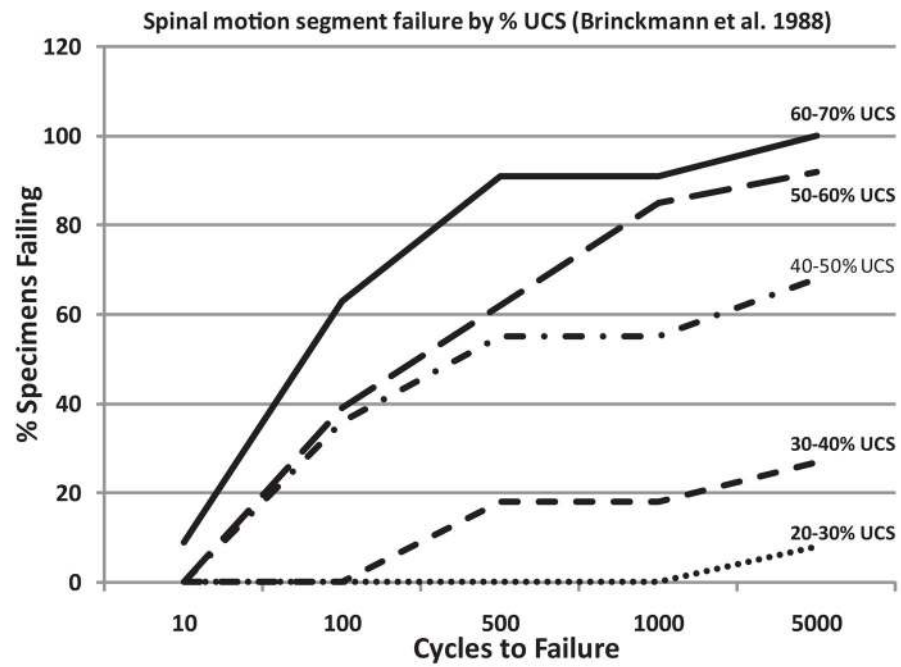


Figure 2. Data on fatigue failure of spinal motion segments by force and cycles of repetition (Brinckmann, Biggemann, & Helweg, 1988).

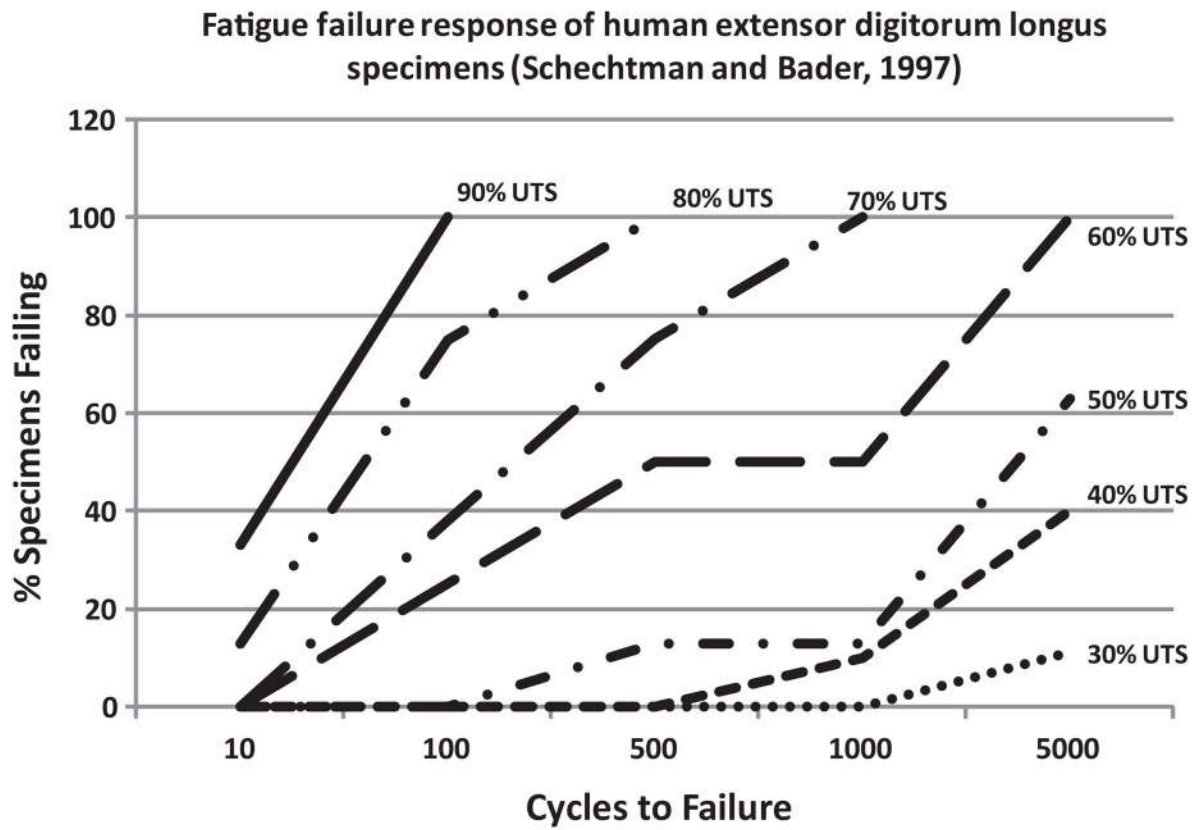


Figure 3. Data on fatigue failure of human extensor digitorum longus tendons by force and cycles of repetition (Schechtman & Bader, 1997). UTS = ultimate tensile strength.

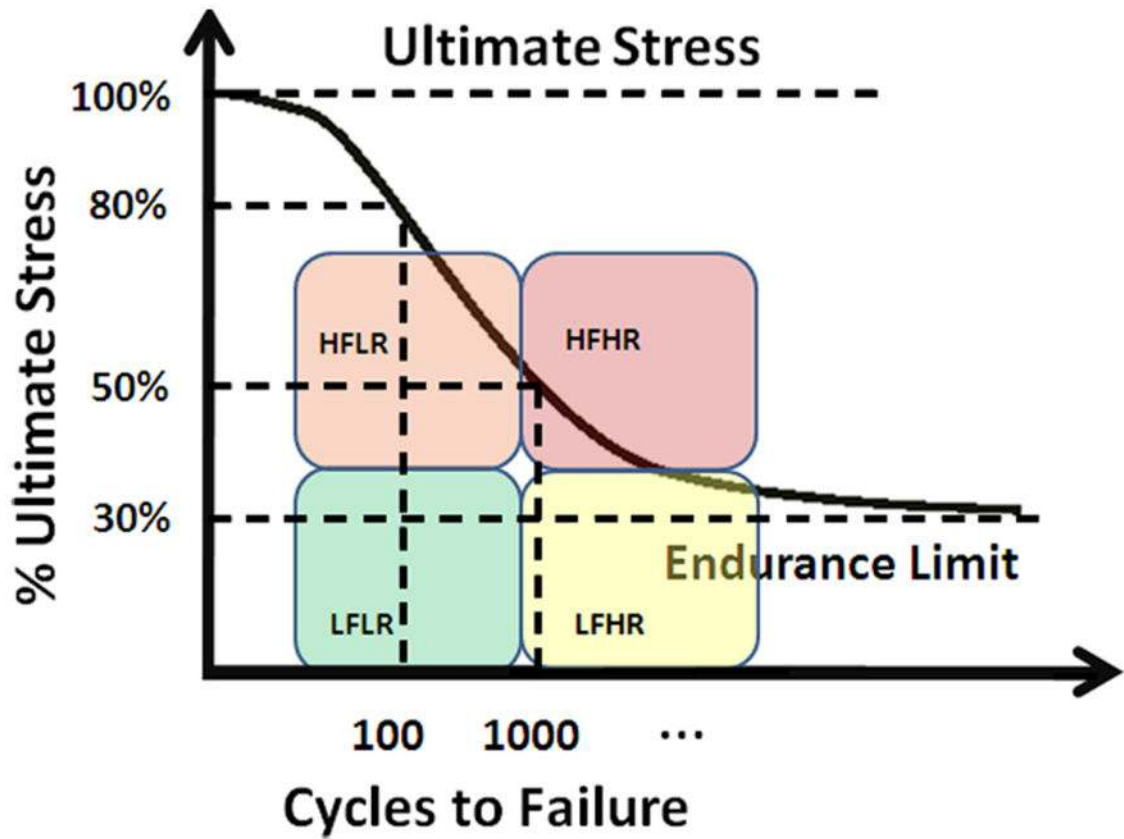


Figure 4. Force \times Repetition quadrants superimposed on a fatigue failure curve. LFLR = low force, low repetition; LFHR = low force, high repetition; HFLR = high force, low repetition; HFHR = high force, high repetition.

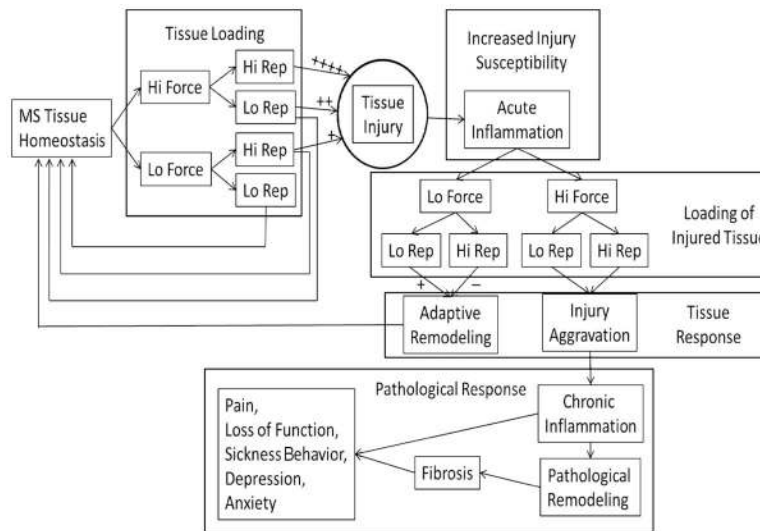


Figure 5. Conceptual model of the effects of force and repetition on musculoskeletal disorder development and recovery. A + indicates an increased likelihood of a following event (more + signs indicate higher likelihood); a – indicates decreased likelihood of a following event.

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TABLE 1**Criteria for Methodological Quality Assessment**

Study population

1. Study groups (exposed and unexposed) are clearly defined
2. Participation > 70%
3. Cases > 50

Assessment of exposure

4. Exposure definition
5. Assessment of exposure
6. Blind for outcome status

Assessment of outcome

7. Outcome definition
8. Assessment method
9. Blind for exposure status

Study design

10. Prospective design
11. Inclusion and exclusion criteria
12. Follow-up period > 1 year
13. Information between completers vs. withdrawals

Analysis and data presentation

14. Data presentation
 15. Consideration for confounders
 16. Control for confounding
-

Note. Criteria were scored as + (positive), – (negative), or ? (unclear).

TABLE 2
Methodological Quality Scores of Epidemiological Studies Investigating a Force × Repetition Interaction

Study	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Score
Armstrong, Fine, Goldstein, Lifshitz, & Silverstein (1987)	+	+	-	+	+	+	+	+	+	-	+	-	-	+	+	+	12
Babski-Reeves & Crumpton-Young (2003)	?	?	-	+	+	+	+	+	+	-	+	-	-	+	+	+	10
Chiang et al. (1993)	+	+	?	+	+	?	+	+	+	-	+	-	-	+	+	+	11
Frost et al. (2002)	+	-	+	+	+	+	+	+	-	-	+	-	-	+	+	+	12
Haahr & Andersen (2003)	+	+	+	+	+	-	+	+	+	-	+	-	-	+	+	+	12
Marras et al. (2003)	+	?	+	+	+	?	+	+	?	-	+	-	-	+	+	+	10
Menzel, Brooks, Bernard, & Nelson (2004)	+	+	+	+	+	-	+	+	-	-	+	-	-	-	-	-	8
Nathan, Keniston, Myers, & Meadows (1992)	+	-	+	+	+	+	+	+	?	+	?	+	+	+	-	-	11
Nathan, Meadows, & Doyle (1988)	+	-	+	+	+	?	+	+	?	-	+	-	-	+	+	+	10
Shiri, Viikari-Juntura, Varonen, & Heliovaara (2006)	+	+	+	+	+	+	+	+	-	-	+	-	+	+	+	+	13
Silverstein, Fine, & Armstrong (1987)	+	+	-	+	+	+	+	+	+	-	+	-	-	+	+	+	12
Thomsen et al. (2007)	+	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+	14

Note. + = positive; - = negative; ? = unclear.

Results of Contrasts Testing Differences (Diff) in Musculoskeletal Disorder Risk Between High-Force (HF) and Low-Force (LF) Exposure Within High- and Low-Repetition Categories for Six Cross-Sectional Studies Reporting 2 x 2 Data

TABLE 3

Study	HF vs. LF for Low-Repetition Tasks			HF vs. LF for High-Repetition Tasks		
	Diff	SE(Diff)	p	Diff	SE(Diff)	p
Armstrong, Fine, Goldstein, Lifshitz, & Silverstein (1987)	.024	.015	.063	.073	.033	.012*
Silverstein, Fine, & Armstrong (1987)	.008	.014	.348	.077	.030	.008*
Haahr & Anderson (2003)	.171	.077	.017*	.564	.058	<.001*
Nathan, Meadows, & Doyle (1988)	.104	.058	.042	.336	.148	.018*
Frost et al. (2002)	-.008	.010	.707	.020	.011	.043
Zurada, Karwowski, & Marras (1997; data from Marras et al., 1993)	.486	.114	<.001*	.594	.114	<.001*

Note. Bonferroni adjustments require that *p* values be less than .025 to achieve significance.

TABLE 4

Data from Schechtman and Bader (1997) on Median Cycles to Failure at Different Percentages of Ultimate Tensile Strength

% Ultimate Tensile Strength	Median Cycles to Failure
35	30,000
40	13,000
45	6,000

Note. Median cycles to failure are rounded to the nearest thousand for ease of computation.

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