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ANATOMY PHYSIOLOGY, PATHOPHYSIOLOGY REVIEW

Ligaments: A source of musculoskeletal disorders

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Summary The mechanical and neurological properties of ligaments are reviewed and updated with recent development from the perspective which evaluates their role as a source of neuromusculoskeletal disorders resulting from exposure to sports and occupational activities. Creep, tension–relaxation, hysteresis, sensitivity to strain rate and strain/load frequency were shown to result not only in mechanical functional degradation but also in the development of sensory–motor disorders with short- and long-term implication on function and disability. The recently exposed relationships between collagen fibers, applied mechanical stimuli, tissue micro-damage, acute and chronic inflammation and neuromuscular disorders are delineated with special reference to sports and occupational stressors such as load duration, rest duration, work/rest ratio, number of repetitions of activity and velocity of movement.

Introduction

There are several ligaments in every joint in the human skeleton and they are considered as the primary restraints of the bones constituting the joint. Ligaments are also sensory organs and have significant input to sensation and reflexive/synergistic activation of muscles. The muscles associated with any given joint, therefore, also have a significant role as restraints. In some joints, such as the intervertebral joints of the spine, the role of the muscles as restraints is amplified. The role of ligaments as joint restraints is rather complex when considering the multitude of physical activities performed by individuals in routine daily functions, work and sports, the complexity of the anatomy of the different joints and the wide range of

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magnitude and velocity of the external loads. The functional complexity of ligaments is amplified when considering their inherent viscoelastic properties such as creep, tension–relaxation, hysteresis and time or frequency-dependent length–tension behavior. As joints go through their range of motion, with or without external load, the ligaments ensure that the bones associated with the joint travel in their prescribed anatomical tracks, keep full and even contact pressure of the articular surfaces, prevent separation of the bones from each other by increasing their tension, as may be necessary, and ensuring stable motion. Joint stability, therefore, is the general role of ligaments without which the joint may subluxate, cause damage to the capsule, cartilage, tendons, nearby nerves and blood vessels, discs (if considering spinal joints) and to the ligaments themselves. Such injury may debilitate the individual by preventing or limiting his/her use of the joint and the loss of function. Unstable joints are also known to drastically modify the intra-articular pressure and the muscular activity pattern about the joint, resulting in early onset of osteoarthritis, pain, disability and eventually the need for joint replacement surgery. Dysfunctional or ruptured ligaments, therefore, result in a complex syndrome, various sensory–motor disorders and other long-term consequences which impact the individual's well-being, his athletic activities, employer, skilled work force pool and national medical expenses.

As axial stretching of a ligament is applied, fibers or bundles with a small helical wave appearance straighten first and begin to offer resistance (increased stiffness) to stretch. As the ligament is further elongated, fibers or fiber bundles of progressively larger helical wave straighten and contribute to the overall stiffness. Once all the fibers are straightened, a sharp increase in stiffness is observed. Over all, the recruitment process gives rise to a non-linear length–tension relationship of a ligament.

Ligament structure

Ligaments consist of closely packed, parallel collagen fibers which appear to have various degrees of undulation (or helical) form along the axis of each fiber at a resting length. There are also short cross fibrils which connect the axial fibers to each other. The helical shape of various wave size of each fiber or group of fibers (bundles) gives rise to a process called "recruitment".

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The geometric shape of a ligament and its insertion into the bones associated with their joint give rise to another "recruitment" process. The medial collateral ligament of the elbow, for example, is a thin fan-shaped structure where the collagen fibers radiate from a relatively small, focal area in the distal humerus, but terminate on a large segment of the ulna. This type of geometric arrangement recruits different bundles of the ligament at different elbow angles. At full extension the anterior fibers are stretched and offer resistance, whereas with flexion, the anterior fibers gradually relax as more posteriorly situated fibers straighten and stretch.

The intraspinous ligament, for example, has a membrane-like arrangement with the fiber direction set diagonally to the axis of the spine, such as to provide the optimal forces during a relevant component of the range of motion of the intervertebral joint in anterior flexion.

Even the simplest, rope-shaped ligaments, such as the anterior cruciate ligament (ACL) undergoes a type of regional recruitment; the rotation (screw home) mechanism during knee extension causes the ligament to twist in addition to its axial stretch, recruiting different fiber bundles.

Overall, the mostly collagen (75%), elastin and other substances structure of ligaments is custom tailored by long evolutionary processes to provide various degrees of stiffness at various loads and at various ranges of motion of a joint, while optimally fitting the anatomy inside (inter-capsular) or outside (extra-capsular) a given joint. The various degrees of helical shape of the different fibers allows generation of a wide range of tensile forces by the fiber recruitment process, whereas the overall geometry of the ligament allows selective recruitment of bundles such as to extend function over a wide range of motion. The large content of water (70%) and the cross weave of the long fibers by short fibers provides the necessary lubrication for bundles to slide relative to each other, yet to remain bundled together and generate stiffness in the transverse directions.

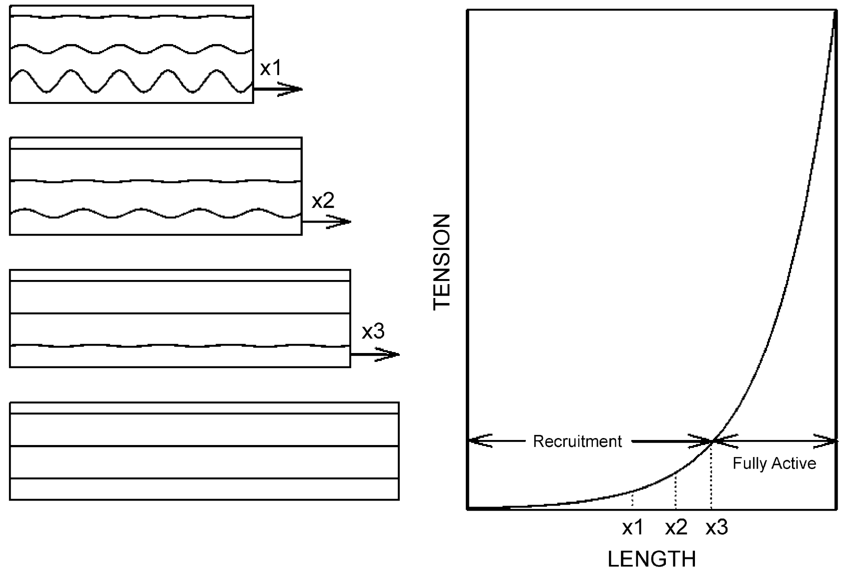

Figure 1 The length–tension behavior of a ligament is shown on the right. On the left, the progressive recruitment of collagen fibers is shown for several elongations.

Mechanical properties

Ligaments are functional (effective) under tension, or when stretched and completely non-functional in compression or when shortened below their resting length. The general response of ligaments to stretch or tension is rather complex and non-linear, and subjected to several phenomena which are time-dependent, such as creep, tension–relaxation, strain rate and hysteresis. Ligament length–tension (or strain–stress) behavior is also temperature-dependent, exhibiting reduced capability to sustain load as temperature increases, while at the same length (Woo and Buckwalter, 1988).

Length–tension and recruitment

The general length–tension (or strain–stress) behavior of a ligament is non-linear as shown in the schematic diagram of Figure 1.

The initial segments of the curve demonstrate rather large strain for very small increase in load. Once all the waves in the collagen fibers of the ligament have been straightened out, and all of the fibers were recruited, additional increase in strain is accompanied with a fast increase in tension. The resting length of ligaments is a difficult issue to establish due to the complexity of measurements in vivo. Some interesting data, however, show that the ACL in the knee has relatively no changes in length between 60° to full flexion, and a fast increase in strain when extending the knee from 60° to full extension (Renstrom et al., 1986). In that study, the authors normalized the measurement to show negative strain in the flexed range, whereas the same data could be presented as zero strain. It is conceivable that the resting length is near or just above the origin of the length–tension curve.

Creep

When a constant load is applied to a ligament, it first elongates to a given length. If left at the same constant load, it will continue to elongate over time in an exponential fashion up to a finite maximum. This elongation over time is termed "creep", and is expressed as the percent elongation relative to the length it arrived to immediately after the load was applied. Figure 2 depicts the response of a ligament to a constant load over time, as well as the creep. The recovery of the creep with rest, after the load was removed, is also shown (Solomonow et al., 2003b).

> When ligaments are subjected to a stretch and hold over time (or constant elongation) the tension–relaxation phenomena is observed. The tension in the ligament increases immediately upon the elongation to a given value. As time elapses, the tension decreases exponentially to a finite minimum while the length does not change.

Tension–relaxation

When ligaments are subjected to a stretch and hold over time (or constant elongation) the

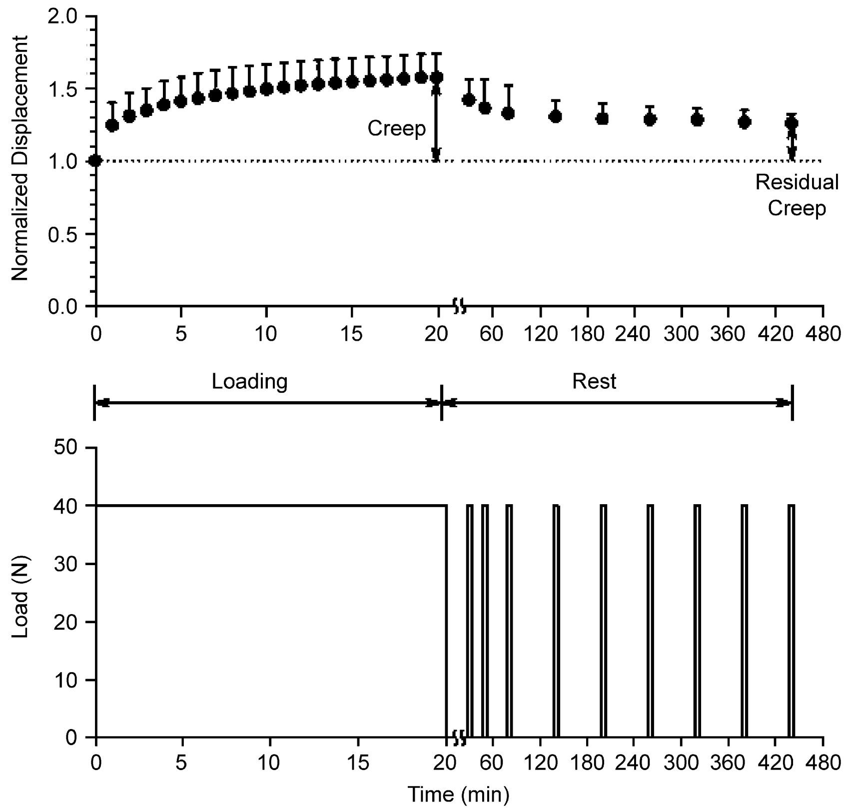

Figure 2 The response of the supraspinous ligament to a constant load applied for a 20 min period exhibits the development of creep. The recovery during 7 h rest was not complete. In the rest period, short (6 s) loading tests were applied to determine the residual creep (Solomonow et al., 2003).

tension–relaxation phenomena is observed. The tension in the ligament increases immediately upon the elongation to a given value. As time elapses, the tension decreases exponentially to a finite minimum while the length does not change. Figure 3 depicts the tension–relaxation phenomena associated with the constant elongation paradigm, as well as its recovery following rest (Jackson et al., 2001).

> In general, slow rates of elongation are associated with the development of relatively low tension, whereas higher rates of elongation result in the development of high tension. Fast stretch of ligaments, such as in high-frequency repetitive motion or in sports activities are known to result in high incidents of ligamentous damage or rupture.

Strain rate

The tension developed in a ligament also depends on the rate of elongation or strain rate (Peterson, 1986). In general, slow rates of elongation are associated with the development of relatively low tension, whereas higher rates of elongation result in the development of high tension. Fast stretch of ligaments, such as in high-frequency repetitive motion or in sports activities are known to result in high incidents of ligamentous damage or rupture. Figure 4 depicts the length–tension curve for a supraspinous ligament stretched at different rates (Eversull et al., 2001). From the figure, it is evident that the supraspinous ligament can develop up to 50% more tension at a given length if stretched at 200%/s, relative to 25%/s. Fast rates of stretch, therefore, may exceed the physiological loads that could be sustained by a ligament safely, yet it may still be well within the physiological length range. Development of high tension in the ligaments may result in rupture and permanent sensory–motor deficit to the joint in addition to deficit in its structural functions.

In occupational activities, minimizing the speed of motion for a given task can contribute toward safer working conditions, especially when such tasks are repetitive. In sports activities, however, high velocity of motion is favored and necessary for success, yet poses a high-risk for injury or damage.

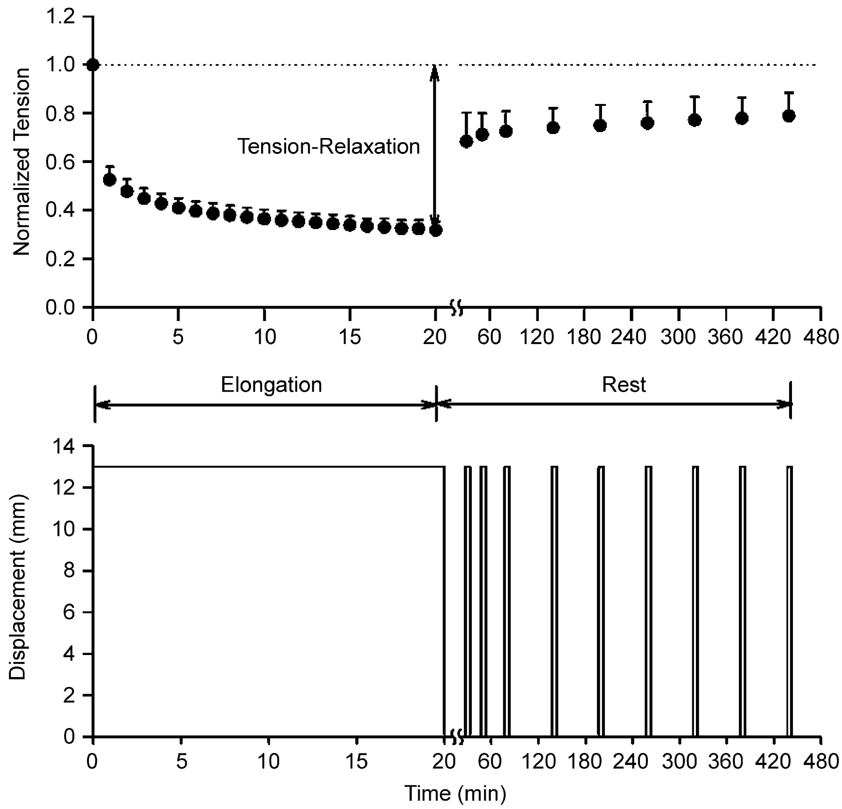

Figure 3 The response of the supraspinous ligament to a constant elongation applied for a 20-min period exhibits the development of tension—relaxation. The tension did not fully recover during the 7 h rest (Jackson et al., 2001).

The impact of progressive hysteresis, therefore, is manifested by gradually decreasing tension in the ligament, development of joint laxity, reduced joint stability and increased risk of injury. Repetitive sports and occupational tasks should be limited in duration and allow sufficient rest periods to facilitate recovery of normal ligament function.

Hysteresis

Another important behavioral property of ligaments is its inability to track the same length—tension curve when subjected to a single stretch—release or load—unload cycle, i.e., hysteresis. This phenomenon is also associated with repetitive motion when a series of stretch—release cycles are performed over time. When the ligament is stimulated repetitively with constant peak load, the hysteresis develops along the length axis, i.e., the ligament length limits increase with each cycle reflecting the hysteresis associated with the development of creep as shown in Figure 5B.

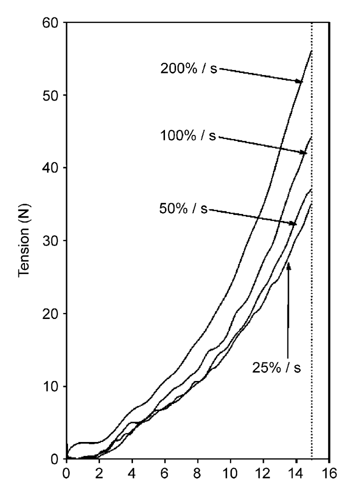

Figure 4 The length—tension relation of a ligament when stretched at different rates. Increasing the rate of stretch from 25%/s to 200%/s develops nearly 50% more tension in the supraspinous ligament (Eversull et al., 2001).

Conversely, when cycles of constant peak stretch are applied, the peak tension decreases in sequential cycles, reflecting the on-going development of tension—relaxation. Figure 5A depicts the hysteresis exhibited under constant elongation whereas

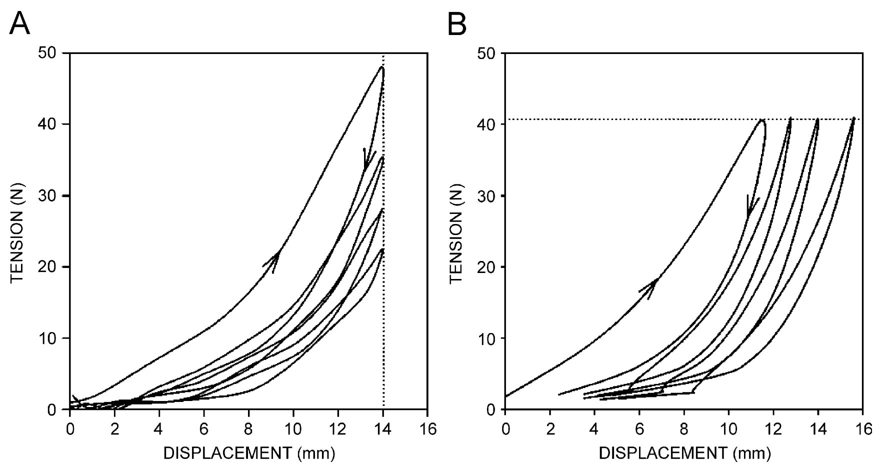

Figure 5 (A) The hysteresis associated with cyclic stretch of the same peak magnitude. (B) The hysteresis developed in a ligament when subjected to cyclic load of the same peak magnitude (Claude et al., 2003; Solomonow et al., 2001).

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Frequency of cyclic motion

Ligament behavior is also dependent on the frequency of load application and unloading, such as in repetitive sports and occupational tasks. Cyclic loading of a ligament with the same peak load, but at a higher frequency, results in larger creep development and longer period of rest required for the full recovery of the creep (Lu et al., 2004). The data in Figure 6 show the peak displacement of the supraspinous ligament subjected to a peak load of 40 N, but at two different frequencies: 0.1 and 0.5 Hz. The data show that the initial displacement at 0.1 Hz is larger than the initial displacement at 0.5 Hz, but the creep developed at the end of 20 min is much larger for the loading frequency of 0.5 Hz. Similarly, the recovery of the creep takes much longer when loading at 0.5 Hz.

Occupational and sports tasks requiring repetitive motion at high frequency, therefore, induce larger creep in the ligaments of the workers, require longer rest time to recover, and probably induce larger risk for cumulative creep from one work session to the next, in the same day and from day-to-day. Larger creep results in increased laxity of the joint as the activity goes on, and the associated risks as discussed above.

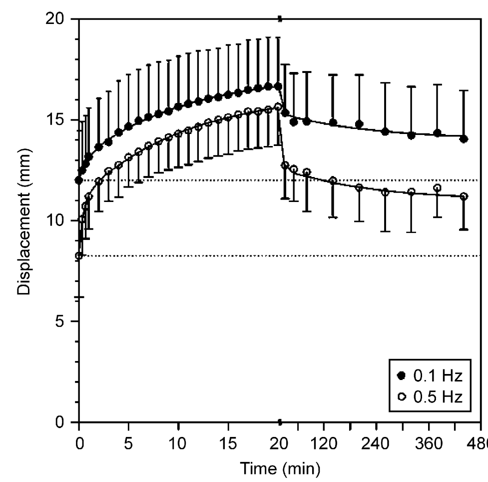

Figure 6 The development of creep and its recovery in the supraspinous ligament subjected to cyclic loading at 0.1 and 0.5 Hz (Lu et al., 2004).

Recovery of creep and tension–relaxation with rest

The recovery of the creep or laxity developed in a ligament during a sustained loading is a relatively unexplored issue. Some early assessments in healthy humans and in vivo animal models show that creep developed over relatively short periods of 10–60 min of loading did not fully recover at the end of up to 2 h of rest (Crisco et al., 1997; Ekstrom et al., 1996; McGill and Brown, 1992). Crisco et al. (1997) observed, however, that nearly full recovery of palm ligaments was measured after 24 h rest. Recent evidence demonstrate that both creep and tension–relaxation induced in a 20–50 min of loading or stretching a ligament, respectively, demonstrated 40–60% recovery in the first hour of rest, whereas full recovery is a very slow process which may require 24–48 h (Claude et al., 2003; Gedalia et al., 1999; Jackson et al., 2001; Solomonow et al., 2003b). Figures 2, 3 and 6 provide experimental illustrations of the recovery of creep and tension–-relaxation over 7–8 h of rest after the loading or stretch of the supraspinous ligament. It is evident, therefore, that loading or stretching a ligament over relatively short periods induces changes in its length–tension behavior that may last 20–40 times longer than the duration of the loading/stretching. This phenomenon has significant implications on the ability of a ligament to protect and stabilize joints in athletes and workers who are subjected to sequential periods of static or cyclic activities during a given day. As the work–rest periods go on, the ligament exhibits cumulative creep and reduction in its ability to protect the joint, causing the latter part of a work period (or day) to be more prone to injury. Since full recovery of the creep with rest also requires more than 24 h, there would be a cumulative creep from the previous work day at the beginning of a new work day. The phenomenon of inter- and intra-day cumulative creep is illustrated with experimental data from the supraspinous ligament in Figure 7, and may provide valuable insights to the mechanical aspects of the development of cumulative trauma disorders.

Responses to increased physical activity and inactivity

Ligaments are adaptive to exercise or series of repetitive functions and to immobilization. Moderate exercise or occupational activities followed with sufficient rest and recovery results, over time, with increase in the strength of a ligament, as well as in its size and collagen content (Gomez, 1988; Tipton et al., 1970; Viidik, 1972, 1967; Viidik and Ekholm, 1968; Woo et al., 1981, 1980; Zernicke

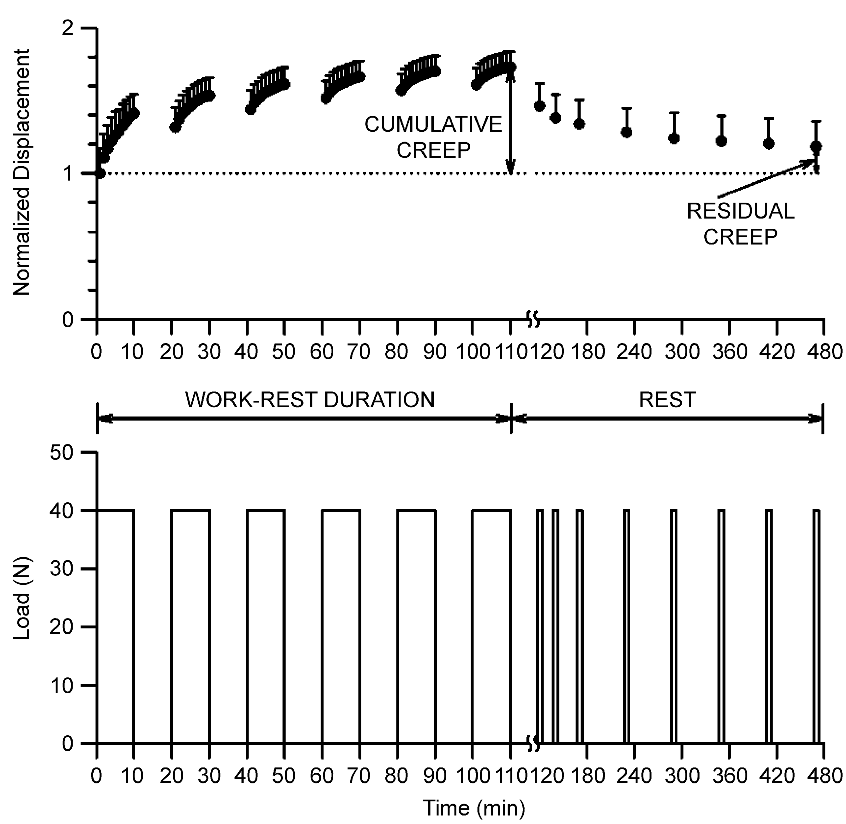

Figure 7 The development of cumulative creep in the supraspinous ligament over a 120 min duration consisting of six sessions of 10 min static flexion followed by 10 min rest and its recovery pattern over 7 h of rest. Note that only partial recovery of creep developed in the first 10 min of load occurred, and that the residual creep, as well as final creep accumulated over the work–rest session. Only partial recovery was seen at the end of 7 h rest, leaving residual creep for the next work day.

et al., 1984). These changes indicate enhanced collagen metabolism in response to the stimulus. Indeed, such stimulus was shown to increase the total number of collagen fibrils in the ligament, as well as in the fibril diameter (Michna, 1984; Mosler et al., 1985; Nemetschek et al., 1983; Oakes et al., 1981; Zernicke et al., 1984). Over all, moderate repetitive stimulation of ligaments coupled with appropriate rest and recovery allows the tissue to hypertrophy, increase its strength and protect joint stability in persons exposed to more demanding physical activity (Suominen et al., 1980).

Conversely, immobilization or reduced physical activity is accompanied with degenerative changes in the ligaments structure and function consisting of decreased collagen fiber diameter, fibril density and fibril number and overall collagen mass and its metabolism (Amiel et al., 1983; Binkley and Peat, 1986; Klein et al., 1982; Tipton et al., 1970).

Furthermore, the immobilization seems to have significant impact on the ligament–bone junction (or insertion to the bone). Immobilization results in increased osteoclastic activity, resorption of bone and disruption of the pattern of diffusion of the ligament fibers into the bone (Woo et al., 1987). Over all, immobilization or decreased physical activity results not only in weaker and thinner ligaments, but also in weaker attachment to the bones of the respective joint, increasing the risk for potential injury if drastic increases in physical activity are implemented. This is important to note when athletes and workers return to activity after prolonged sickness, periods of lapse in training or unemployment or long holiday. Similarly, changing position from one job to another or one sports category to another where different types of physical functions are performed requiring relatively dormant joints to be fully engaged may result in high exposure to injury. A gradual ''work in'' period in such circumstances may be a safe method to avoid exposure to injury.

Ligament inflammation

Inflammatory response in ligaments is initiated whenever the tissue is subjected to stresses which exceed its routine limits at a given time. For example, a sub-injury/failure load, well within the physiological limits of a ligament when applied to the ligament by an individual who does not do that type of physical activity routinely. The normal homeostatic metabolic, cellular, circulatory and mechanical limits are therefore exceeded by the load, triggering an inflammatory response.

Similarly, static or repetitive loading of a ligament, within its physiological limits, when extended over a period of time result in creep which is an expression of cumulative micro-damage within the collagen fibers structure of the tissue. The accumulated micro-damage triggers inflammatory responses as well (Bryant, 1977; Frank et al., 1985; Gamble, 1988; Martinez-Hernandez, 1988).

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Inflammatory signs consisting of swelling, redness, elevated temperature and pain demonstrate that a healing process is underway. The collagen fibers are undergoing changes in cellular, metabolic and vascular condition in order to improve the mechanical properties of the ligament such that it may be able to negotiate with the increased demand to physical activity. The inflammation also manages the breakdown and removal of damaged protein and the importation of new protein to repair and reconstruct the micro-damage and hypertrophy the tissue.

Acute inflammation, therefore, represents the healing or upgrading of the ligament's properties and if left undisturbed by additional overexposure to stress or intervention of anti-inflammatory drugs will allow recovery and upgrading of the ligament (Leadbetter, 1990).

Another case where acute inflammation is present is when physical activities presenting sudden overload/stretch cause a distinct damage to the tissue which is felt immediately. Such cases, as a sudden loss of balance, a fall, collision with another person, exposure to unexpected load, etc., may result in what is called a sprain injury or a partial rupture of the ligament. Acute inflammation sets in within several hours and may last several weeks and up to 12 months. The healing process, however, does not result in full recovery of the functional properties of the tissue. Mostly, only up to 70% of the ligaments original structural and functional characteristics are attained by healing post-injury (Woo et al., 1980).

The inflammation process described above is designated as acute inflammation, which is distinctly different from a chronic inflammation.

Chronic inflammation is an extension of an acute inflammation when the tissue is not allowed to rest, recover and heal. Repetitive exposure to physical activity and reloading of the ligament over prolonged periods without sufficient rest and recovery represent cumulative micro-trauma. The resulting chronic inflammation is associated with atrophy and degeneration of the collagen matrix leaving a permanently damaged, weak and non-functional ligament (Leadbetter, 1990). The dangerous aspect of a chronic inflammation is the fact that it builds up silently over many weeks, months or years (dependent on a presently unknown dose-duration levels of the stressors) and appears one day as a permanent disability associated with pain, limited motion, weakness and other disorders (Safran, 1985). Rest and recovery of as much as 2 years allows only partial resolution of the disability (Woo and Buckwalter, 1988). Full recovery was never reported.

Ligaments as sensory organs

While ligaments are primarily known as mechanical apparatus responsible for joint stability, they have equally important sensory functions. Anatomical studies demonstrate that ligaments in the extremity joints and the spine are endowed with mechanoreceptors consisting of: Pancinian, Golgi, Ruffini and bare nerve endings (Burgess and Clark, 1969; Freeman and Wyke, 1967a, b; Gardner, 1944; Guanche et al., 1995; Halata et al., 1985; Jackson et al., 1966; Mountcastle, 1974; Petrie et al., 1998, 1997; Polacek, 1966; Proske et al., 1988; Schulz et al., 1984; Sjölander, 1989; Skoglund, 1956; Solomonow et al., 1996; Wyke, 1981; Yahia and Newman, 1991; Zimney and Wink, 1991). The presence of such afferents in the ligaments confirms that they contribute to proprioception and kinesthesia and may also have a distinct role in reflex activation or inhibition of muscular activities.

Studies of patients with ruptured ACL exhibit decreased ability to accurately position/reposition their limbs, indicating defective kinesthetic sensation (Skinner and Barrack, 1991). Similarly, such patients also demonstrate defective reflexive responses to joint loading that may disturb stability indicating that a deficit in proprioception is present as well (Beard et al., 1994; Solomonow et al., 1987; Solomonow and Krogsgaard, 2001). Overall, the decrease or loss of function in a ligament due to rupture or damage does not only compromise its mechanical contributions to joint stability, but also sensory loss of proprioceptive and kinesthetic perception and fast reflexive activation of muscles and the forces they generate in order to enforce joint stability.

Ligamento-muscular reflex

It was suggested, as far back as the turn of the last century, that a reflex may exist from sensory receptors in the ligaments to muscles that may directly or indirectly modify the load imposed on the ligament (Payr, 1900). Experiments performed in the 1950s resulted in conflicting data and no conclusion (Andersson and Stener, 1959; Ekholm et al., 1960; Palmer, 1938, 1958; Stener, 1959; Stener, and Petersen, 1962). A clear demonstration of a reflex activation of muscles by stimulation of the ACL was finally provided in 1987 (Solomonow et al., 1987) and reconfirmed several times since then (Beard et al., 1994; Dyhre-Poulsen and Krogsgard, 2000; Raunest et al., 1996; Johansson et al., 1989; Kim et al., 1995). It was further shown that such a ligamento-muscular reflex exists in most extremity joints (Freeman and Wyke, 1967b; Guanche et al., 1995; Knatt et al., 1995; Schaible and Schmidt, 1983; Schaible et al., 1986; Solomonow et al., 1996; Phillips et al., 1997; Solomonow and Lewis, 2002) and in the spine (Indahl et al., 1995, 1997; Stubbs et al., 1998; Solomonow et al., 1998).

Biomechanical data demonstrate that the muscular activity elicited by the reflex from the ACL always acts to prevent the distraction of the joint (Hirokawa et al., 1991, 1992; Louie and Mote, 1987; Markolf et al., 1978; Markolf et al., 1976) as well as reduce the strain in the ACL (Renstrom et al., 1986), establishing the functional objective of such reflex; synergistic activity of muscles and ligaments to maintain joint stability.

Recently, new evidence supports that the ligamento-muscular reflex may also have inhibitory effects on muscles associated with that joint (Solomonow and Krogsgaard, 2001; Voigt et al., 1998; Chu et al., 2003). Indeed, such inhibition may prevent extremely large forces from developing in muscles that increase the stress in and overwhelm the ligaments. A typical case is demonstrated by inhibition of large quadriceps forces during extension in the range of motion of 60° to full knee flexion (Chu et al., 2003). It is well established that quadriceps force in that range of motion contributes toward the anterior distraction of the tibia (Hirokawa et al., 1992), as well as increasing the strain in the ACL (Renstrom et al., 1986). The reflex inhibition, therefore, also serves to protect the ligament.

Ligamento-muscular reflexes, therefore, may be inhibitory or excitatory, as may be fit to preserve joint stability; inhibiting muscles that destabilize the joint or increasing antagonist co-activation to stabilize the joint.

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Indirect control of joint stability, via the ligamento-muscular reflex, by activating muscles that do not cross the joint is observed in the ankle joint. Stimulation of the medial collateral ligament of the ankle results in activation of the intrinsic muscles of the foot. The force generated by these muscles increases the arch of the foot and thereby corrects or prevents eversion and the associated joint instability (Solomonow and Lewis, 2002). To date, this unique case represents how muscles which do not cross a joint can have pronounced impact on its stability.

Another special case is the ligaments associated with the shoulder. The capsule surrounding the joint exhibits thickening bands on its superior, anterior and posterior region, as well as in its inferior region which constitutes relatively weak ligaments. In some cases the thickening is hardly noticeable, confirming the relatively minor mechanical role of these ligaments. The four bands, however, are well endowed with the four types of mechanoreceptors, indicating an increased importance of their sensory role in perception of joint position and in ligamento-muscular reflex activation (Guanche et al., 1999; Solomonow et al., 1996). Similarly, there are several articular nerves supplying the afferents in these ligaments and a complex, vivid reflexive activation of the many muscles associated with the rotator cuff (Guanche et al., 1995; Knatt et al., 1995; Solomonow et al., 1996). The muscles, therefore seem to be a major component in maintaining the stability of the shoulder.

The reflex from the ligaments, therefore, can provide muscular assistance for the preservation of joint stability directly (by muscles crossing the joint) or indirectly (by muscles not crossing the joint) using muscular activation or inhibition.

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Neuromuscular disorders

Considering the ligaments' mechanical properties (length–tension, creep, tension–relaxation, hysteresis, etc.), together with its sensory–motor functions (kinesthesia, proprioception and reflex activation/inhibition of muscles) and biological behavior (hypertrophy, degeneration, inflammation and healing) can motivate one to form several hypothesis regarding its role in triggering neuromusculoskeletal disorders.

Athletes and workers engaged in daily performance of static or repetitive activities over periods of weeks, months or years will exhibit first hypertrophy of the ligaments, but still subjected to creep, tension–relaxation and hysteresis. The ligament becomes lax over a day's work and cannot exert sufficient tension to maintain the motion of the bones on the correct track and maintain even pressure distribution on the cartilage surface, while supporting the same external loads. Such degradation of function can cause increased exposure to injury as the work day progresses, while at the same time causing gradual degeneration of the articular surfaces of the joint, leading to osteoarthritis.

The development of cumulative creep in the ligament over prolonged periods may build up at some point to trigger sufficient micro-damage in the collagen fibers with the acute inflammation becoming chronic and consequently degeneration of the ligament and permanent disability (Leadbetter, 1990; Safran, 1985).

While the two disorders presented above are widely recognized due to long experience in the orthopedic and rehabilitation clinics, the interaction of the mechanical and sensory (reflexive) properties of ligaments and the potential disorders that can result is still unexplored. As ligaments develop creep, tension–relaxation and hysteresis, the length or tension sensory thresholds of the various afferents are shifted significantly in the range of motion and with the loads experienced by the ligament through the same motion (Eversull et al., 2001; Solomonow et al., 2001). The direct results of such sensory thresholds shift is degradation in proprioception and kinesthetic perception that lead to inaccuracies of movement and dysfunctional reflexive activation of muscles.

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Acute neuromuscular disorder

Solomonow et al. (2003b) described an acute neuromuscular disorder, consisting of five distinct components, associated with cyclic or static loads applied to lumbar ligaments. The first component consists of a gradually decreasing reflexive muscular activity, which is directly related to the laxity and creep developed in the ligaments, eliciting a shift in the sensory trigger thresholds of the reflex.

The second component consists of spasms observed during the cyclic or static loading period, elicited by the micro-damage in the collagen fibers and relayed reflexively by pain receptors.

The third component was observed in the first hour of rest after the static loading. This was expressed as a minor transient hyperexcitability of reflexive muscular activity. The hyperexcitability was attributed to the attempt of the musculature to protect the severely stretched ligament from any further development of micro-damage until substantial recovery of creep took place.

The fourth component consisted of a relatively prolonged reflex muscular hyperexcitabiltiy that gradually increased from the second to the sixth hour of rest after static loading of the lumbar ligaments. The amplitude of this "morning after" hyperexcitability was much stronger than the initial hyperexitability by two- to three-fold and seemed to last well over 24 h. This component was correlated to the development of inflammation in the supraspinous ligament (Solomonow et al., 2003b, c), the magnitude of which dictated the duration or the time constants of the development and decay of the hyperexcitability.

The fifth component of the disorder is the slow exponential recovery of the reflexive EMG to its normal (initial) level as rest time progresses.

Similar responses were observed by Claude et al. (2003), Navar et al. (2006), Le et al. (2007), and Hoops et al. (2007) when cyclic loading of lumbar viscoelastic tissues were performed.

Figure 8 shows recording of reflexive EMG from the multifidus muscles while the lumbar spine and the supraspinous ligaments are subjected to cyclic anterior flexion for 20 min followed by 7 h of rest. The development of creep and its recovery and the corresponding spasms and two hyperexcitabilities are noticeable in the different phases.

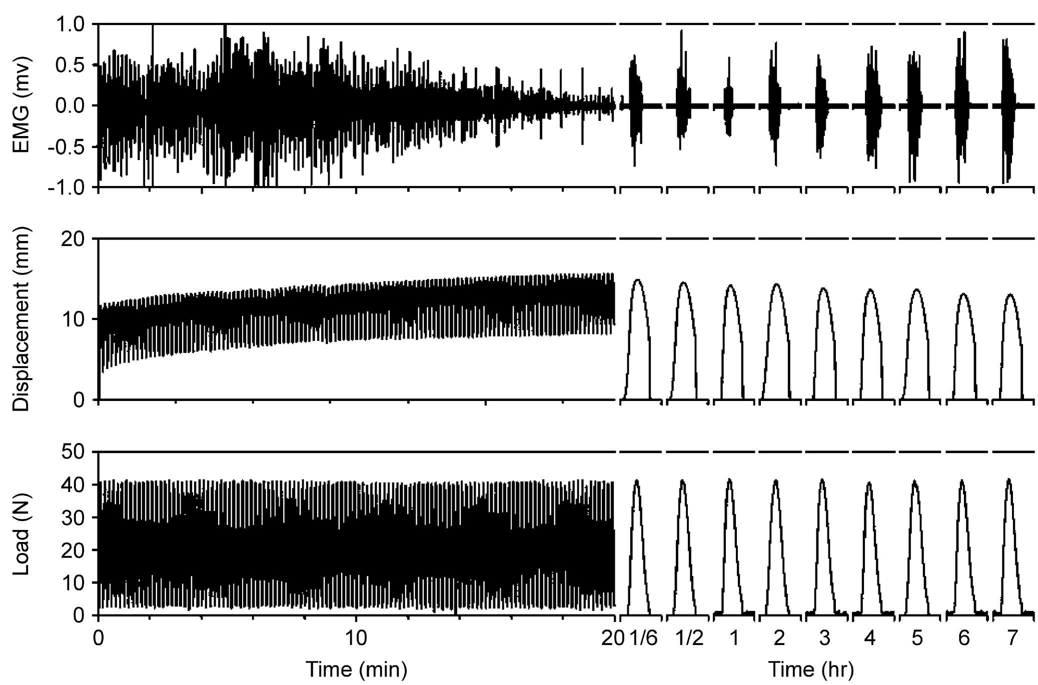

Figure 8 Experimental recordings of multifidus reflexive EMG during 20 min of static lumbar flexion followed by 7 h of rest. Note the simultaneous development of creep and its recovery.

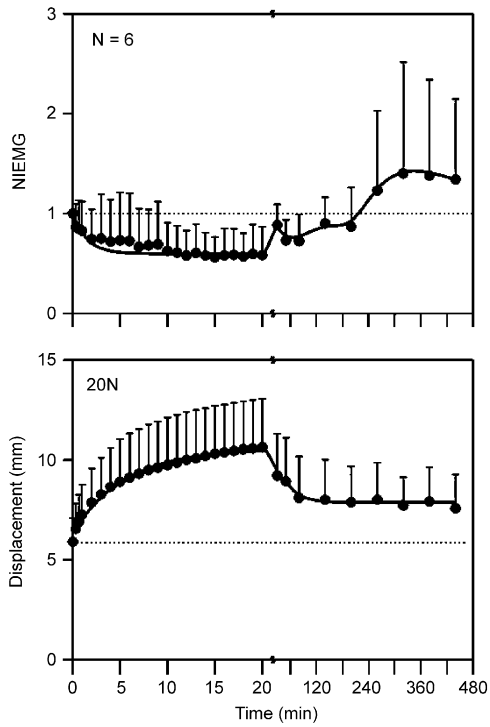

Figure 9 The pooled mean normalized and integrated EMG and mean displacement from Figure 8, together with few other preparations subjected to the same protocol.

Figure 9 shows the pooled, processed data of Figure 8, together with a few other in vivo specimens subjected to the same cyclic anterior flexion of the lumbar spine. Note the creep and its recovery with rest as well as the five components of the neuromuscular disorder.

Figure 10 shows a schematic of the five components of the neuromuscular disorder associated with creep during the loading period and the following rest.

The mechanical properties of the viscoelastic tissue of ligaments (and other such tissues as discs, facet capsules, doroslumbar fascia, etc.) could give rise to or be the source of a neuromuscular disorder. Prolonged exposure of a joint to cyclic or static activities allows the development of creep (in a constant load condition) or tension–relaxation (in a constant displacement condition). Data obtained from normal, healthy young subjects show that spasms develop in the musculature during the static and cyclic activity and significant modification of muscular activity, primarily hyperactivity, is observed after the loading period (Chu et al., 2003; Solomonow et al., 2003a; Olson et al., 2004, 2006, in press; Li et al., 2007). The above results obtained from the ACL in the knee and from the lumbar spine reinforce the assertion made earlier concerning the similar behavior of the ligamento-muscular reflex in most, if not all, major joints.

Risk factors for neuromuscular disorder

The epidemiology demonstrates statistical correlation between the static and cyclic physical activity performed over long periods to the occurrence of musculoskeletal disorders (Silverstein et al., 1986; Hoogendoorn et al., 2000). Such statistical relationships do not offer the process by which the disorder develops nor the biomechanical, neurophysiological and inflammatory evidence verifying the relationships. Furthermore, the relative contributions of the load magnitudes, the duration of their application, the number of repetitions and the rest periods (or work to rest ratios) which constitute a threshold above which a high-risk for the development of a disorder are not delineated.

The impact of such risk factors was studied in recent years and a wealth of information was derived, shedding light on the etiology of the musculoskeletal disorders developing from static and cyclic physical activities.

Load magnitude

The effect of load magnitude is delineated in Figure 11A and B. Figure 11A (Sbriccoli et al., 2004a) shows that for static loading at a work/rest schedule of 1:1 (or 10 min work followed by 10 min rest) repeated six times. Light and moderate loads of 20 and 40 N, respectively, did not elicit a delayed hyperexcitability during the 7 h recovery period, whereas the high load of 60 N did elicit an hyperexcitability indicative of an acute inflammation due to excessive micro-damage to the viscoelastic tissues. High loads, therefore, are a relative risk factor compared to light and moderate loads applied at the same work/rest schedule.

From Figure 11B (Le et al., 2007), it is evident that for cyclic lumbar loading, moderate and high loads of 40 and 60 N, respectively, result in delayed excitability indicative of an acute inflammation, whereas light loads of 20 N, did not.

Two major conclusions could be drawn from the data:

1. High loads are a risk factor for the triggering of muscular hyperexcitability and the associated acute inflammation in the viscoelastic tissues when compared to lighter static and cyclic loads applied at the same work/rest schedule.
2. Cyclic loading seems to be more deleterious to the viscoelastic tissues compared to static loading, as it triggers delayed muscular hyperexcitability at moderate and high loads, whereas static loading triggers it only at high loads.

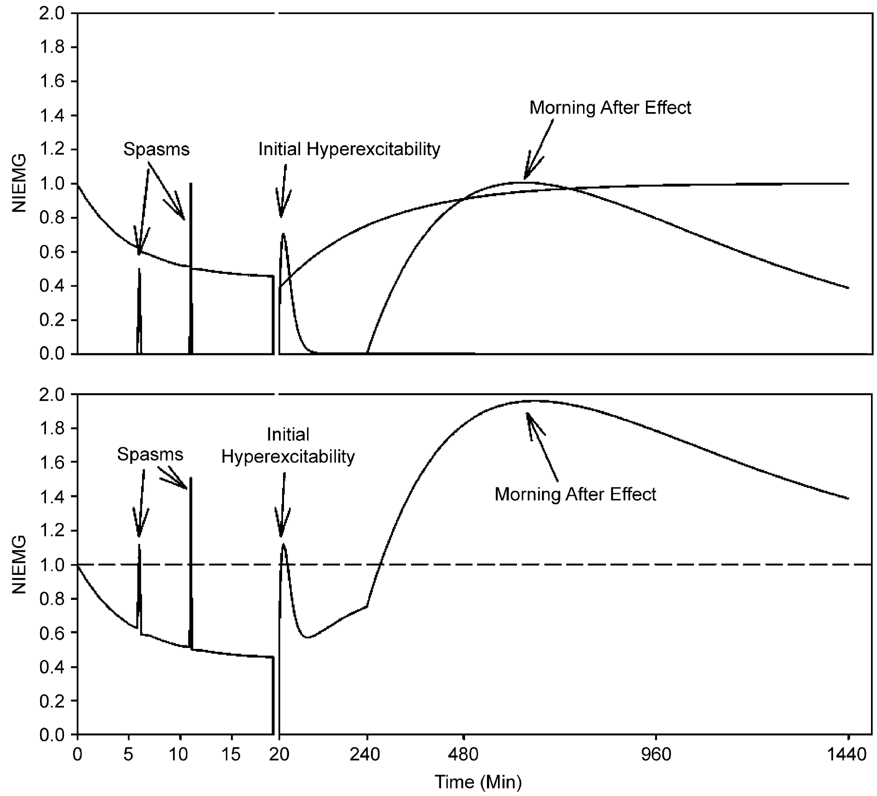

Figure 10 A schematic of the five components neuromuscular disorder resulting from static load applied to the ligaments.

The first conclusion provides the biomechanical and neurophysiological confirmation of the epidemiology which predicted that handling high loads result in more complaints of musculoskeletal disorders.

The second conclusion was rather surprising. One can assume that in static loading, such as in performing long anterior lumbar flexion, the posterior viscoelastic structure will stretch one time and remain stretched for the duration, slowly accumulating micro-damage to the collagen chains. Conversely, during cyclic loading, one can assume that the peak load will be fully applied only during a brief moment at the peak of the flexion, which intuitively will be considered as minimal or only partial exposure. This intuitive predication was invalidated by the data. In retrospect the data offers the explanation that in the static loading case, the viscoelastic tissues were stretched only once and remained stretched during each 10 min work session, whereas in the cyclic loading paradigm, the tissues were stretched every 4 s (frequency of the cyclic test was 0.25 Hz), which amounts to 15 stretches every minute or a grand total of 150 stretches during every 10 min loading. Apparently, the act of stretch is the phase where the major micro-damages occur, or at least, the act of stretch induces substantially more damage than occurs when remaining stretched during a prolonged period.

Whichever is the current explanation, cyclic lumbar flexion is more deleterious to the posterior viscoelastic tissues than a static flexion of the same duration.

Number of repetitions

Figure 12A and B, delineates the EMG changes during the 7 h recovery post-static and cyclic loading, respectively, of the lumbar spine in anterior flexion with a moderate load of 40 N. The loading schedule of 10 min, followed by 10 min rest was repeated 3, 6 and 9 times.

Figure 12A (Sbriccoli et al., 2004b) indicates that a static loading sequence of 10 min work/10 min rest, repeated 3 and 6 times did not result in a delayed hyperexcitability during the 7 h recovery period, whereas 9 repetitions did elicit hyperexcitability indicative of an acute inflammation.

When cyclic loads were applied at the same schedule, Figure 12B (Navar et al., 2006) indicates that 3 repetitions did not elicit delayed

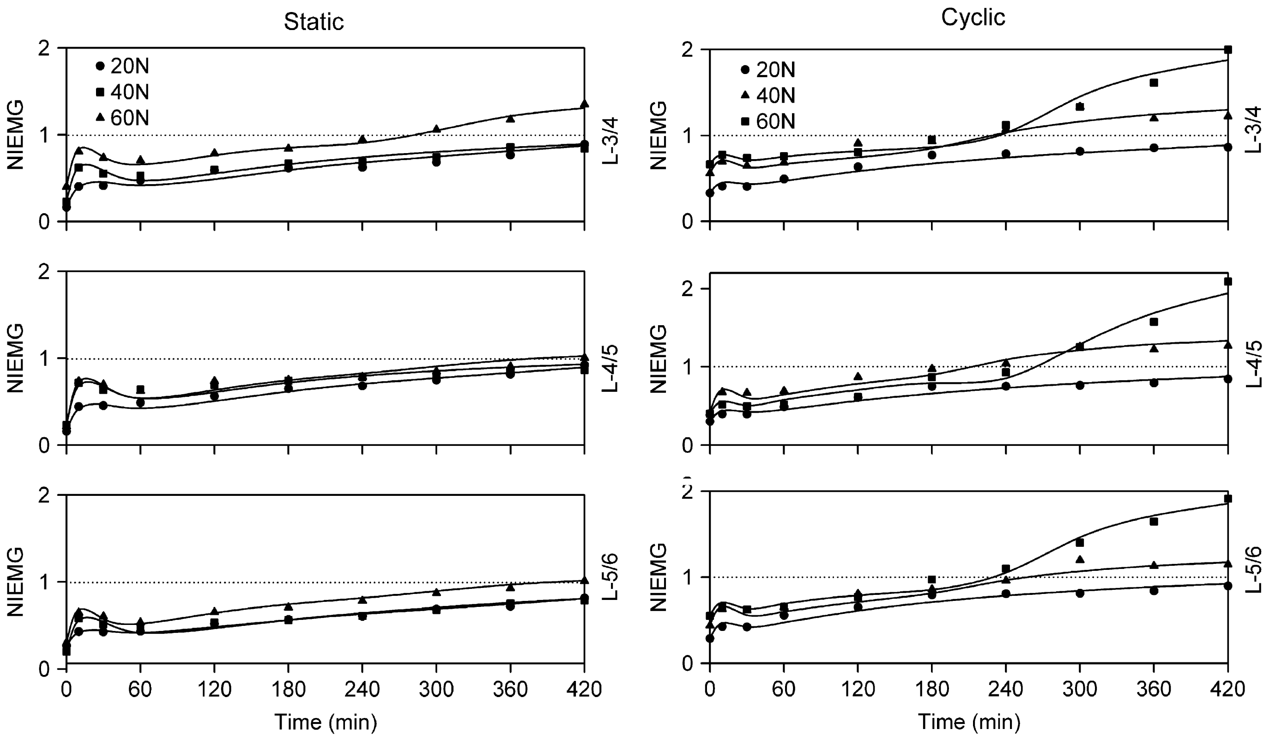

Figure 11 The EMG of the reflexive muscular activation is shown during even hours of rest post-static (A) and cyclic (B) activity of different load magnitudes. Note the hyperexcitability near the end of the 7 h for high loads.

hyperexcitability indicative of an acute inflammation, whereas 6 and 9 repetitions did.

The conclusions, again, provide biomechanical and neurophysiological validation for the epidemiological prediction that repeating a specific static or cyclic movement many times results in more complaints of musculoskeletal disorders.

Furthermore, our earlier conclusion that cyclic stretching is more deleterious for the viscoelastic tissues receives further reinforcement. For cyclic anterior flexion, 6 and 9 repetitions induced a disorder whereas in static flexion at the same load and schedule, only 9 repetitions did.

Work and rest

The effect of rest periods and their relationship to the work/loading periods was not addressed in earnest by the epidemiology, nor biomechanically or neurophysiologically. The importance of appropriately selected rest duration for a given exertive motion is intuitively paramount if one considers that the robustness of viscoelastic tissues depends on carefully proportioned work and following rest as outlined by Woo et al. (1980, 1981, 1987), Woo and Buckwalter (1988). The impact of various work/rest paradigms on the triggering of a neuromuscular disorder was studied for static and cyclic loading/rest of the lumbar spine with the attempt to identify what are the risk/no risk boundaries.

Figure 13A and B provides the EMG responses of several work/rest paradigms for static and cyclic lumbar flexion.

For static flexion/rest, Figure 13A (Courville et al., 2005) depicts that combinations of 10 min rest followed by 10 or 20 min rest are free of delayed hyperexcitability and its associated acute inflammation during the 7 h recovery period. A paradigm of 10 min work followed by only 5 min rest did, however, elicit a delayed hyperexcitability. The data leads one to conclude that a ratio of 1:1 or 10 min work followed by 10 min rest is optimal, as it contains the minimal rest duration necessary to prevent a neuromuscular disorder.

With such tentative conclusion, one may ask; is a 1:1 ratio for work/rest periods empirically correct for long work periods? Intuitively, if a performed physical activity, like anterior lumbar spine flexion is maintained for 8 continuous hours, it would be doubtful if the damage done to the viscoelastic tissues would be offset by 8 h of rest.

Testing in vivo spinal ligaments using 1:1 paradigms such as 10:10, 20:20, 30:30 and 60:60 min of load to rest revealed that the 1:1 ratio for work and rest is indeed preventive with respect to the triggering of a neuromuscular disorder up to the 60 min limits. Once a straight 60 min load period

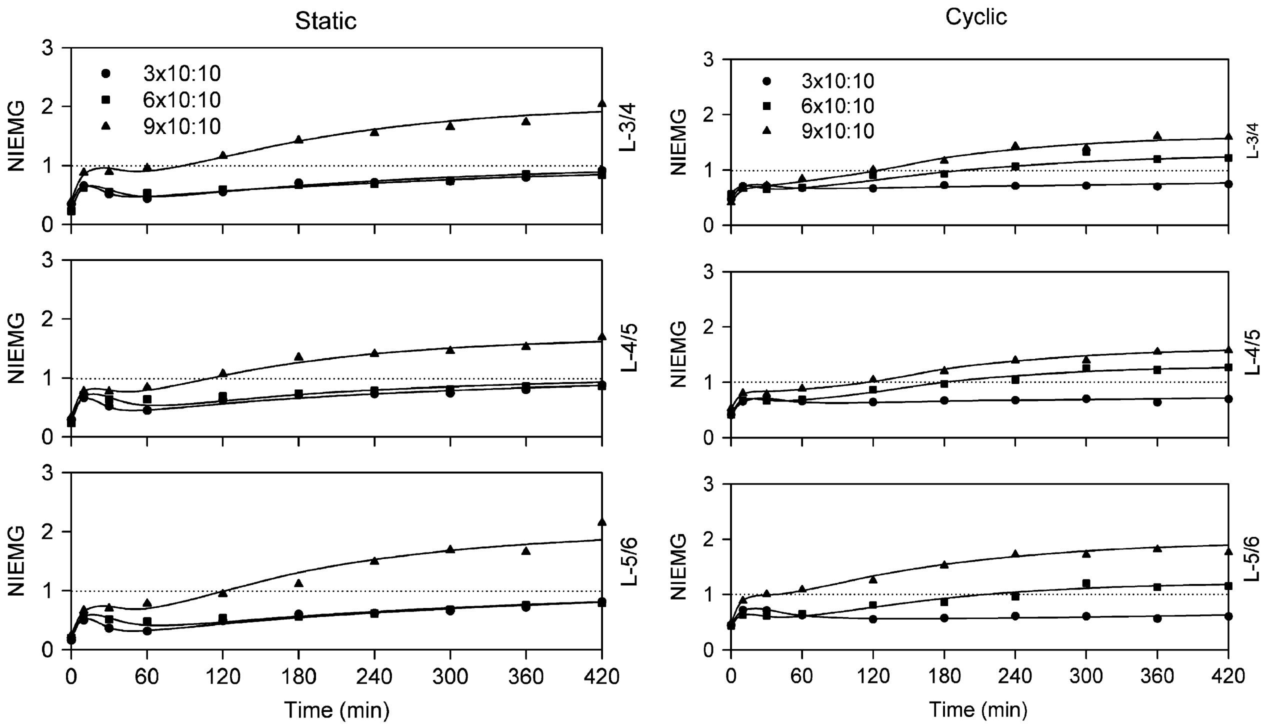

Figure 12 The neuromuscular hyperexcitability is shown during the 7 h recovery post 3, 6 and 9 repetitions of static (A) and cyclic (B) activity.

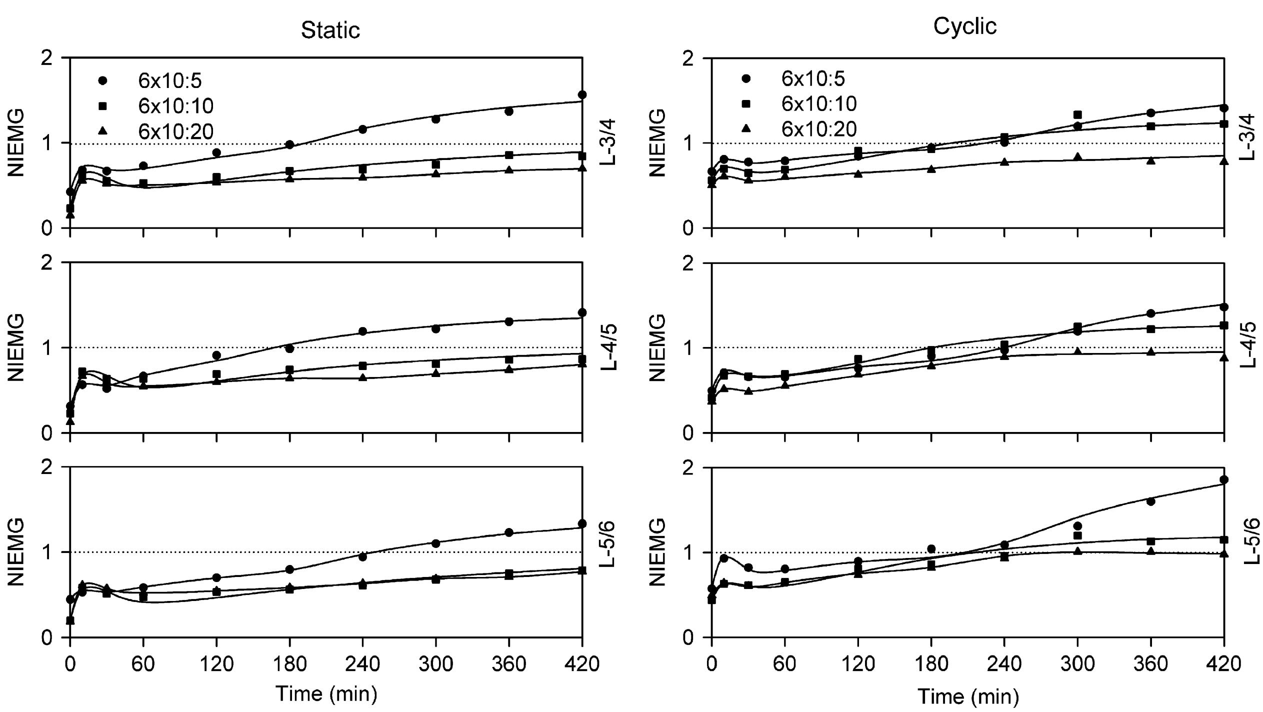

Figure 13 The neuromuscular hyperexcitability is shown during the 7 h recovery period post-static (A) and cyclic (B) activity of different work: rest ratios.

was applied, it did develop delayed hyperexcitability and a neuromuscular disorder (Sbriccoli et al., 2007).

The conclusion is that for static work, a work to rest ratio of unity is optimal, as it presents the minimal rest required to prevent a neuromuscular disorder due to overexposure of the viscoelastic tissues to micro-damage. This remains valid for work periods up to 1 h, after which, a disorder will be triggered due to the long, continuous work period.

For cyclic loading, a work/rest ratio of unity did not apply from the start. A unity ratio did elicit a neuromuscular disorder at a 10 min work: 10 min rest sequence. A 10 min work to 20 min rest, however, prevented the disorder (Hoops et al., 2007) as shown in Figure 13B.

The deleterious effect of cyclic loading was so far evident from the testing for load magnitude, number of repetitions and the longer rest it required to offset or prevent a disorder, and now for the disproportionate work: rest ratio.

Risk factors for developing cumulative trauma disorder are:

- Cyclic loading at high frequency.
- Long work duration.
- Short periods of rest.
- High number of repetitions.
- Static or cyclic work with heavy loads.

Work duration

The duration in which activity is performed apparently bears a pronounced impact on the development of a neuromuscular disorder as a result of excessive continuous viscoelastic tissue strain. LaBry et al. (2004) assessed the duration of continuous static loading of the lumbar spine, showing that regardless of the rest provided, work duration in excess of 30 min tended to elicit a disorder in comparison to shorter durations with cumulative periods regardless of the load magnitude. The findings provide partial explanation to the failure of the 1:1 work to rest ratio paradigm to prevent a disorder for work durations near 1 h or above. Rest apparently, is of significant impact as long as the duration of continuous work is not excessive. Long work periods apparently induce substantial damage in the viscoelastic tissues such that any reasonable rest cannot attenuate or prevent a disorder.

Frequency

When cyclic activity is performed, the rate or the frequency at which the activity is repeated was identified by the epidemiology as a risk factor: higher frequencies resulting in high number of patients with neuromuscular disorders.

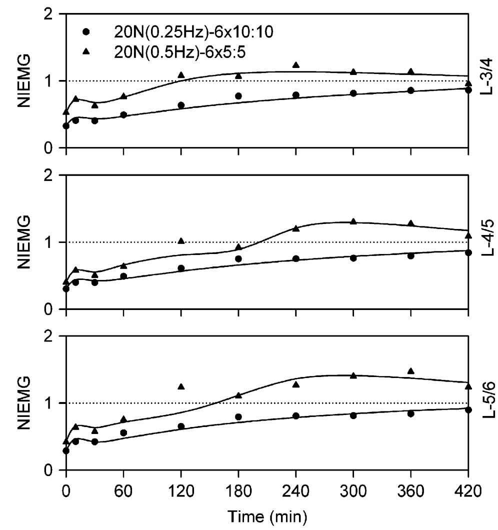

Figure 14 The neuromuscular hyperexcitability in the 7 h rest post-cyclic loading at 0.25 and 0.5 Hz.

Figure 14 displays the EMG response to anterior lumbar flexion at a low load of 20 N, performed at 0.25 and at 0.5 Hz in a cyclic load sequence of 10 min load, followed by 10 min rest, repeated six times. A delayed hyperexcitability is observed in the recovery period of the 0.5 Hz response, indicating that doubling the frequency of cyclic motion, elicits a disorder (Lu et al., 2004, in press).

Conclusion

It is evident that ligaments evolved to become the optimal biological passive tissue to provide the function of joint stability. Ligaments are also adaptive to the extent that increase and decrease in physical activity is accompanied with hypertrophy and atrophy, respectively. Their normal function, however, is dependent on a dose–duration–rest-repetition formula which received an initial address in this review and is not fully known at the present. Sufficient rest between periods of physical activity seems to be of paramount importance for long-term healthy, normal function, and such data are just becoming available.

Due to the mechanical properties of viscoelastic tissue, two classes of disorders originate from ligaments; mechanical and neuromusculoskeletal. Mechanical deficits such as joint laxity, instability, osteoarthritis, sprain, rupture, etc., are the direct result of creep, tension–relaxation, hysteresis and time/frequency dependence of the length–tension of ligaments.

The same mechanical factors are also manifested with complex sensory–motor disorders (or syndromes) associated with changes in proprioception and kinesthetic perception, reflex activation of muscles, joint stability and overall performance. Inflammatory responses of viscoelastic tissues, a result of complex combination of mechanical stimuli seems to be a significant factor in the development of cumulative trauma disorders in athletes and workers maintaining activities that require daily performance of static and repetitive motion.

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