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Acute repetitive lumbar syndrome: A multi-component insight into the disorder

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Summary *Purpose:* Repetitive Lumbar Injury (RLI) is common in individuals engaged in long term performance of repetitive occupational/sports activities with the spine. The triggering source of the disorder, tissues involved in the failure and biomechanical, neuromuscular, and biological processes active in the initiation and development of the disorder, are not known. The purpose is, therefore, to test, using *in-vivo* feline model and healthy human subjects, the hypothesis that RLI due to prolonged exposure to repetitive lumbar flexion—extension is triggered by an acute inflammation in the viscoelastic tissues and is characterized by lingering residual creep, pronounced changes in neuromuscular control and transient changes in lumbar stability. This report, therefore, is a summary of a lengthy research program consisting of multiple projects.

Methods: A series of experimental data was obtained from *in-vivo* feline groups and normal humans subjected to prolonged cyclic lumbar flexion—extension at high and low loads, high and low velocities, few and many repetitions, as well as short and long in-between rest periods, while recording lumbar displacement and multifidi EMG. Neutrophil and cytokines expression analysis were performed on the dissected feline supraspinous ligaments before loading (control) and 7 h post-loading. A comprehensive, time based model was designed to represent the creep, motor control, tissue biology and stability derived from the experimental data.

Results: Prolonged cyclic loading induced creep in the spine, reduced muscular activity, triggered spasms and reduced stability followed, several hours later, by acute inflammation/tissue degradation, muscular hyperexcitability and hyperstability. Fast movement, high loads, many repetitions and short rest periods, triggered the full disorder, whereas low velocities, low loads, long rest and few repetitions, triggered only minor but statistically significant pro-inflammatory tissue degradation and significantly reduced stability.

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Conclusion: Viscoelastic tissue failure via inflammation is the source of RLI and is also the process which governs the mechanical and neuromuscular characteristic symptoms of the disorder. The experimental data validates the hypothesis and provides insights into the development of potential treatments and prevention.

Introduction

Repetitive Lumbar Injury (RLI), also known as Cumulative Trauma Disorder (CTD), is diagnosed with pain, weakness, limited range of motion and stiffness/spasms in the muscles associated with the respective joint. Common diagnostic procedures produce negative indications for deficits such as prolapsed disc, facet impingement, vertebral fracture, stenosis, etc., potentially placing RLI as a major contributor to the non-specific back pain category. The epidemiological evaluation suggested a strong relationship between repetitive occupational/sports activities over long periods and RLI. In specific, activities under high load magnitudes, large number of repetitions, and high rates of motion were identified as risk factors (Hoogendoorn et al., 2000; Marras, 2000; Orchard et al., 2009; Punnett and Wegeman, 2004; Silverstein et al., 1986; Smoljanovic et al., 2009). Biomechanical and physiological validation of the observational statistics (epidemiology) is missing, as well as the etiology of the development of RLI (e.g., what tissues failed, failure mode, neurological and biological pathways and interactions). Viscoelastic tissues' tolerance to load and the associated strain over many repetitions was suspected to be the source of the disorder, but experimental validation was not available (Kumar, 2001, 2008).

It is hypothesized that repetitive/cyclic anterior lumbar flexion strains the posterior viscoelastic tissues (ligaments, facet capsule, discs, fascia) and induces creep (McGill and Brown, 1992; Sanchez-Zuriaga et al., 2010; Solomonow et al., 1999, 2000) and micro-fractures in their collagen fibers (Woo et al., 1981, 1982, 1999; Fung et al., 2009) with parallel changes in reflexive neuromuscular function (Stubbs et al., 1998). An acute inflammation is

tissue biology) obtained from a long series of experimental research projects in animal models (Williams et al., 2000; Eversull et al., 2001; Solomonow et al., 2003b, 2008, 2011; Claude et al., 2003; Hoops et al., 2007; Le et al., 2007; Lu et al., 2004, 2008; Navar et al., 2006; Youssef et al., 2008; Le et al., 2009; Ben-Masaud et al., 2009; King et al., 2009; D'Ambrosia et al., 2010; Pinski et al., 2010) and healthy humans (Solomonow et al., 2003a; Olson et al., 2004, 2006, 2009; Li et al., 2007) in order to provide a comprehensive model of the multi-factorial etiology of RLI, offer validating support for the acute phase of the hypothesis and allow the potential developments of science based methods for its treatment and prevention.

Methods

Animal experiments

In-vivo feline groups were used as the model for studying the various aspects of RLI and its relationship to load magnitudes, duration of loading, rest duration in-between loading periods, number of repetitions and movement velocity (or frequency) of the lumbar flexion–extension. Feline anaesthetized with chloralose is the classical model in neurophysiology of movement and was approved by the NIH-OLAR and the local IACUC. The preparations were supported by standard respiration, hydration and monitoring during the experiments to maintain proper body functions and metabolism. Exact details of the set up and loading are rather lengthy and provided in the separate publications on the various aspects of the loading (Williams et al., 2000; Eversull et al., 2001; Solomonow et al., 2001,

Repeated bending activities in daily living appear to change both structure (ligaments, discs) and function (protective spinal reflexes)

triggered as the micro-damage exceeds a certain threshold (Leadbetter, 1990) simultaneously with spasms, reflexive hyperexcitability of the muscles (Williams et al., 2000) and changes in stability. Continuous exposure of the lumbar spine to repetitive activities can eventually convert the acute inflammation into a chronic inflammation, collagen fibers degeneration into fibrous tissue and permanent disability (Leadbetter, 1990).

2003a, 2008, 2011; Claude et al., 2003; Hoops et al., 2007; Le et al., 2007; Lu et al., 2004, 2008; Navar et al., 2006; Youssef et al., 2008; Le et al., 2009; Ben-Masaud et al., 2009; King et al., 2009; D'Ambrosia et al., 2010; Pinski et al., 2010) and healthy humans (Solomonow et al., 2003b; Olson et al., 2004, 2006, 2009; Li et al., 2007).

In general, anesthetized preparations were set up in a fixture that allowed loading of the lumbar spine in flex-

If ignored, repeated bending is not just painful, it appears to trigger detrimental structural changes.

The objective of this paper is to provide a systematic integration of the various components active in the hypothesis (creep, neuromuscular control, stability, inflammation/

ion–extension within the physiological range under various load magnitudes, load durations, number of repetitions, intermittent rest periods and different loading rates/

frequencies. The displacement of the spine and the load applied were recorded.

Simultaneously, the wire EMG from the lumbar multifidi was recorded from the L-3/4 to L-5/6 levels in order to assess changes in neuromuscular functions. Following prolonged load/rest sessions, a 7 h rest period was allowed in order to assess post-loading changes such as creep recovery, changes in muscle function and development of inflammatory condition. Single flexion—extension tests were applied every hour over the 7 h rest. At the end of the 7 h rest period, the supraspinous ligaments of the L-3/4, L-4/5 and L-5/6 as well as the unloaded T-10/11 (self control) were dissected, frozen immediately and subjected to neutrophil density or pro-inflammatory cytokines (IL-1β, IL-6, IL-8, TNFα and TGFβ) expression analysis for determination of inflammatory status.

Human experiments

Additional experiments were conducted with healthy human subjects with local IRB approval. The purpose of these experiments was to confirm that results and conclusions derived from the feline model may be applicable to humans loading their spine under similar conditions. The experimental details are also provided in the individual reports (Solomonow et al., 2003a; Olson et al., 2004, 2006, 2009; Li et al., 2007).

In general, healthy human subjects were required to perform repetitive or static anterior flexion—extension or trunk rotation over a period of time while recording the flexion or rotation angles and surface EMG from various muscles via. Experimental conditions varied from flexion—extension in the standing upright position, to performing the same from the supine position to assess effect of gravity and in repetitive lateral twisting.

Cumulative results

Animal experiments

A typical recording of repetitive cyclic flexion at 0.25 Hz over three 10 min sessions with 10 min in-between rest

Figure 2 The mean (±SD) displacement (bottom) and the associated calculated mean creep (top) of the lumbar spine during the loading and after 7 h of rest post-loading.

followed by single 4 s single cycle tests over the following 7 h rest is shown in Fig. 1.

The data from groups subjected to the same loading conditions (eg, load magnitude, load duration, in-between rest, number of repetitions and rates of flexion—extension) were pooled and resulted in the individual models described in Figs. 2—4, encompassing creep, EMG and stability values.

Creep

The typical mechanical response of the lumbar spine to prolonged cyclic flexion—extension is the development of creep (laxity) during the loading periods, its partial recovery during periods of in-between rest and further development of creep in a following loading session as shown in Fig. 2. During the 7 h recovery, the creep demonstrates continuous substantial recovery, yet a complete recovery is never achieved, leaving a residual creep ranging from 5 to 35% at the end of 7 h rest. Mild loads, few repetitions, low cyclic frequency and
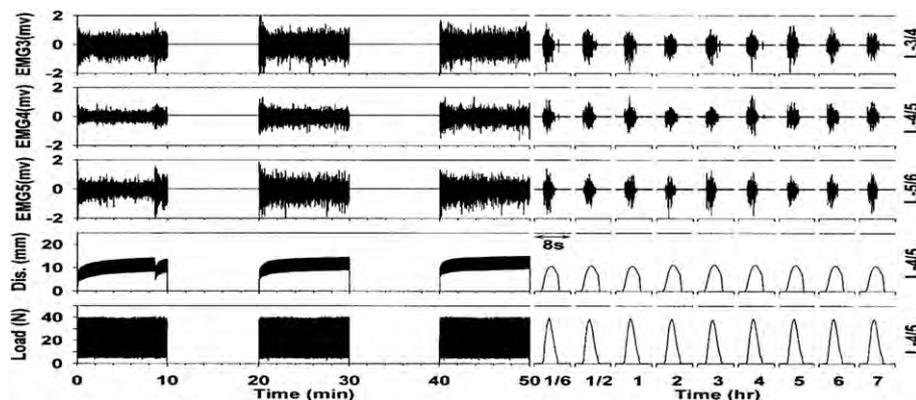

Figure 1 A typical recording of three 10 min sessions of cyclic flexion—extension of the feline lumbar spine showing the load, displacement and the EMG from the L-3/4, L-4/5 and L-5/6 multifidi exhibiting spasm during the flexion as well as 7 h after the work cessation.
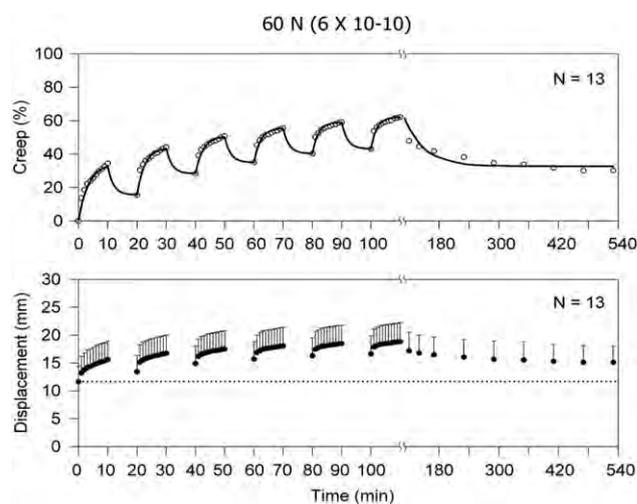
Tissues that are subjected to repeated loading, appear to only partially recover, with some tissue changes being long lasting or permanent
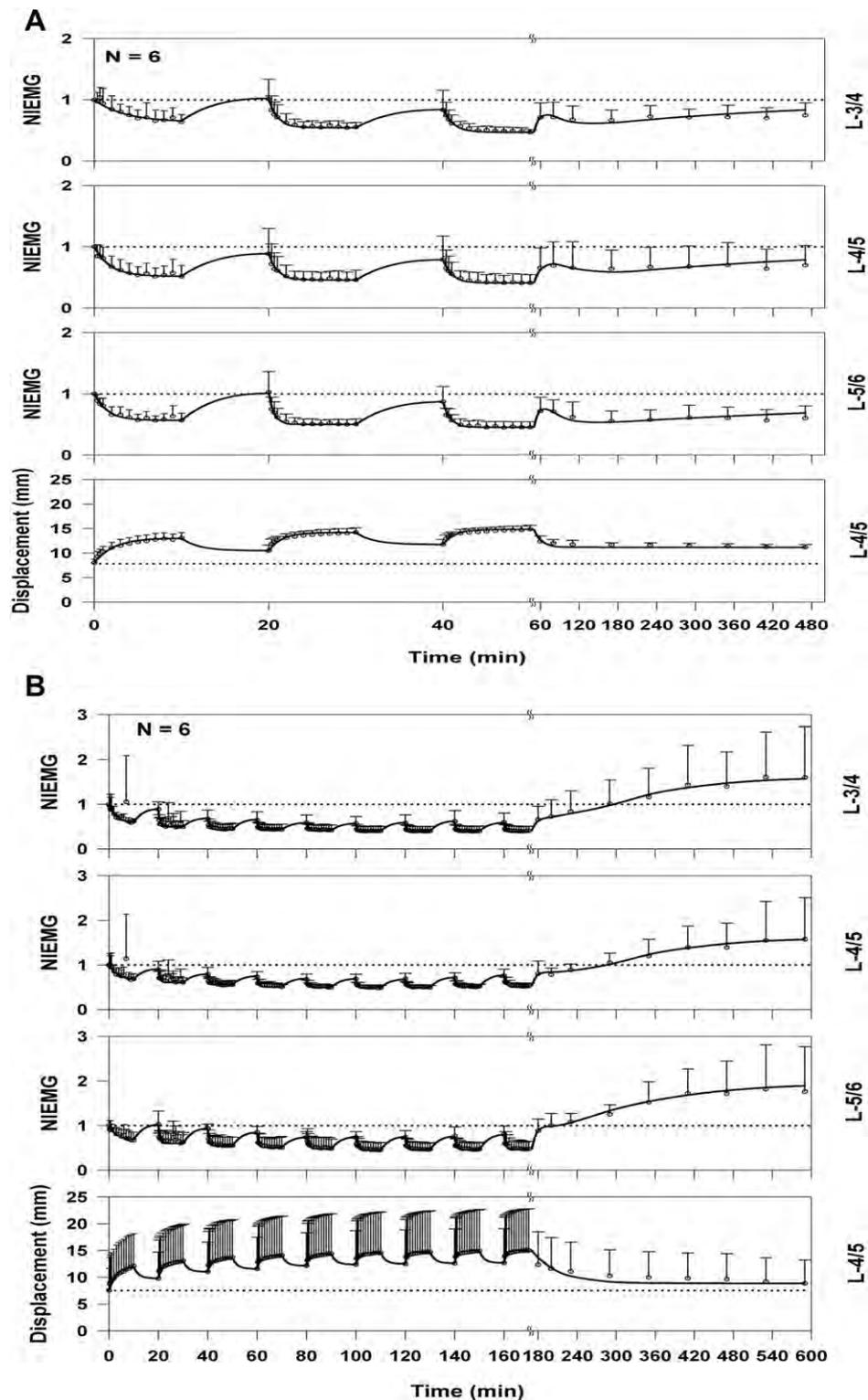

Figure 3 The EMG during loading and the following 7 h rest. The top set (3A) is for low risk condition of three repetitions of 10 min work and 10 min rest at 20N load, demonstrating gradual recovery of the NIEMG to baseline over the 7 h rest. The lower set (3B) is for a high risk condition of nine repetitions of 10 min work and 10 min rest under 60N load. The NIEMG exceeds the baseline after 2 h and reaches to near double the baseline by the 7th hour, expressing the hyper-excitability.
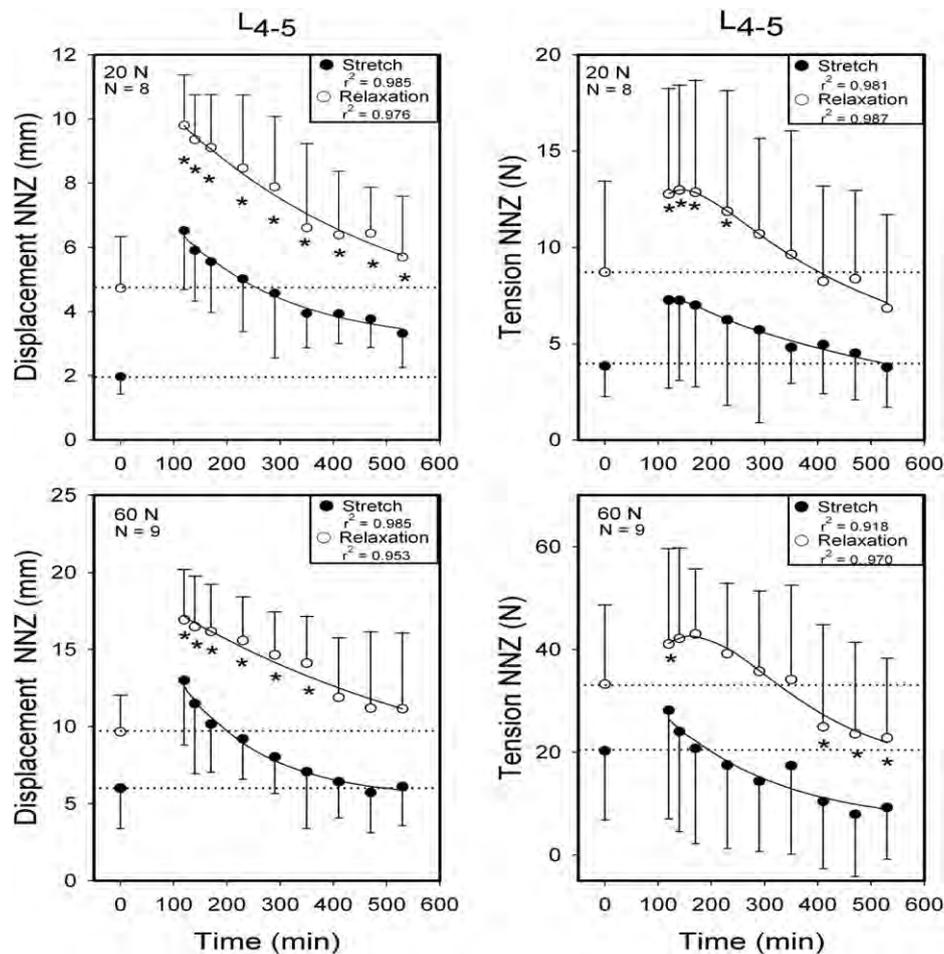
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Figure 4 The Displacement and Tension NNZ during the 7 h rest for mild loads of 20N (top row) and for high loads of 60N on the bottom row. Note that the DNNZ in the top row remains significantly above baseline for the complete 7 h rest whereas it reaches the baseline within the 4th hour for the high risk load. Similarly, The TNNZ for low loads remains large for several hours post-loading whereas it becomes significantly smaller than baseline within an hour post-loading for high loads.

ample in-between rest commonly exhibit about 5% residual creep after 7 h rest whereas high loads, high cyclic frequency, many repetitions and short in-between rest exhibit 25—35% residual creep at the end of 7 h rest. The model constructed for the creep during loading consists of exponential representation which is the classical response of viscoelastic materials and is as follows

$$\text{CREEP}(t) = C_0 + C_L\left(1 + e^{-t/T_2}\right)$$

Where;

CREEP (t) is the calculated creep as a function of time (%).
C_0 is the elastic component amplitude of creep (%).
C_L is the viscoelastic component amplitude (%).
T_2 is the time constant (in minutes), and t is time.

The model for the creep during the recovery period is;

$$\text{CREEP}(t) = C_0 + R + (C_L - R)e^{-t/T_3}$$

Where;

C_0 is the elastic component amplitude of displacement (%).
C_L is the viscoelastic component amplitude at the end of loading (%).
R is the residual creep at the end of recovery (%).
T_3 is the recovery time constant (in minutes).

The parameters for all models fitted were obtained by using the Marquardt—Levenberg nonlinear regression algorithm.

Neuromuscular function
The EMG was full-wave rectified, integrated and normalized with respect to the initial EMG at the beginning of loading to yield the NIEMG (Normalized Integrated EMG). The NIEMG pattern during the loading period and during the following 7 h recovery for paradigms of 3 repetitions and 9 repetitions is shown in Fig. 3(A&B). The following typical EMG behavior was observed;

1. Gradual decrease of EMG amplitude during the loading period.
2. Partial recovery of the EMG amplitude during the in-between rest periods.

3. Continuous decrease in EMG amplitude during each consecutive loading period.
4. Random super-imposed spasms during the loading periods, *regardless of load magnitude, frequency of loading, number of repetitions and in-between rest* (see Fig. 1).
5. Spasms were more intense in amplitude and duration when *high loads or high velocity flexion* were applied.
6. During the 7 h rest period following the loading, the EMG displayed a gradual recovery to baseline amplitude by the 7th hour for *mild loads, low cyclic frequency, few repetitions and long rest*.
7. For *high loads, high frequency, many repetitions and short in-between rest paradigms*, the EMG amplitude gradually increased during the first 2–3 h post-loading and then exhibited a sharp increase, reaching 140–200% that of baseline, indicated *hyperexcitability* of the muscles.

The NIEMG during the loading period was modeled as follows:

$$\text{NIEMG}(t) = A e^{-t/T_1} + \text{NIEMGss}$$

Where;

A is the exponential component initial amplitude (unit-less).
T_1 is the exponential decay time constant (in minutes).
NIEMGss is the steady-state NIEMG amplitude (unit-less), and t is time.

The parameters for the models fitted were also obtained by using the Marquardt–Levenberg nonlinear regression algorithm.

Stability

The stability of the lumbar spine was assessed using the Neuromuscular Neutral Zones (NNZ) concept (Eversull et al., 2001 Solomonow et al., 2001; Solomonow et al., 2008; Ben-Masaud et al., 2009). The Displacement and Tension NNZs (or DNNZ and TNNZ, respectively) for low and high loads are shown in Fig. 4 top and bottom rows, respectively.

In general, immediately after the loading;

1. Significant *increases* in TNNZ and DNNZ were observed in the first 1–7 h postloading, indicating *significant decrease in muscular stabilizing function*.
2. For *high loads and frequencies*, the decreased stability was short, lasting 1–2 h post-loading.
3. For *mild loads and low frequencies*, the decreased stability lasted 3–7 h post-loading.

Since the overall stability of the spine is composed of the functions of the viscoelastic tissues and the musculature, the creep/laxity observed together with the decreasing EMG amplitude and the increase in the TNNZ and DNNZ during the loading and the following 7 h rest indicate a gross time dependent deficit in stability. Cyclic loading, therefore, results in a *Transient Instability Disorder (TISD)*.

Temporary instability appears to occur through a combination of deficient muscular reflex and tissue laxity.

The NIEMG during the recovery period, the model format was:

$$\text{NIEMG}(t) = E\left(1 - e^{-t/T_4}\right) + tBe^{-t/T_5} + C(t - Td)e^{-(t-Td)/T_6} + \text{NIEMG}_0$$

Where;

$E(1 - e^{-t/T_4})$ represents the steady-state recovery component.
tBe^{-t/T_5} is a transient hyperexcitability component.
$C(t - Td)e^{-(t-Td)/T_6}$ the delayed transient hyperexcitability only for $t \geq Td$.
NIEMG_0 represents the residual response at the end of the loading period (unit-less).

In this model, the constraint of $E + \text{NIEMG0} = 1$ is used to ensure that full recovery results in a normal (unity) response. E, B, and C are unit-less. T_4, T_5, T_6, and Td are expressed in minutes.

The second and third terms, therefore, are transient features that first increase and then reverse (decrease) over time to finally arrive to near zero as the effect of hyperexcitability diminishes with rest. Furthermore, the third term, which represents the delayed hyperexcitability, becomes effective only after $t \geq Td$; that is, the effect of this term is null until recovery time exceeds Td. Overall, the model provides a unique prediction of the NIEMG at any given time during a rest period following a cyclic loading period.

The time-course Model of the DNNZ thresholds during the stretch phase and relaxation phase of the test cycles during the recovery period were described by:

$$\text{DNNZ}(t) = D_0 + (t - T_r)D_L e^{-(t-T_r)/T_1} + D_m e^{-(t-T_r)/T_1}$$

For all t values during 7 h recovery post-loading.
Where: Do is the intercept of the displacement (mm)

D_L affects the rise amplitude (mm/sec)
D_m is the amplitude of the decay dominating the end of the recovery period (mm)
$t - (T_r D_L e^{-(t-T_r)/T_1})$ allows for a transient rise at the beginning of the recovery period
T_1 affects the rates of rise and fall (sec)
T_2 is the exponential time-constant of the decay that dominates the end of the recovery period (min).

The time-course of the TNNZ thresholds during the flexion and extension phases of the test cycles during the recovery period were described by:

$$\text{TNNZ}(t) = T_0 + (t - T_r)T_L e^{-(t-T_r)/T_3} + T_M e^{-(t-T_r)/T_4}$$

For all t values during 7 h recovery.
Where: T_0 is the intercept of the tension (N)

T_L affects the rise amplitude (N/sec)

T_M is the amplitude of the decay dominating the end of the recovery period (N)

$(t - T_r)T_L e^{-(t-T_r)/T_3}$ allows for a transient rise at the beginning of the recovery period.

demonstrating the complexity of this disorder and justifying its designation as a syndrome. Fig. 8 displays a flow-chart exhibiting the interactive relationships of the different components.

> It is suggested that a comprehensive insight into the acute phase of RLI demonstrates the complexity of this disorder, justifies its designation as a syndrome. A flow chart, exhibiting the interactive relationships of the different components, is shown in Fig. 8.

T_3 affects the rates of rise and fall (sec)

T_4 is the exponential time-constant of the decay that dominates the end of the recovery period (min).

Tissue biology

Neutrophil analysis indicated that under high magnitude loads, over $\times100$ fold increase in neutrophil density was present in the ligaments after several hours rest. According to standard pathology definitions, this was an acute inflammation. Mild loads resulted in minor increase in neutrophils short of acute inflammation.

The changes in cytokines expression associated with the repetitive loading of the lumbar spine under mild/high loads and low/high frequencies are shown in Figs. 5 and 6, respectively.

The typical responses were as follows;

1. Cyclic loading under both *high and low magnitude* loads demonstrated *significant increase* in pro-inflammatory cytokines expression 7 h following the loading period. IL-1b, IL-6, IL-8, TNFα and TGFβ were all *significantly higher* than controls, indicating pro-inflammatory tissue degradation in the ligaments.
2. The increases in cytokines expression post-loading in ligaments subjected to *high magnitude loads was significantly higher from those under low loads for IL-6, IL-8 and TGF*β. No significant differences were observed for IL-1b and TNFα. Together with the over $\times100$ increase in neutrophil density, *a full acute inflammation* was present in the ligaments subjected *to high loads*.
3. *High frequency* loading with a moderate load result in *significantly higher cytokines expression* relative to *low frequency* loading.

The overall model

Fig. 7A provides a common time base overview of the models for creep, muscular activity, stability and tissue inflammation for a low risk lumbar exposure, eg, mild loads, slow motion, few repetitions and ample rest. Fig. 7B provides the simultaneous models of the same components after exposure to high risk conditions (high loads, fast motion, many repetitions, little rest). Together, a comprehensive insight of the acute phase of RLI is obtained,

Human experiments

Experiments using healthy normal subjects, 21—35 years old assessed the EMG and kinematics during flexion—extension in upright as well as supine position and during lateral rotation (twisting) in a repetitive manner. The overall findings were as follows;

1. *Creep was developed* over time when under static or cyclic loading.
2. There was *a shift in the time when EMG was observed to cease* during *flexion* and *the time when EMG was initiated* during *extension*. This is consistent with the changes in NNZ observed in the feline.
3. Distinct *spasms were observed* as the static/cyclic activity was continued.
4. Re-orientation with respect to the *gravity* vector *changed the motor control scheme* and activated muscles in a different mode.
5. Twisting also resulted in evidence of *creep* and *increase/decrease in muscles activity* level as repetitive activity was continued, further confirming the interaction of muscles with viscoelastic tissues.

Overall, the human experiments confirmed the presence of creep and spasm; finding interaction of viscoelastic tissues with the musculature, modified motor control and changes in stability under prolonged repetitive activity.

Discussion

The major findings of this project consist of the following interactive components;

1. The source of the RLI was found to be *inflammation of the viscoelastic tissues* of the lumbar spine, e.g. the *viscoelastic tissues failed and the mode of failure is inflammation (or degradation)*.
2. High magnitude loads, long loading durations, large number of repetitions, high movement velocities and short in-between rest periods are *risk factors for RLI* as they trigger inflammation.
3. Of the several risk factors listed above, the *most prominent one is high cyclic loading frequency, e.g., high loading rates or high velocity motion*.
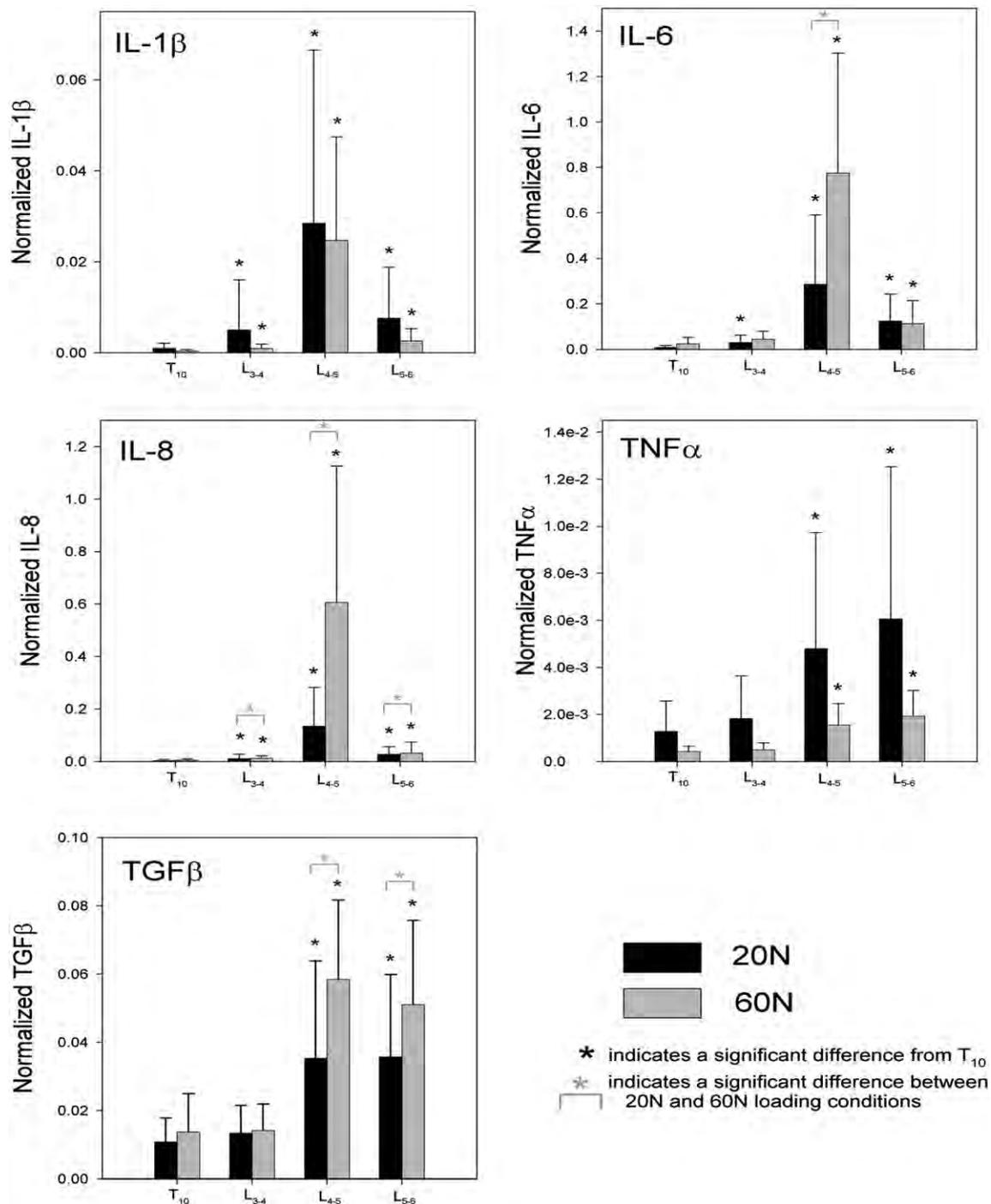
Figure 5 Pro-inflammatory cytokines expression in the supraspinous ligaments of L-3/4, L-5/6 and L-5/6 relative to the unloaded T-10/11 ligament (control). The expression of cytokines is given for high and low loads at the end of the 7 h rest post-loading. Note that both high and low loads induce significant increase in cytokines expression 7 h post-loading and that there is significant increase in expression for high loads relative to low loads.

4. The inflammation triggers a powerful *muscular hyper-excitability* which compensates for *deficient stability due to significant viscoelastic laxity and decreased reflexive muscular activity*. This allows for protecting the tissues from further exposure and also allows for effective repair.[cond1]

Low magnitude loads, short loading durations, long in-between rest, low movement velocity and few repetitions were not found to constitute significant risk factors, yet trigger noticeable long transient deficit in stability and pro-inflammatory tissue degradation. It would be more appropriate to designate these conditions as low risk instead of no risk.

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High magnitude loads, long loading durations, large number of repetitions, high movement velocities and short in-between rest periods appear to be *risk factors for RLI,* as they trigger inflammation.

Of the several risk factors listed above, the *most* prominent one is high cyclic loading frequency, e.g., high loading rates or high velocity motion.

The inflammation triggers a powerful muscular hyperexcitability which compensates for deficient stability due to significant viscoelastic laxity and decreased reflexive muscular activity. This allows for protecting the tissues from further exposure and also allows for effective repair.

Low magnitude loads, short loading durations, long in-between rest, low movement velocity and few repetitions *were not found to constitute* significant risk factors, yet trigger noticeable long transient deficit in stability and pro-inflammatory *tissue degradation*. It would be more appropriate to designate these conditions as *low risk* instead of *no risk*. In perspective, *Repetitive Lumbar Injury is a complex multi-factorial syndrome*.

In perspective, *RLI is a complex multi-factorial syndrome* consisting of biomechanical, neuromuscular, tissue biology and stability components undergoing drastic changes during the multiple phases of the loading, in-between rest and for many hours post-work. Designating RLI as syndrome is justified due to the complex interaction and interdependency of the various tissues/components.

Pro-inflammatory degradation of the ligaments seems to be an anticipated response to prolonged activity under any loading condition as the strain of the ligaments produces micro-ruptures within the collagen matrix (Woo et al., 1981, 1982, 1999 and Fung et al., 2009) and triggers the reflexive repair/healing process associated with inflammation (Leadbetter, 1990). The scientific data presented in this paper indicates that minor inflammatory degradation is associated with low level loading, not only with severe stresses. Although only the ligaments were analyzed in this research, it is intuitive that other viscoelastic tissues, such as discs, facet capsules, dorso-lumbar fascia, etc, could be affected via the same biomechanical and biochemical route. The distinguishing difference between high risk and low risk loading conditions seems to be that the accumulation of pro-inflammatory cytokines in the affected tissues exceeds a certain threshold above which a strong acute inflammation is triggered. Indeed, the literature supports that high levels of IL-6 and IL-8 are associated with pain in humans with an acute inflammation (Wang et al., 2009) and this could vary between healthy, athletic, obese or subjects with previous history of back trouble. IL-8 is also considered a chemokine since it attracts neutrophils to the inflammation cite (Namen et al., 1988). Overall, the significantly higher expression level of these two cytokines in the tissues exposed to high risk conditions explains the presence of neutrophil density at inflammation level and the possibility of inflammatory pain. Inflammation was shown to induce hyperexcitability in neural elements within the tissue (Bove et al., 2003; Cavanaugh et al., 2006; Dilley and Bove, 2008). This explains the hyperexcitability of the musculature observed several hours post-work. Since the inflammation requires some time to develop fully, the 2–3 h delay in the appearance of the hyperexcitability is evident. Once the inflammation matured, the neural components within the

viscoelastic tissues became over-sensitive, triggering the observed stronger compensatory reflexive muscular contractions in the multifidi. It is not clear if the triggering source of the pronounced compensatory changes in neuromuscular control and stability are the inflammation or its associated pain. Nevertheless, since acute inflammation is associated with pain, then it can be considered as the central process that affects changes in motor control and stability.

Clinical relevance

Two clinically relevant observations could be made. Clinicians should, therefore, avoid prescribing exercise therapy that may engage the lumbar spine at this stage until both inflammation and pain has decreased, as these two processes are the drivers of motor impairment. Furthermore, since the inflammation is a biological healing/repair process, the administration of non-steroidal anti-inflammatory medication can retard, prolong or even prevent healing. It may be advantageous to prescribe common pain medication to provide comfort to the patient while not interfering with the inflammation. Similarly, if muscle spasms are overwhelming, relaxants may be prescribed to allow activities of daily living.

The neuromuscular hyperexcitability seems to be a compensatory response for several deficits. The damage in the viscoelastic tissues requires rest for spontaneous repair as well as to prevent additional damage (Leadbetter, 1990). The increased stiffness afforded by the hyper-excitable muscles minimizes the exposure of the joint to motion and accumulation of further injury while providing a modicum of rest. The same increase in stiffness also reduces the NNZs, compensates for the laxity associated with the creep and increases the stability to above normal levels. Such compensation was not observed in the tissues exposed to low risk conditions with only a mild pro-inflammatory degradation. Employing clinical methods which aim to reduce neuromuscular hyperexcitability at this stage may not be appropriate until healing and tissue repair is completed. It should be recalled that the hyper-excitability compensates for the significantly decreased stability of the spine and that without this compensation the spine may be exposed to additional injury.

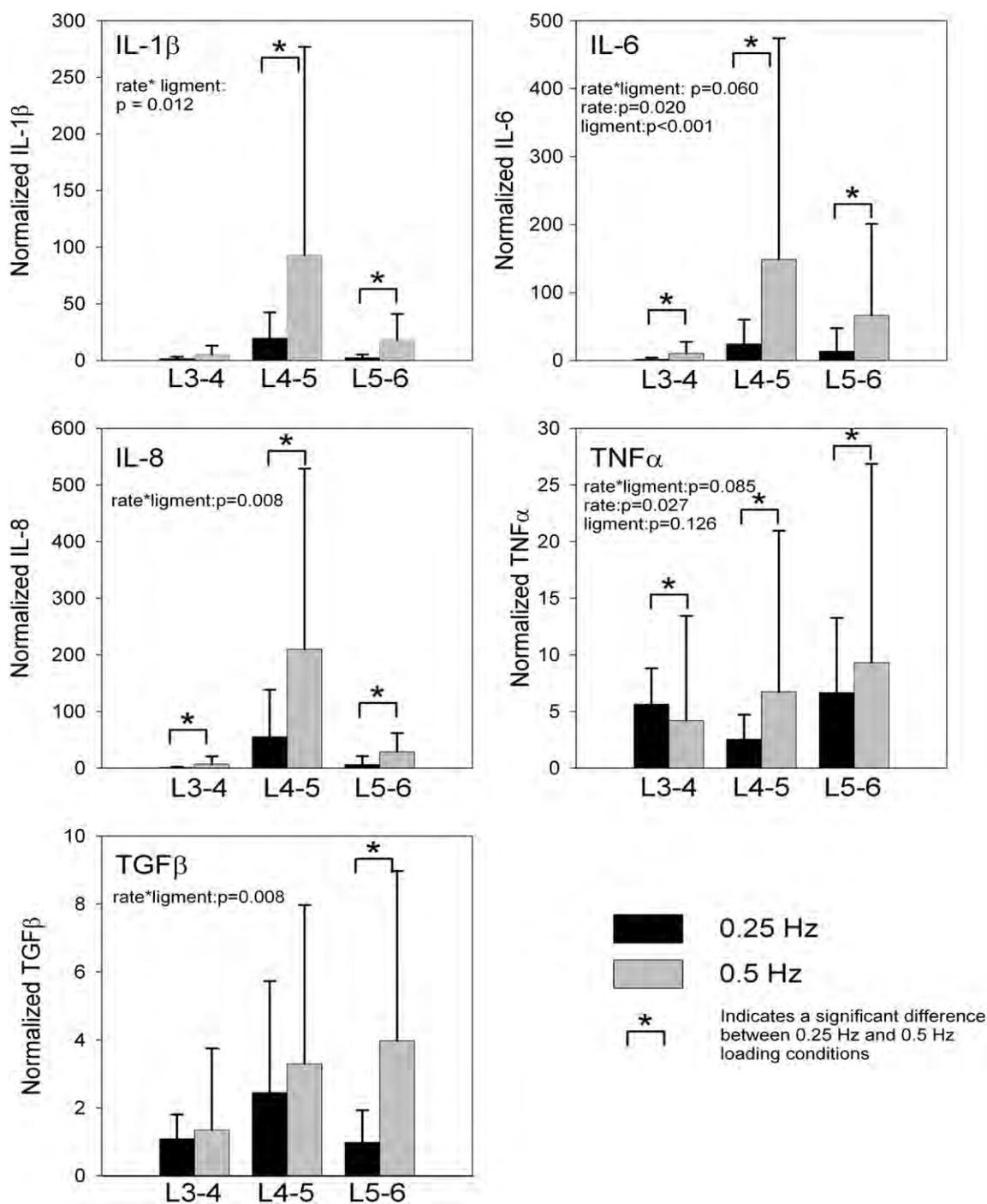Neural inflammation and tissue inflammation coexist.

Figure 6 Pro-inflammatory cytokines expression 7 h post cyclic loading with a moderate load of 40N but under low (0.25 Hz) and high (0.5 Hz) frequency. In most cases, there is significant increase in expression in ligaments subjected to high loads.

The significant laxity of the viscoelastic tissues together with significant reduction of muscular activity and stability immediately post work render these 2—3 h as highly

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> Awareness of this high risk period, should alert workers, work managers, athletes and coaches to take appropriate steps to prevent injury post activity.

exposed to accidental instability, injury, re-injury and the development of detrimental motor impairment. Now that

work managers, athletes and coaches take appropriate steps to prevent injury post activity. For example, simple elastic or
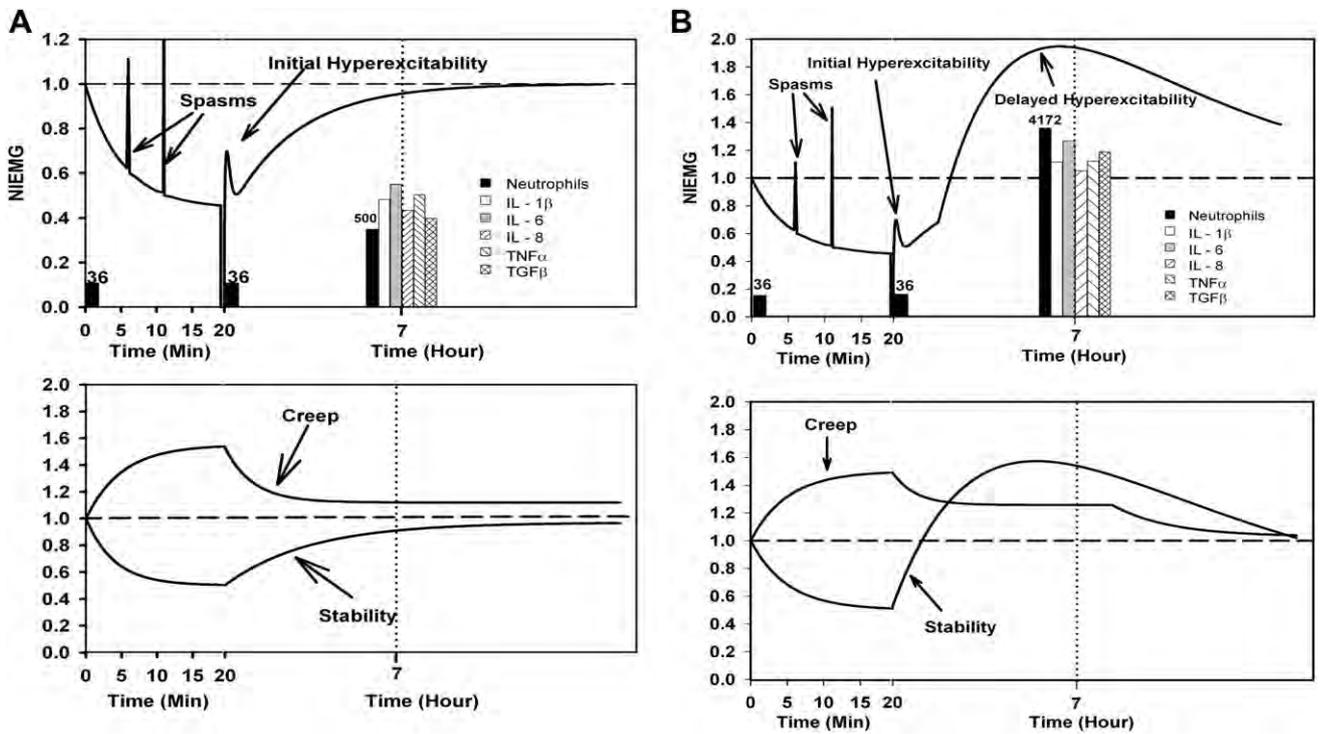
Figure 7   The comprehensive model of the various components of CTD for low (A) and for high (B) risk load conditions.
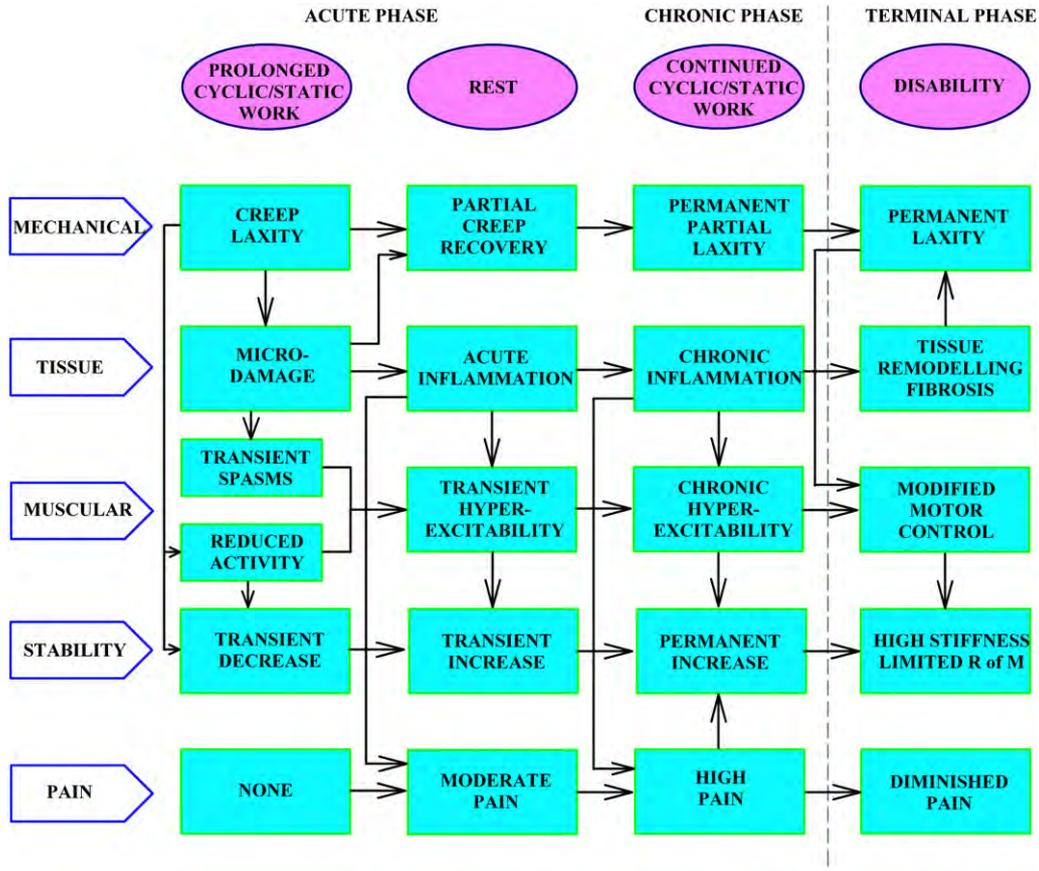

Figure 8   A flow-chart identifying the interdependency and chain reaction between the various components of the disorder during the development of the acute phase and into the chronic phase.

support braces could be worn for 2—3 h post work to add stiffness to the lumbar spine. Preventive measures, such as appropriate in-between work sessions rest can minimize creep, allow for its better recovery and avoid inflammation or long transient instability. Furthermore, work rotation requiring alternating activity of the spine, upper and lower extremity can minimize the exposure time of any given joint and prevent the development of the RLI/syndrome.

Clinical implications of the findings are of interest. Since excessive amount of motion trigger the disorder, it is intuitive that long period of rest can allow for spontaneous or forced resolution of the inflammation and return to normal function. In this case, exercise or physical therapy may be contra-indicated while rest could be highly effective.

The majority of the findings and their implications described in this report were obtained from the feline model with some verification from healthy human subjects. The feline model was selected as the spearhead of this long term research project for many reasons. For example, in order to provide direct scientific evidence that the creep and the associated inflammation come from the lumbar ligaments, it was necessary to surgically harvest the ligaments post-stimulation to conduct the cytokine analysis. Surgical removal of lumbar ligaments from healthy human subjects is devastating and not acceptable as an option. Direct measurement of creep from the ligaments is also not possible without resorting to invasive techniques. Furthermore, neuromuscular responses in humans are an integrated response to a multitude of factors such as direction of the

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In this case, exercise or *active* physical therapy may be contra-indicated while rest could be highly effective. Rest, in this context, implies avoidance of the stimuli that triggered the disorder, but not common activities of daily living.

Rest, in this context, implies avoidance of repetitive motion, heavy loads or fast flexion/extension, since they are the stimuli that may have triggered the disorder. Activities of daily living, however, should be encouraged to avoid muscle atrophy.

Furthermore, it should be recalled that there are several types of idiopathic low back pain and the one uncovered in this paper, the repetitive lumbar disorder, was until now one of them. It is widely accepted that special exercise or physical therapy is effective for non-specific low back pain with over 50% success rate. RLI, however, most likely belongs in the remaining 50% category where success was elusive. The scientific data presented in this paper provide an insight into the possible etiology of RLI and the most appropriate therapeutic modalities that can bring resolution of this disorder. Furthermore, it is suggested that with the newly available etiology, RLI should no longer be classified as a non-specific/idiopathic low back pain.

Recent evidence encourages some types of spinal manipulations, as they were shown to reduce cytokines expression levels in the blood of human subjects (Teodorczyk-Injeyan et al., 2006, 2008; Omos et al., 2009). Additional research in this area may be required to validate and optimize this promising approach.

The development of excessive creep in the viscoelastic tissues is a silent process and may not be easily perceived by individuals engaged in repetitive work/sports until it is too late. As a preventive measure, a great need exists for additional research in two areas. It may be possible to train such individuals to perceive over-exertion and the associated viscoelastic laxity using various sensory techniques. Individuals, then, can discontinue activity once they perceive that their exertion limit is reached. Ergonomists should expand this area of research to identify safe dose-duration combinations (load magnitudes, number of repetitions, work duration, in-between rest, etc.) in humans. This could be accomplished by monitoring increased cytokines concentration in the circulatory system above some threshold levels, as harvesting live tissues from humans is destructive and not an option. This will allow safe work and prevention of repetitive injury syndromes. Similar approaches could be employed in sports research, preventing the syndrome in athletes.

gravity vector during flexion—extension, muscular co-activation, vestibular, visual and auditory inputs to mention a few. Direct linkage of neuromuscular responses to creep and inflammation are virtually impossible in such conditions, in humans. The acute feline model allowed us to obtain direct evidence from many components as well as their interaction.

The validity and applicability of the feline model to humans is justified. The biomechanical literature encompassing spine research provides ample *in-vivo* demonstrations of the applicability of various quadrupeds including feline (Ianuzzi et al., 2009, 2010), sheep (Wilke et al., 1997), goat (Smit, 2002) etc, spine, as a model of the human spine. Furthermore, the feline is a classical neurophysiological model for neuromuscular research and has been repeatedly validated in humans over the last century.

Verifications of the development of creep and changes in neuromuscular responses in humans exposed to repetitive/cyclic loading was provided from independent laboratories (Sánchez-Zuriaga et al., 2010; Dickey et al., 2003; Little and Khalsa, 2005; McGill and Brown, 1992; Shin and Mirka, 2007; Granata et al., 1999, 2005; Hendershot et al., 2011). Obviously, differences exist, but they are probably related to size and stimulus magnitudes. Such differences are expressed in our model in the time constants and magnitudes, in the equations presented above but not in the modus operandi of the repetitive syndrome.

In conclusion, it was experimentally shown that RLI is triggered by the development of an acute inflammation in viscoelastic tissues exposed to prolonged cyclic high risk loading conditions. The acute phase is reversible but can be transformed to an irreversible and degenerative chronic phase if the tissues are further exposed to high risk loading over time. As this scientifically based insight is now available, vigilance could be exercised by workers and employers to identify the acute phase in time and avoid its progression to the chronic phase. The new multi-factorial, interactive model also provides confirmation of the risk factors and new insights that may allow scientifically justified prevention measures, manipulative (Teodorczyk-Injeyan et al., 2006, 2008; Omos et al., 2009) or pharmacological (anti-inflammatory) therapy and ergonomic design of optimal work schedules.

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Acknowledgment

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