Biomechanics of back pain

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Abstract

This paper offers a mechanistic account of back pain which attempts to incorporate all of the most important recent advances in spinal research. Anatomical and pain-provocation studies show that severe and chronic back pain most often originates in the lumbar intervertebral discs, the apophyseal joints, and the sacroiliac joints. Psychosocial factors influence many aspects of back pain behaviour but they are not important determinants of who will experience back pain in the first place. Back pain is closely (but not invariably) associated with structural pathology such as intervertebral disc prolapse and endplate fractures, although age-related biochemical changes such as those revealed by a 'dark disc' on MRI have little clinical relevance. All features of structural pathology (including disc prolapse) can be re-created in cadaveric specimens by severe or repetitive mechanical loading, with a combination of bending and compression being particularly harmful to the spine. Structural disruption alters the mechanical environment of disc cells in a manner that leads to cell-mediated degenerative changes, and animal experiments confirm that surgical disruption of a disc is followed by widespread disc degeneration. Some people are more vulnerable to spinal degeneration than others, largely because of their genetic inheritance. Age-related biochemical changes and loading history can also affect tissue vulnerability. Finally the concept of 'functional pathology' is introduced, according to which, back pain can arise because postural habits generate painful stress concentrations within innervated tissues, even though the stresses are not high enough to cause physical disruption.

Keywords

Low back pain, anatomy, intervertebral disc, apophyseal joint, sacroiliac joint.

Introduction

Low back pain is one of the most frequent medical causes of absence from work, and disability arising from chronic back pain is now a major welfare and economic problem. Of course back pain can be cited as a convenient excuse for malingering, but there can be little doubt that many people have real and severe problems. Mechanical influences must be important because specific types of mechanical loading constitute the greatest known risk factors for acute disc prolapse,[1] and for low back pain in general.[2] However, there is growing evidence that back pain is a phenomenon which affects both mind and body.

The motivation for writing this review paper, and indeed a book with a similar name,[3] is to attempt to put into context all of the influences which contribute to the natural history of back pain. The word 'bio-mechanics' in the title is not intended to suggest a preoccupation with mechanical influences, but a desire to construct a mechanistic explanation of the various chains of events, including biological and psychological ones, that result in back pain. As we have urged previously:[3] 'Back pain should be explained, not explained away!'

In what follows, Sections 1 and 2 tackle the problem of where back pain comes from by considering the relevant functional anatomy, together with evidence from pain-provocation and pain-blocking studies. Section 3 attempts to distinguish spinal degeneration (and in particular, disc degeneration) from the more-or-less inevitable consequences of ageing. Structural disruption is seen as a key component of 'degeneration', and Section 4 considers how mechanical loading can most easily disrupt the tissues and structures of the lumbar spine. Section 5 points out that living tissues do not behave like inert engineering materials: they respond

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ORIGINAL ARTICLE

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A hypothesis of chronic back pain: ligament subfailure injuries lead to muscle control dysfunction

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Abstract Clinical reports and research studies have documented the behavior of chronic low back and neck pain patients. A few hypotheses have attempted to explain these varied clinical and research findings. A new hypothesis, based upon the concept that subfailure injuries of ligaments (spinal ligaments, disc annulus and facet capsules) may cause chronic back pain due to muscle control dysfunction, is presented. The hypothesis has the following sequential steps. Single trauma or cumulative microtrauma causes subfailure injuries of the ligaments and embedded mechanoreceptors. The injured mechanoreceptors generate corrupted transducer signals, which lead to corrupted muscle response pattern produced by the neuromuscular control unit. Muscle coordination and individual muscle force characteristics, i.e. onset, magnitude, and shut-off, are disrupted. This results in abnormal stresses and strains in the ligaments, mechanoreceptors and muscles, and excessive loading of the facet joints. Due to inherently poor healing of spinal ligaments, accelerated degeneration of disc and facet joints may occur. The abnormal conditions may persist, and, over time, may lead to chronic back pain via inflammation of neural tissues. The hypothesis explains many of the clinical observations and research findings about the back pain patients. The hypothesis may help in a better understanding of chronic low back and neck pain patients, and in improved clinical management.

Keywords Low back pain · Neck pain · Whiplash · Biomechanics · Hypothesis

Introduction

Low back pain is an important societal problem with significant costs. Up to 70–85% of the population in industrialized societies experience low back pain at least once in their lifetime, with point prevalence of about 30% [1, 24]. The total cost of low back pain has been estimated to exceed 50 billion dollars per year in the USA [17]. Although neck pain due to whiplash-associated disorder is less common and less costly, awareness of this disorder, diagnosis and treatment are equally baffling [63]. The term ''back pain'' as used here does not include back pain due to known infections, tumor, systemic disease, fractures or fracture dislocations [73]. Further, the term used here refers generally to the entire spine but in particular to the cervical and lumbar regions.

Back pain is complex. The exact cause of most back (low back and neck) pain remains unproven [72]. The multi-factorial nature of back pain is well recognized with respect to its causes, diagnosis, chronicity, disability and treatment [73]. Abnormal mechanics of the

spinal column has been hypothesized to lead to back pain via nociceptive sensors [72]. The path from abnormal mechanics to nociceptive sensation may go via inflammation [8, 11], biochemical and nutritional changes [6], immunological factors [44], and changes in the structure and material of the endplates [6] and discs [40, 41], and neural structures, such as nerve ingrowth into diseased intervertebral disc [15, 16]. The abnormal mechanics of the spine may be due to degenerative changes of the spinal column [18] and/or injury of the ligaments [43]. Most likely, the initiating event is some kind of trauma involving the spine. It may be a single trauma due to an accident or microtrauma caused by repetitive motion over a long time. It is also possible that spinal muscles will fire in an uncoordinated way in response to sudden fear of injury, such as when one misjudges the depth of a step. All these events may cause spinal ligament injury. Adverse psycho–social factors may also play an important role in transforming the back pain into disability [3].

The research literature on chronic back pain is vast. However, there are some important and common observations. Chronic low back pain patients have delayed muscle response when asked to perform a task [65] or when the spine is suddenly loaded [35], or in anticipation of raising an arm to horizontal position [20], and also delayed muscle shut-off after the external challenge has been withdrawn [52]. Further, they show poorer spinal posture control and balance, especially during complex tasks, when compared to subjects without back pain [10, 33, 53]. The findings in neck pain patients are similar, although the number of studies is fewer. Patients with whiplash-associated disorders have disrupted neck motion [2, 4, 14, 27, 34, 49, 51] and less efficient muscle control [14, 19, 22, 31, 34].

A few hypotheses have attempted to explain the clinical observations and research findings in back pain patients. As the nociceptive sensors are present in most components of the spinal column, the hypotheses have focused on disruption of the spinal column and its components, such as spinal column degeneration [25], injury and clinical instability [47, 73]; facet joint injury [13], and inferior facet-tip impingement on the lamina [77], and Schmorl's nodes [29]. Others have focused on spinal muscles. The pain adaptation [32] and pain–spasm–pain [54] hypotheses were evaluated in a recent review article [69]. The evidence was mixed, and authors suggested that other models, such as spinal instability [46, 47], may be explored. The role played by the injury to the mechanoreceptors embedded in the ligaments of the spinal column has not been explored by any hypothesis.

The spinal column, consisting of ligaments (spinal ligaments, discs annulus and facet capsules) and vertebrae, is one of the three subsystems of the spinal stabilizing system [46]. The other two are the spinal muscles and neuromuscular control unit, Fig. 1. The spinal column has two functions: *structural* and *transducer*. The structural function provides stiffness to the spine. The transducer function provides the information needed to precisely characterize the spinal posture, vertebral motions, spinal loads etc. to the neuromuscular control unit via innumerable mechanoreceptors present in the spinal column ligaments [26, 58], facet capsules [11, 36, 76] and the disc annulus [26]. These mechanical transducers provide information to the neuromuscular control unit which helps to generate muscular spinal stability via the spinal muscle system and neuromuscular control unit. [46] The criterion used by the neuromuscular unit is hypothesized to be the need for adequate and overall mechanical stability of the spine. If the structural function is compromised, due to injury or degeneration, then the muscular stability is increased to compensate the loss. What happens if the *transducer* function of the ligaments of the spinal column is compromised? This has not been explored. There is evidence from animal studies that the stimulation of the ligaments of the spine (disc and facets [21], and ligaments [59, 62]) results in spinal muscle firing. The mechanoreceptor-muscle firing relationships are modulated by several factors, such as ligament fatigue [61], static flexed posture [60], and cumulative microtrauma [75].

The observations from animal studies just mentioned, together with the possibility of transducer dysfunction in back pain patients, form the basis of a new back pain hypothesis. The purpose is to describe the hypothesis, use the hypothesis to explain the various important research findings, and suggest possible treatment options.

The hypothesis

The hypothesis consists of the following sequential steps:

1. Single trauma or cumulative microtrauma causes *subfailure injury* of the spinal ligaments and injury to the mechanoreceptors embedded in the ligaments.
2. When the injured spine performs a task or it is challenged by an external load, the transducer signals generated by the mechanoreceptors are corrupted.
3. Neuromuscular control unit has difficulty in interpreting the corrupted transducer signals because there is spatial and temporal mismatch between the normally expected and the corrupted signals received.
4. The muscle response pattern generated by the neuromuscular control unit is corrupted, affecting the spatial and temporal coordination and activation of each spinal muscle.
5. The corrupted muscle response pattern leads to corrupted feedback to the control unit via tendon organs of muscles and injured mechanoreceptors, further corrupting the muscle response pattern.

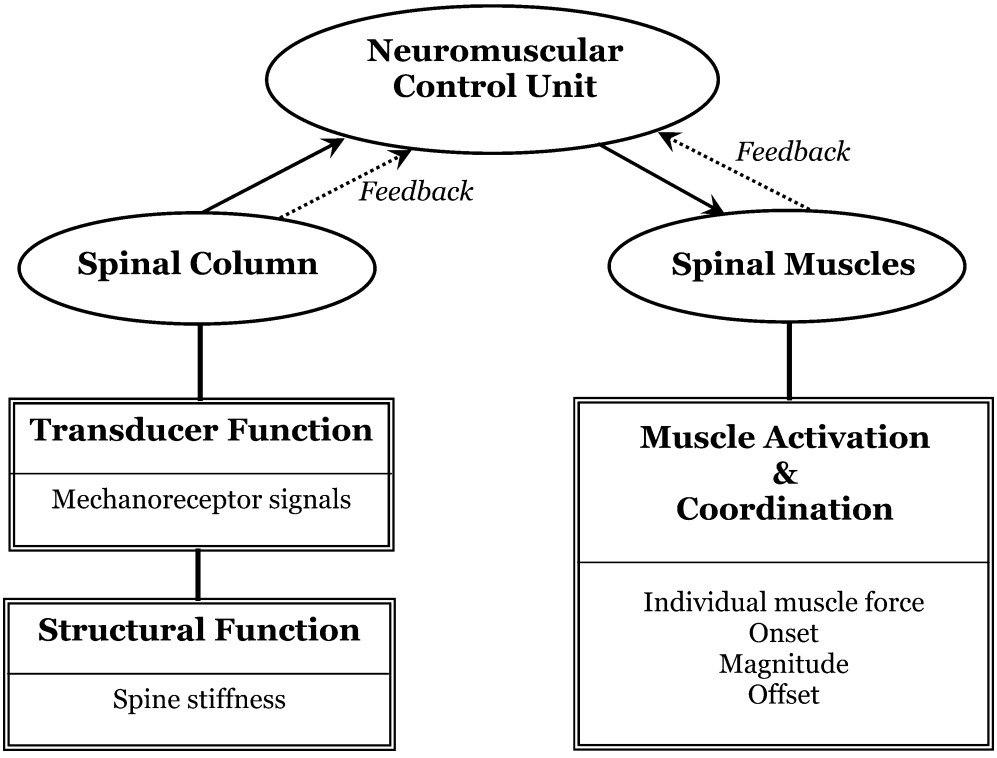

Fig. 1 Spinal stabilizing system. It consists of three subsystems: spinal column, spinal muscles, and neuromuscular control unit. The spinal column has two functions: structural—to provide intrinsic mechanical stability, and transducer—to generate signals describing spinal posture, motions, loads etc. via the mechanoreceptors. The neuromuscular control unit generates muscle response pattern to activate and coordinate the spinal muscles to provide muscle mechanical stability. There is feedback from the spinal muscles and mechanoreceptors to the control unit. (Adapted from Panjabi 1992)

6. The corrupted muscle response pattern produces high stresses and strains in spinal components leading to further subfailure injury of the spinal ligaments, mechanoreceptors and muscles, and overload of facet joints.
7. The abnormal stresses and strains produce inflammation of spinal tissues, which have abundant supply of nociceptive sensors and neural structures.
8. Consequently, over time, chronic back pain may develop. The *subfailure injury* of the spinal ligament is defined as an injury caused by stretching of the tissue beyond its physiological limit, but less than its failure point [48].

Under normal circumstances, to perform a task or to respond to an external challenge, the mechanoreceptors generate a complex and redundant set of transducer signals describing vertebral position, spinal motion, spinal load, and so forth, at each spinal level (Fig. 2). The signals are transmitted to the neuromuscular control unit for interpretation and action. The neuromuscular control unit evaluates the signals and produces a normal muscle response pattern, based upon several factors, including the need for spinal stability, postural control, balance, minimal stress/stain in various spinal components, and so forth. This is achieved via feedback from the muscle spindles and golgi tendon organs of the muscles as well as the mechanoreceptors of the ligaments. The muscle response pattern includes all the information needed to dynamically orchestrate the muscles: to choose the individual muscles needed, and to activate each muscle in a defined sequence with respect to its onset, activation level and shut-off. The entire dynamic procedure is relatively quick, non-injurious and leads to no adverse consequences.

The injured spine behaves differently (Fig. 3). The subfailure injuries of the ligaments disrupt and/or injure the embedded mechanoreceptors. When the spine performs a routine task or responds to an external challenge, the disrupted/injured mechanoreceptors produce *corrupted* transducer signals, describing vertebral position, motion, spinal loads etc. for each spinal level. There is loss of spatial and temporal integrity of the transducer signals received from multiple redundant mechanoreceptors distributed through the spinal column. The neuromuscular control unit, not affected by the injury itself, senses a mismatch between the normally expected and the received transducer signals, and, therefore, has difficulty in choosing the appropriate muscle response pattern. However, it must act. Consequently, the neuromuscular control unit produces a *corrupted* muscle response pattern, which is the closest match it can determine to the corrupted transducer signals. The corrupted muscle response pattern affects the choice of the spinal muscles to activate, and the individual muscle activation: force onset, intensity and shut-off. The orchestration of the various spinal muscles responsible for spinal stability, posture and motion is disrupted.

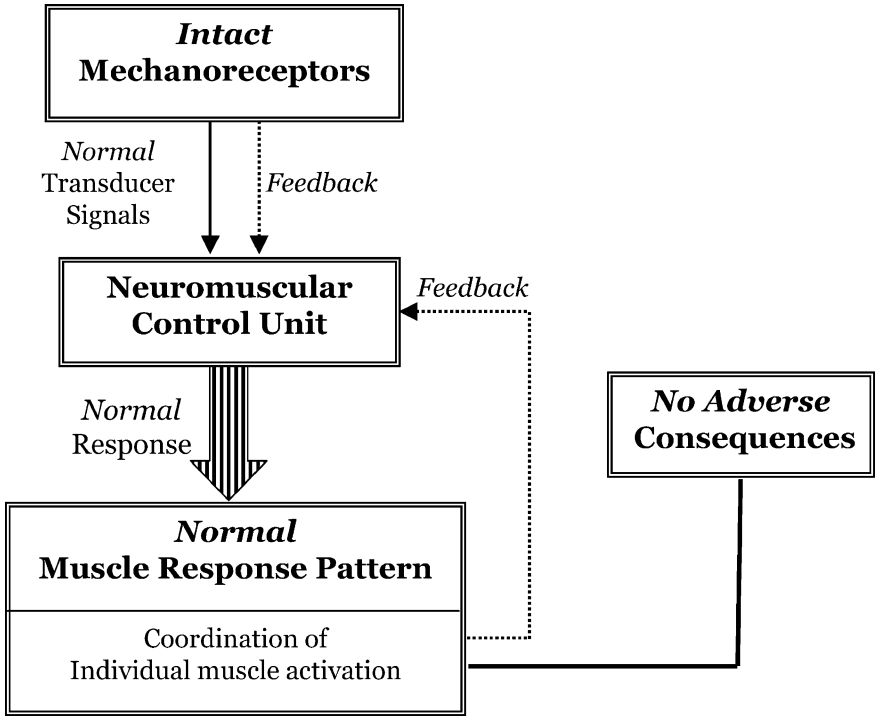

Fig. 2 Normal circumstances. The intact mechanoreceptors send transducer signals to the neuromuscular control unit, which evaluates the transducer signals and sends out muscle response pattern to coordinate the activation of individual spinal muscles. There is feedback from the muscle spindles and golgi tendon organs of the muscles and mechanoreceptors of the ligaments to the neuromuscular control unit. Under normal circumstances, there are no adverse consequences

Additionally, the feedback to the neuromuscular control unit and mechanoreceptors is also negatively affected, further corrupting the muscle response pattern. This has several adverse effects. Higher stresses, and strains and injuries may develop in the spinal ligaments, and mechanoreceptors. The facet joints may be overloaded, and the spinal muscles may fatigue or be injured. Over time, these injurious stresses and strains can initiate inflammation of neural tissues [12], and accelerate disc [40] and facet joint [9] degeneration. Thus, a vicious cycle is set up, leading to chronic dysfunction of the entire spinal system, resulting in back pain.

Discussion

The underlying concept of the spinal instability hypothesis was the need for adequate spinal stability provided by vertebrae and ligaments of the spinal column, and augmented by the spinal muscles under the neuromuscular control [46, 47]. In the present hypothesis, the focus is on the disruption of the mechanoreceptors due to ligament injury leading to corrupted transducer signals and muscle response pattern, and overall system dysfunction. What follows is an attempt, using the new hypothesis, to explain some of the observations concerning low back and neck pain patients, and to suggest treatment options.

Delayed muscle response is a common observation in low back pain patients. When low back pain patients were challenged by a sudden external load, the delayed muscle onset was observed [35], and delayed muscle shut-off was seen when the load was removed [52]. Similarly, the anticipatory response of the transverse abdominis was delayed [20]. These findings can be explained by the hypothesis. An individual with intact spinal system, when challenged by a sudden change in its load or posture, will produce a quick and normal muscle response pattern, specific to the challenge (Fig. 2). However, when the neuromuscular control unit receives corrupted transducer signals, it may take a longer time to choose a muscle response pattern that most closely matches the corrupted transducer signals, taking into account a multitude of factors such as spinal stability, postural balance, tissue overload and so forth (Fig. 3). Additional factors, such as muscle fatigue, complexity of the task, mental distraction, and so forth, may further decrease the efficiency of the neuromuscular control unit leading to the delayed muscle system response.

Balance and postural control are deficient in low back pain patients [10, 33, 53]. The balance and postural control includes a three-step process: generation of transducer signals by the mechanoreceptors; selection of appropriate muscle response pattern by the neuromuscular control unit based up mechanoreceptor signals; and feedback from the mechanoreceptors and muscle spindles and golgi tendon organs (Fig. 2). Therefore, subfailure injuries of the ligaments disrupt all the three steps involving the mechanoreceptors thereby resulting in poor balance and postural control.

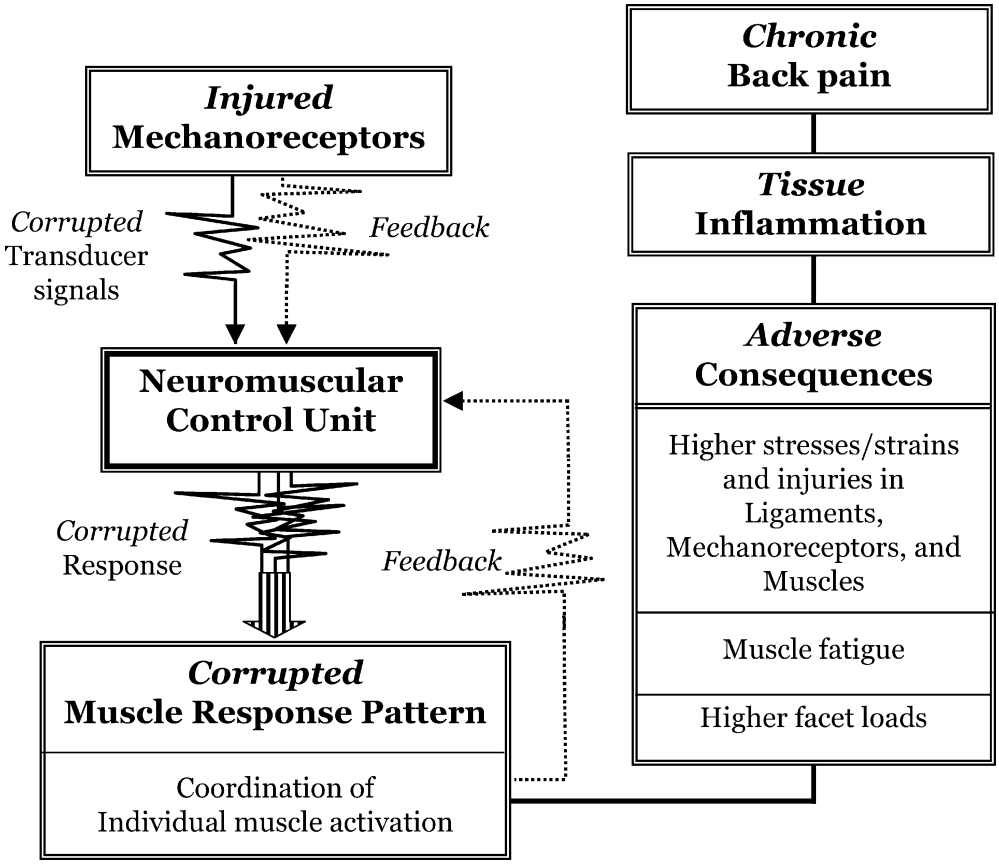

Fig. 3 Subfailure injuries of the ligaments. The injured mechanoreceptors send out *corrupted* transducer signals to the neuromuscular control unit, which finds spatial and temporal mismatch between the expected and received transducer signals, and, as a result, there is muscle system dysfunction and *corrupted* muscle response pattern is generated. Consequently, there are adverse consequenses: higher stresses, strains, and even injuries, in the ligaments, mechanoreceptors, and muscles. There may also be muscle fatigue, and excessive facet loads. These abnormal conditions produce neural and ligament inflammation, and over time, chronic back pain

Re-positioning error has been consistently found in both low back pain [7, 38, 42] and whiplash [19, 31] patients. The error occurs when the patient is asked, starting from an initial posture, to first bend or twist the spine to a certain posture, and then to return to the initial posture. Based upon the hypothesis presented, this is to be expected. The muscle response pattern generated to bring back the trunk or head to the initial posture makes use of the mechanoreceptor transducer signals, in the three-step process described above. With the ligament injury in back pain patients, the corrupted mechanoreceptor information and the corrupted muscle response pattern will both lead to the re-positioning error.

Among chronic whiplash patients, decreased neck motion has been observed in most studies [2, 4, 14, 34, 49, 51]. These were active motion studies in which the subject was encouraged to produce the motion. However, when the subject was relaxed and the motion was produced passively by the examiner, the motion was found to be increased in the whiplash patients compared to the control group [27]. How can one explain these contrasting findings? In the active motion studies, corrupted muscle response pattern (generated due to corrupted mechanoreceptor signals) applies higher muscle forces on the cervical spine. Such forces stiffen the spine and reduce the motion [50, 68, 74]. In the relaxed passive motion studies, care was taken to decrease the influence of muscle guarding, pain and lack of motivation by relaxing the neck and shoulder muscles with application of vapor coolant, and then letting the examiner move the patient's head into maximum flexion. Thus, when the abnormal muscle forces were minimized in the passive examination, the intrinsic injury of the spinal column was exhibited as the increased motion.

Muscle spasm is commonly observed in both low back pain [5, 30] and whiplash patients [39, 55, 67]. Muscle coordination may be thought of as an orchestrated activation of various spinal muscles to stabilize the spinal column and accomplish a certain task. The orchestration consists of activation of individual muscles with respect to the onset, magnitude of the force generated, and offset. With the injury of the ligaments, the mechanoreceptors generate corrupted transducer signals, and therefore, there is a mismatch between the expected and the received corrupted transducer signals. The neuromuscular control unit senses the mismatch and may fire simultaneously both the agonist and antagonist muscles at its command to temporarily stabilize the spine and minimize the intervertebral motions, corrupted transducer signals, and pain. If the situation does not improve with time,

then the muscle action may become chronic. Such simultaneous firing of agonistic and antagonist muscles has been observed in low back pain patients.

Greater variability has been observed in almost all parameters measured in low back [28, 33, 37, 42, 53] and whiplash [14, 34] patients. The new hypothesis can explain this increased variability. The subfailure injuries of ligaments are incomplete injuries, which may range between tearing of a few fibers to a nearly complete rupture of a ligament. Importantly, a complex joint, such as a functional spinal unit, includes many ligament structures. This collection of ligament structures may encompass a wide range of injuries, each structure with different injury severity, depending upon the magnitude and mode of the trauma. The density of the mechanoreceptors imbedded in the various ligament structures may also vary. The result of all these numerous variations can produce a wide spectrum of corrupted muscle response patterns for seemingly similar injury-causing events. Further, each low back pain patient is unique, for example with respect to the anatomy, mechanical properties of ligaments, and muscle response to the trauma, adding further to the muscle response pattern variability.

There are limitations to the hypothesis. Back pain is a complex multifactorial problem, and a single hypothesis cannot explain each and every clinical and research observation, and there may also be alternative explanations, such as instability [46, 47], and/or pain [32, 54]. It is recognized that the pain is a subjective experience. Besides affecting the muscle system via the corrupted mechanoreceptor signals, ligament injury may also result in muscle atrophy and weakness due to disuse, thus directly affecting the spinal system function. Additionally, muscle injury, fatigue, atrophy, and so forth may aggravate the spinal system dysfunction. As the muscles participate in the feedback loop via the mechanoreceptors in the form of muscle spindles and golgi tendon organs (Fig. 3), their disruption could further corrupt the muscle response pattern. However, an injured muscle may heal relatively quickly due to abundant blood supply, and, therefore, may not be the main cause of *chronic* back pain. In contrast, the ligament injuries heal poorly and, therefore, may lead to tissue degeneration over time [40, 41]. Thus, the ligament injuries are more likely to be the major cause of the chronic back pain. The corrupted transducer signals may be the result not only of the ligament injury, but also due to ligament fatigue and viscoelastic creep stretch [61], but such an effect is often reversible given sufficient rest, and, therefore, may not always lead to chronic back pain. The clinical and research studies presented constitute only a small, but an important and quite representative sample, of the vast literature available on the subject of back pain. It is recognized that there may be other studies whose explanation may or may not fit the new hypothesis. In general, hypotheses and models are extremely difficult, if not impossible, to fully validate [45]. They can only attempt to explain the available findings, and may be used to predict outcomes in specific situations.

Can the system adapt to the subfailure injury of the mechanoreceptors? A minor subfailure injury is probably repaired or compensated with no long-term consequences. A mild subfailure injury, on the other hand, may be successfully compensated in the short-term by temporarily modifying the chosen muscle response pattern. However, the modification may be difficult to maintain overtime, as it is likely to produce excessive tissue loads and muscle fatigue. Lapses in the maintenance of the modified muscle response pattern may occur from time to time. Could this be the mechanism for recurrent episodes of back pain that many patients experience? [57, 71] On the other hand, if the corrupted muscle response pattern becomes permanent, then it may result in abnormal posture, disturbed intervertebral motion pattern, altered gait, and, in general, a less efficient system to perform every day spinal functions.

One can speculate as to the possible treatment options based upon the hypothesis. The incoming corrupted transducer data may never become normal, even though the ligaments, incorporating the injured mechanoreceptors, may heal/scar over time. After breaking the cascade of injury, inflammation, and pain by suitable drug treatment, the patient may be encouraged to retrain the neuromuscular control unit to produce an altered muscle response pattern that is suited to both the corrupted transducer signals and activities of daily living. The criterion for the altered muscle response pattern may be the reduction of stresses and strains of the ligaments, loads on facet joints, and muscle forces, which may reduce the back pain. A set of tasks may be designed for this purpose. The tasks may be repeated and varied. Improvement in the efficiency of the neuromuscular control unit may develop over time, with concomitant relief of back pain. Several clinical studies have incorporated these and similar ideas. Re-training exercises involving muscle control have shown promising results in both chronic low back pain [22, 23, 70], and neck pain [56, 64, 66] patients, compared to traditional therapies. More research is needed in this area. I hope that the presentation of this hypothesis will stimulate discussion among clinicians and researchers in biomechanics to evaluate the usefulness of the hypothesis towards better understanding of back pain, development of more precise diagnostic methods, and design of more efficient treatments for back pain patients.

Conclusions

A new hypothesis of chronic back pain based upon muscle system dysfunction due to ligament injuries is

described. Subfailure injuries of the ligaments and embedded mechanoreceptors generate *corrupted* mechanoreceptor signals. Consequently, the neuromuscular control unit produces *corrupted* muscle response pattern, resulting in excessive loading and, possibly, injuries of the spinal structures, including additional injuries of the mechanoreceptors. The hypothesis accounts for many of the common and important experimental observations and clinical findings seen in low back pain and whiplash patients. In the low back pain patients, it explains findings of delayed muscle response, poor balance, inefficient postural control, greater error in re-positioning the trunk, muscle spasm, and greater variability in the tasks performed. In the whiplash patients, both the decreased motion in active testing and increased motion in passive-relaxed testing are explained. The hypothesis proposes that the dysfunction of the muscle system over time may lead to chronic back pain via additional mechanoreceptor injury, and neural tissue inflammation.

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Sensory – Motor control of ligaments and associated neuromuscular disorders

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Abstract

The ligaments were considered, over several centuries, as the major restraints of the joints, keeping the associated bones in position and preventing instability, e.g. their separation from each other and/or mal-alignment. This project, conducted over 25 years, presents the following hypothesis:

1. Ligaments are also major sensory organs, capable of monitoring relevant kinesthetic and proprioceptive data.
2. Excitatory and inhibitory reflex arcs from sensory organs within the ligaments recruit/de-recruit the musculature to participate in maintaining joint stability as needed by the movement type performed.
3. The synergy of the ligament and associated musculature allocates prominent role for muscles in maintaining joint stability.
4. The viscoelastic properties of ligaments and their classical responses to static and cyclic loads or movements such as creep, tension–relaxation, hysteresis and strain rate dependence decreases their effectiveness as joint restraint and stabilizers and as sensory organs and exposes the joint to injury.
5. Long-term exposure of ligaments to static or cyclic loads/movements in a certain dose-duration paradigms consisting of high loads, long loading duration, high number of load repetitions, high frequency or rate of loading and short rest periods develops acute inflammatory responses which require long rest periods to resolve. These inflammatory responses are associated with a temporary (acute) neuromuscular disorder and during such period high exposure to injury is present.
6. Continued exposure of an inflamed ligament to static or cyclic load may result in a chronic inflammation and the associated chronic neuromuscular disorder known as cumulative trauma disorder (CTD).
7. The knowledge gained from basic and applied research on the sensory – motor function of ligaments can be used as infrastructure for translational research; mostly for the development of ''smart orthotic'' systems for ligament deficient patients. Three such ''smart orthosis'', for the knee and lumbar spine are described.
8. The knowledge gained from the basic and applied research manifests in new physiotherapy modalities for ligament deficient patients.

Ligaments, therefore, are important structures with significant impact on motor control and a strong influence on the quality of movement, safety/stability of the joint and potential disorders that impact the safety and health of workers and athletes.

1. Historical background

For centuries the role of the ligaments was thought to be that of mechanical structures that maintain the bones associated with the joint in a relative position to each other, e.g. prevent the separation of the bones. Over the years additional information was obtained providing more details on the properties of the ligaments, their anatomy and mechanical functions. The collagen fibers of the ligaments were shown to be viscoelastic and the fibers were shown to be at various levels of laxity or tension such that

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elongation created a process of recruitment which increased with length allowing increase in tension (Woo and Buckwalter, 1988; Woo et al., 1980, 1981, 1987). Furthermore, the position, orientation and shape of a specific ligament was shown to also increase and decrease its tension at specific range of motion, providing resistance to joint separation in that range (Renstrom et al., 1986). It was also shown that interaction of several ligaments associated with the same joint provided joint stability for most of the range of motion in several axis, allowed equal pressure distribution of the two cartilage surfaces and kept the surfaces moving on a prescribed track. Such data confirmed the mechanical properties of ligaments as joint stabilizers.

As far back as the early 20th century, Payr (1900) suspected that ligaments may have a neurological function in addition to their mechanical properties. His hypothesis went without experimental proof for nearly 50 years until several anatomical studies demonstrated the existence of mechanoreceptors in ligaments (Gardner, 1944; Wrete, 1949; Freeman and Wyke, 1967a,b; Ekholm et al., 1960; Patridge, 1924).

Together with the earlier demonstration of articular nerves emerging from ligaments (Rudinger, 1857), the possible neurological role of the ligaments as a sensory element was emerging.

2. The ligamento-muscular reflex

At about the same time, in the mid-20th century, groups of Swedish researchers were attempting to demonstrate the possibility of a reflex arc from the knee ligaments to the thigh muscles. Palmer (1938, 1958) developed tension in the knee's medial collateral ligament of humans and was able to see some muscle activity in the semimembranosus, sartorius, and vastus muscles and noted decreasing activity as the transverse tension via a ligature was shifted distally along the ligament. Stener (1959, 1962) and Andersson and Stener (1959), failed to observe the reflex in the anesthetized feline, yet were able to record nerve activity in the articular nerves of the feline and unanaesthetized humans upon ligament loading, but no muscle activity. In patients with ligament rupture, pain sensation and some muscular activity was observed upon stretch of the damaged ligaments. It was assumed that ligament innervation was to deliver pain sensation upon damage.

The conflicting and confusing results from the two groups remained until 1987 when we were able to demonstrate a distinct reflex activity from the anterior cruciate ligament to the hamstrings in the in vivo feline and in unanaesthetized humans as shown in Fig. 1a–c (Solomonow et al., 1987). Several groups went on to independently confirm the existence of a reflex arc from various knee ligaments to the leg muscles in humans and animal models (Grabiner and Weiker, 1993; Beard et al., 1994; Raunest et al., 1996; Sjolander, 1989).

As the neurological functions of the knee ligaments and its reflexive activation of the thigh muscles were established, several new questions emerged; are all ligaments in the major joints innervated and capable of eliciting a reflex? And what is the biomechanical/physiological function of the reflex arc from the ligaments to the muscles?

Over the following years we have been able to demonstrate that mechanoreceptors exist in the ligaments of the major joints (Guanche et al., 1999; Solomonow et al., 1996; Petrie et al., 1997, 1998) and that a reflex arc could be elicited by either electrically stimulating the articular nerve emerging from the ligaments or applying tension directly to the ligaments. Mechanoreceptors and a reflex arc were demonstrated in the knee, elbow, shoulder, ankle, palmar wrist, and lumbar spine as shown in Figs. 2 and 3 (Solomonow et al., 1996, 1998, 2002; Phillips et al., 1997; Knatt et al., 1995; Guanche et al., 1995; Stubbs et al., 1998). It is, therefore, a fair conclusion that most ligaments are also a sensory organ and a source of reflex arc to relevant muscles.

Several interesting issues were also revealed. All ligaments are innervated with the same four types of afferents; Golgi, Pacinian Corpuscles, Ruffini endings, and bare endings. Furthermore, in some ligaments these afferents are distributed homogenously throughout the length of the ligament, whereas in other ligaments most afferents are distributed near the two insertions of the ligament to the bone with otherwise poor presences in their mid-substance. For example, afferents are evenly distributed throughout the annular and transverse medial ligaments but near the insertions of the radial posterior and anterior ligaments of the elbow (Petrie et al., 1998).

Such findings give rise to several suggestions regarding the role of the ligamento-muscular reflex. One possibility suggests that if afferents are distributed only at the bony insertion of the ligaments, where the higher tissue stiffness results in less strain, the excitation threshold of the afferents will be elevated and the reflex will become active only at high strains/tensions. This may be at levels which pose a risk for ligament damage and then the reflexively recruited muscular activity may serve to reduce the strain/stress in the ligament by load sharing. Conversely, if a ligament is evenly distributed with afferents, that may indicate an ongoing service as a sensory organ for detection of angle, position, load, joint velocity, etc., e.g. kinesthetic sensing organ. This may also indicate an ongoing synergistic reflexive activation of muscles during movement.

The absence of Pacinian afferents in the radial collateral ligament of the elbow may emphasize its role as a high threshold strain detector or a nociceptive role where near injurious loads may directly trigger a reflex response from the muscles (Petrie et al., 1998), assisting in preventing injury.

3. Biomechanical functions

The biomechanical function of the reflex initiated by the ligaments was proposed by us to be that of a joint

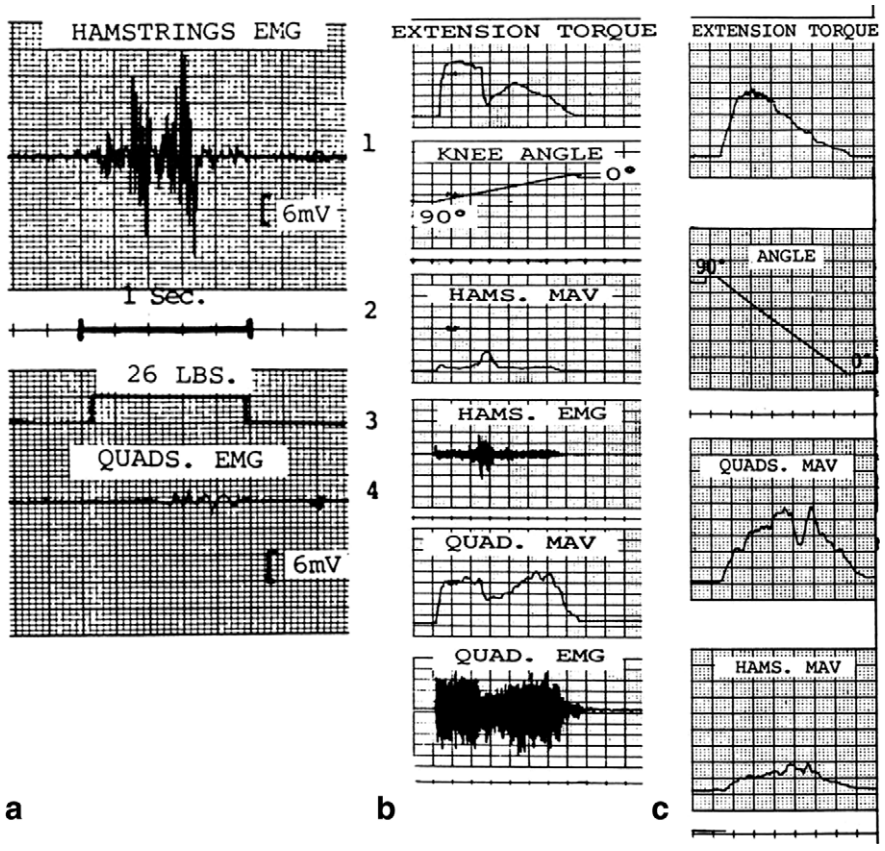

Fig. 1. (a) The substantial increase in EMG activity of the cat's hamstring (Trace 1) over 1 s duration (Trace 2) of direct load application (Trace 3) to the ACL. The quadriceps EMG (Trace 4) exhibits short initial low-level activity and then becomes inhibited for the duration of the ligament's loading. (b) Extension torque, knee angle, hamstring MAV (mean absolute value of the EMG) and EMG, and quadriceps MAV and EMG obtained from a patient with a midsubstance tear of the ACL. Note the large subluxation torque failure near 42°, which appears simultaneously with decrease in quadriceps EMG/MAV and increase in hamstring EMG/MAV, indicating the reflexive attempt of the muscles to correct the instability. (c) Extension torque, knee angle, quadriceps MAV, and hamstring MAV taken from an ACL deficient patient 2 weeks postarthroscopy. Note that the torque does not show any sign of failure, while the reflexive decrease in quadriceps MAV and increase in hamstring MAV do take place near 37° of flexion. The patient had abnormally tight hamstrings. Identical responses were obtained from subjects with hypertrophic knee muscles due to continuous participation in various exercise and sports activity.

stabilizer as well as the source of co-contraction which is so necessary for refined and controlled motion. Hirokawa et al. (1991, 1992) conducted a two stage study to assess the interaction of the thigh muscles, quadriceps and hamstrings, and the relative position of the distal femur and proximal tibia. Sequential X-rays of cadaver knee were taken while loading the quadriceps tendon at different loads and then applying loads to the hamstrings tendon simulating co-contraction, while the quadriceps were fully loaded as shown in Fig. 4. Small metal spheres embedded in the bones, as in the X-ray of Fig. 5a and b, served as markers that were analyzed geometrically. The study shows that anterior translation of the tibia was elicited in the range of motion of 60° flexion to full extension with quadriceps loading as shown in Fig. 6a. As the hamstrings were simultaneously loaded as shown in Fig. 6b, a substantial decrease in the anterior translation of the tibia occurred. It was clear, therefore, that the quadriceps can elicit instability and strain in the ACL due to anterior translation of the proximal tibia from 60° flexion to full extension, and that the hamstrings can substantially attenuate the anterior translation with just a few percent of co-activation.

We concluded that reflexive activation of the hamstrings as we observed in the feline and humans (Solomonow et al., 1987) could decrease the anterior translation of the tibia and decrease the tension in the ACL. This is specifically applicable for the range of motion from 60 degrees flexion to near full extension. In full extension both quadriceps and hamstrings could stiffen the joint and minimize instability, but without having direct impact on opposing anterior forces as was shown by Markolf et al. (1976, 1978) and Shoemaker and Markolf (1982).

4. Effects of velocity and training

Clear evidence was provided to explain the function of the ligamento-muscular reflex as a synergistic sensory-motor control scheme for maintaining joint stability, decreasing and/or preventing risk of damage to the

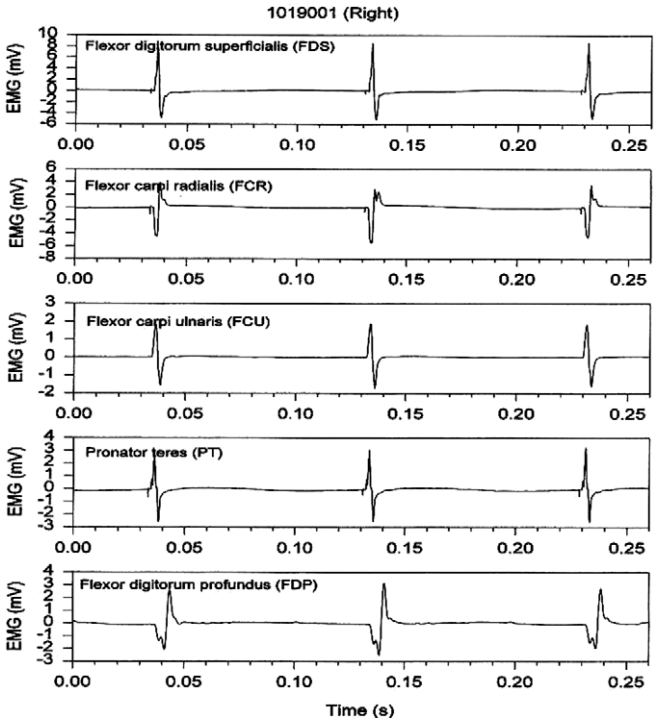

Fig. 2. Typical myoelectric discharge of the flexors digitorum superficialis and profundu, flexors carpi radialis and ulnaris, and the pronator teres in response to stimulation of the median articular nerve to the medial ligaments of the elbow.

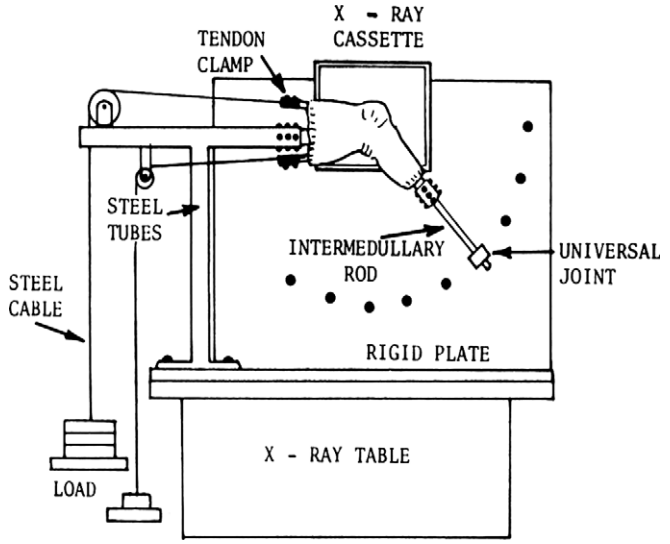

Fig. 4. Experimental apparatus constructed to fix the cadaver knee while permitting loading of the quadriceps and hamstring tendons and change in joint angle.

ligament via co-activation. In addition, one of the roles of ongoing co- activation during various types of joint movement was determined to be preserving joint stability in addition to allowing for joint acceleration, dynamic braking and smooth, controlled motion as shown in Fig. 7a

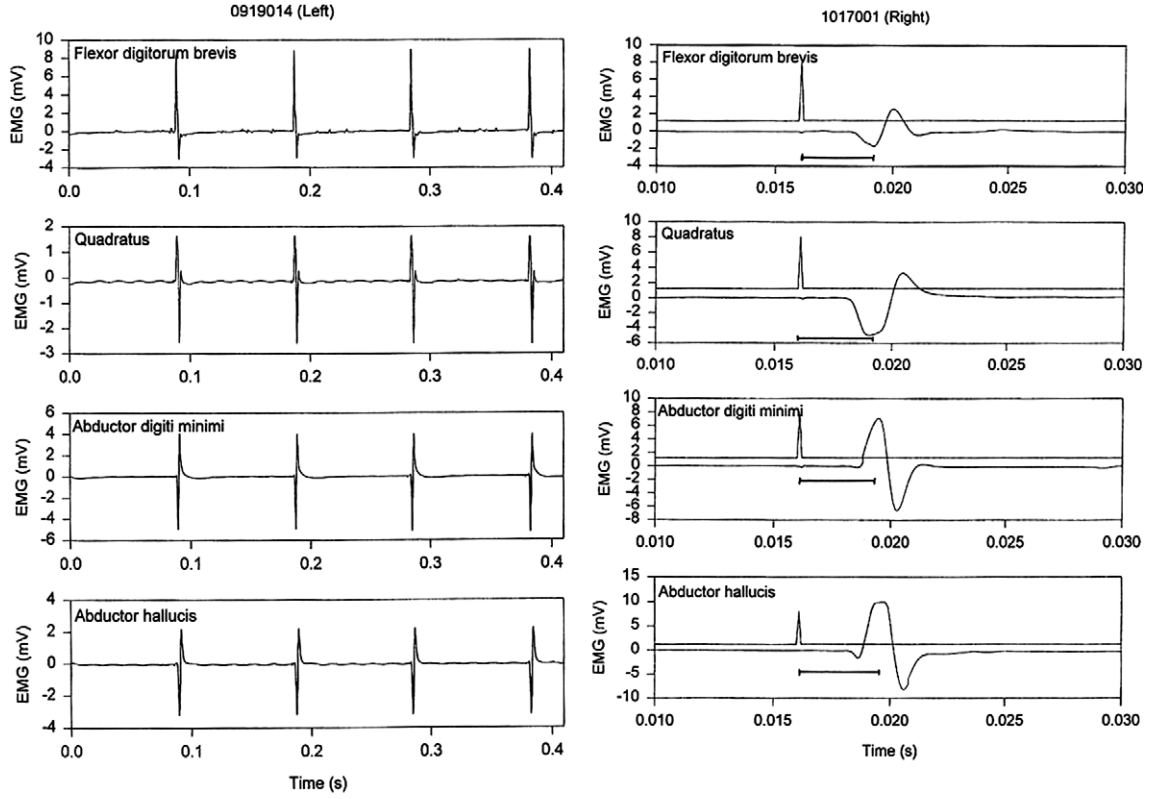

Fig. 3. (a) A typical EMG response of the four intrinsic foot muscles (FDB, Q, ADM, and AH) to a stimulus train of 10 pps. (b) A typical EMG response to one pulse showing the calculated time delay from the peak of the stimulus artifact to the peak of the resulting EMG.

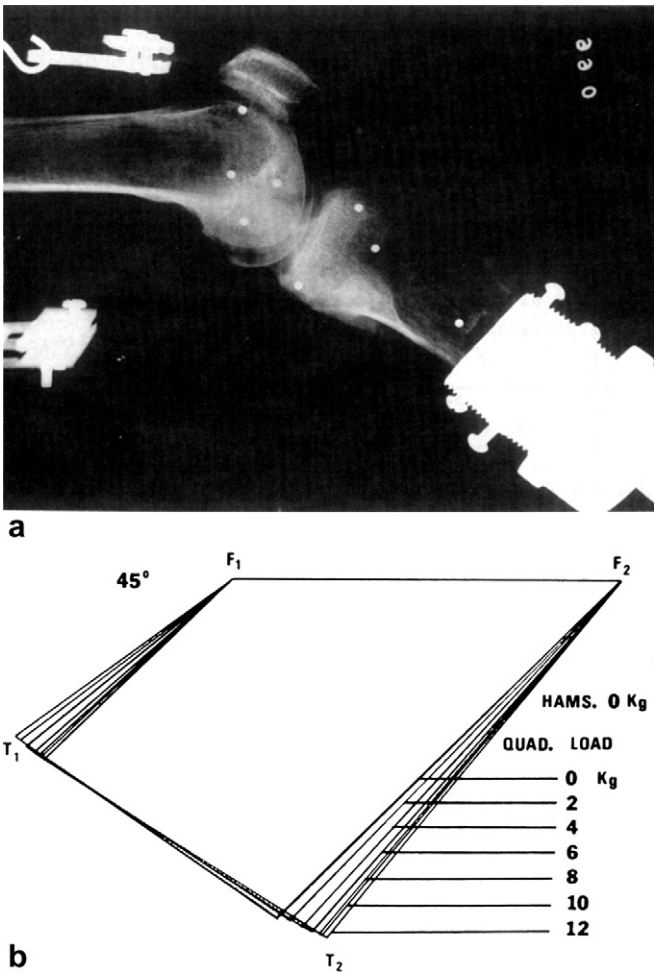

Fig. 5. (a) Typical radiograph of a cadaveric knee positioned at 45° of knee flexion. Note the four metal spheres in the femur and the four metal spheres in the tibia. (b) Seven sequential quadrangles generated from loading the cadaveric knee (set at 45° of flexion) from passive (no load) up to 12 kg load in the quadriceps tendon. Note the deformation of the quadrangle of the passive state in the anterior direction as the load is increased, pointing out the anterior displacement of the tibia. F_1, F_2, T_1, and T_2 correspond to points on the femur and tibia (see Fig. 3).

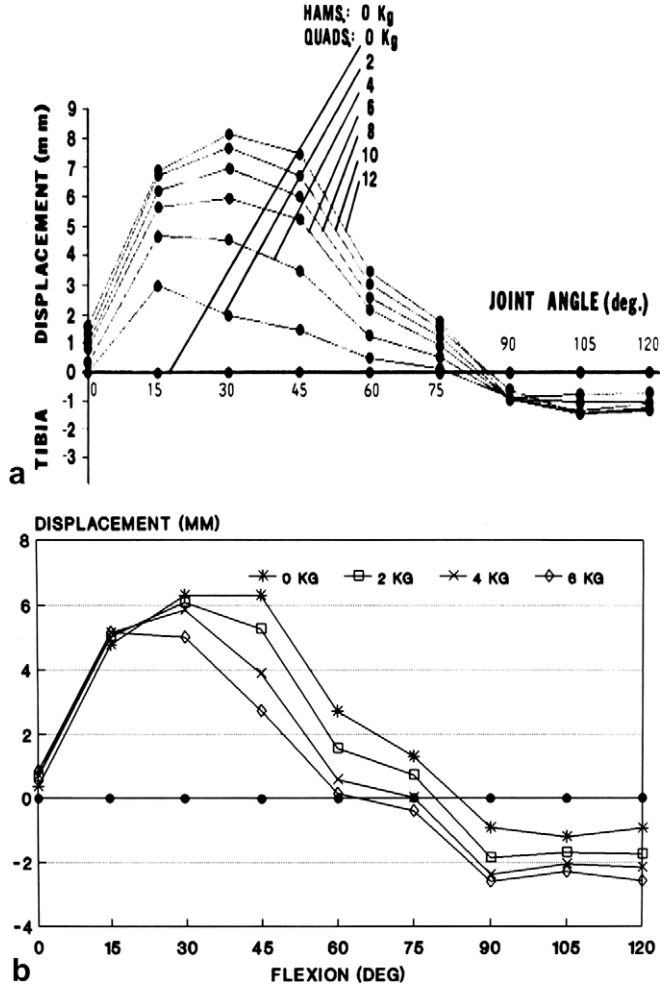

Fig. 6. (a) Anterior–posterior displacement of the tibia versus joint angle for various load levels in the quadriceps. The horizontal axis displays the data of the passive knee (no load). Positive displacement indicates anterior shift, while negative displacement indicates posterior shift. (b) Mean tibia displacement versus joint angle for constant 12 kg quadriceps load and simultaneous hamstrings loads of several magnitudes. Note decrease in anterior translation of the tibia as hamstrings load increases.

and b (Hagood et al., 1990; Solomonow et al., 1986, 1988, 1989; Baratta et al., 1988). While co-contraction allows for a measure of joint stability throughout normal motion, the triggering of the ligamento-muscular reflex can provide a fast dose of increase in joint stability when unexpected movement occurs, eliciting sudden increase in ligament tension. It is a protective reflex. We also demonstrated as seen in Fig. 8, that in athletes; jumping activity can decrease the hamstrings coactivation but that could be reversed by three weeks of hamstring retraining (Baratta et al., 1988).

Any protective reflex responding to a potentially damaging or risky stimulus must be a fast-acting one and generate forces in the appropriate muscles. Review of the studies we conducted on the ligamento-muscular reflexes in the elbow, knee, shoulder, ankle, and spine reveal a response time (or latency) ranging from 2.5 to 5 ms (see Fig. 3b for example). Considering the length of the nerves from the spine to the respective joints, a conduction velocity of 120 ms (for large afferents such as Golgi and Pacinian, Mountcastle, 1974) and a 0.5 ms for synaptic transmission, only a monosynaptic or bisynaptic reflex could be assumed. This may emphasize the importance of this reflex as a fast-acting, protective reflex, preventing damage to the ligament and potential risk to the joints.

So far it was shown that the ligaments of the major joints and the lumbar spine are equipped with sensory organs; that there are two patterns of the sensory organ distribution along the ligament with functional neurological implications; that a reflex arc exists from the sensory receptors to muscles associated with the respective joint and that the function of the muscular activation and co-activation is to unload the ligament from overload and prevent potential injury or damage.

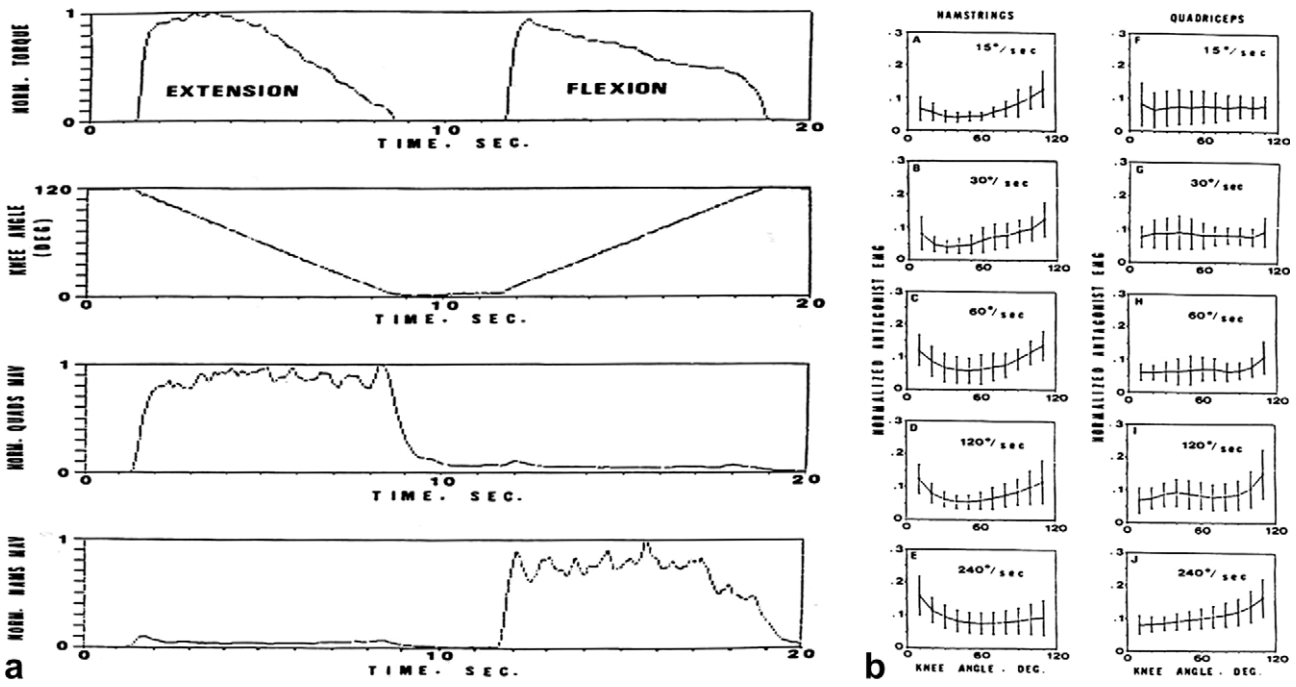

Fig. 7. (a) Typical recording of actual trial from one subject at isokinetic knee velocity of 15 degree/s. Traces show (from top to bottom) extension and flexion normalized torque, knee angle, normalized quadriceps MAV of its EMG during extension and flexion, and the hamstrings normalized MAV of its EMG during extension and flexion. Note that the quadriceps MAV during extension and the hamstrings MAV during flexion were nearly constant (despite the typical fluctuations at maximal force levels) throughout extension and flexion. (b) The antagonist coactivation patterns of the hamstrings (left column) and quadriceps (right column) are shown for increasing joint velocity as normalized antagonist EMG (MAV) versus knee angle. The plots are based on the data pooled from all subjects. The vertical bars indicate the standard deviation for each angle and the curve connects the mean value of the MAV value throughout the range of motion. Note the increase in hamstrings coactivation with increasing velocity just before full extension and decreasing coactivation at the initiation of the motion.

5. Neuromuscular neutral zones

Viscoelastic tissues, such as ligaments, have classical responses to elongation and tension which includes hysteresis and elongation rate dependence (Solomonow, 2004). Ligaments can display large elongations and relatively low associated tension when stretched slow. Fast rates of stretch, however, develop very high tensions that can result in severe damage (known as sprain) or rupture at relatively short elongations. Furthermore, when subjected to a stretch and release cycle, the length versus tension trajectory during the stretch is different than the trajectory during the release, e.g. hysteresis. These two mechanical factors are expected to have a substantial impact on the sensory-motor functions of the ligaments as expressed by the ligamento-muscular reflex.

The above issues were studied and reported in two reports (Eversull et al., 2001; Solomonow et al., 2001). We found that during a single sinusoidal stretch-release cycle of the supraspinous ligament, the reflex was initiated only after a certain length and tension were developed. The length–tension range prior to the triggering of the reflex was properly designated as a ''neutral zone'' indicating that small perturbation (1–2 mm) in the ligament length around its resting length are probably inconsequential for joint stability and do not require co-commitant muscular activation (see Fig. 9).

During the relaxation phase, the reflex disappeared at a different length and different associated tension, much larger than the length and tension thresholds observed during the stretch phase as seen in Fig. 9.

During the stretch phase, past the activation threshold of the ligamento-muscular reflex, the EMG gradually increased to the peak and then gradually decreased during the relaxation phase. It was clear that increasing length and tension in the ligament required an increase in muscular force in order to sustain joint stability. This emphasized the synergistic relationships of ligaments and muscles in maintaining that stability.

From Fig. 9, one can also see that as the frequency of the sinusoidal cycle increased from 0.1 Hz to 1.0 Hz, the length and tension thresholds of the reflex decreased (e.g. reflex was triggered earlier) during the stretch phase. During the relaxation phase, the length and tension thresholds increased (e.g. the reflex terminated earlier). Furthermore, as the stretch-release cycle frequency increased, the peak to peak EMG and its corresponding mean absolute value (MAV) increased as seen in Fig. 10, indicating that fast elongations of ligaments require much larger con-committant muscle force to maintain stability and minimize the potential risk of rupture. For fast ligament elongation, therefore, higher stiffness from the muscles protect the ligament from development of high tension and strain and potential rupture.

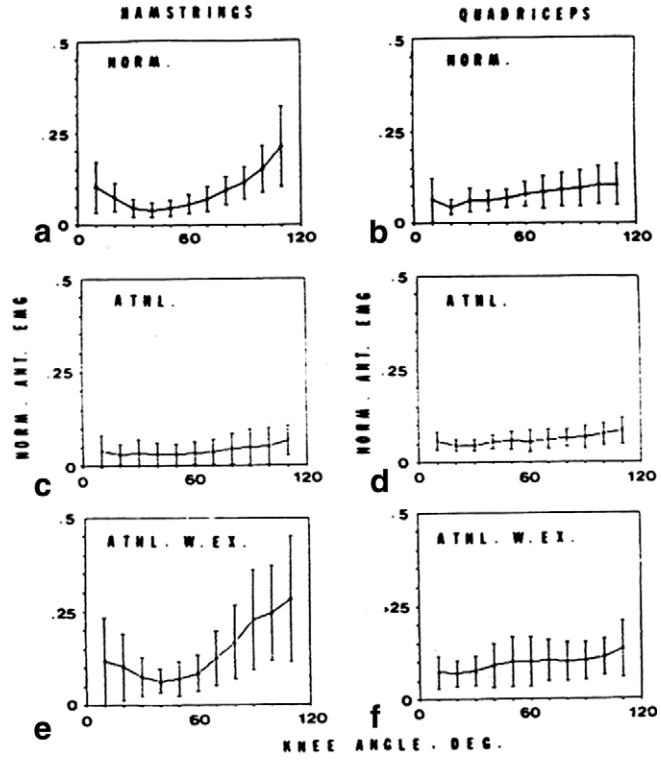

Fig. 8. The average normalized antagonist MAV versus knee angle for the hamstrings (a) and quadriceps (b) of normal subjects compared with the hamstrings and quadriceps MAV versus knee angle of verified athletes (c and d) and athletes who routinely exercise their hamstrings (e and f). The athletes had hypertrophied quadriceps, which resulted in inhibition of the hamstrings motor drive (EMG) when extension movement was performed (see c versus a and e). Quadricep coactivation patterns of normal subject group and athletes were nearly identical. The vertical bars at each data point represent the standard deviation from the mean of all subjects tested in that category.

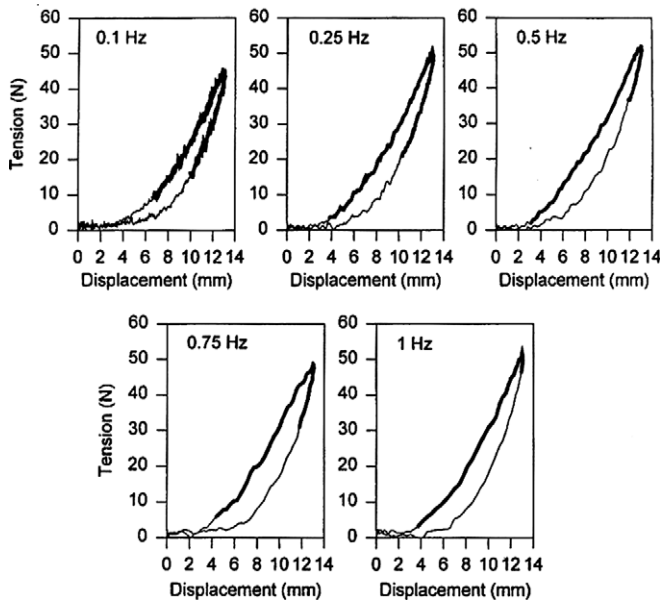

Fig. 9. Typical hysteresis curves where the tension versus displacement of a single cycle at each of the frequencies employed is shown; the period where the EMG was recorded from its initiation in the stretch phase to its termination in the release phase is designated in boldface on the curve.

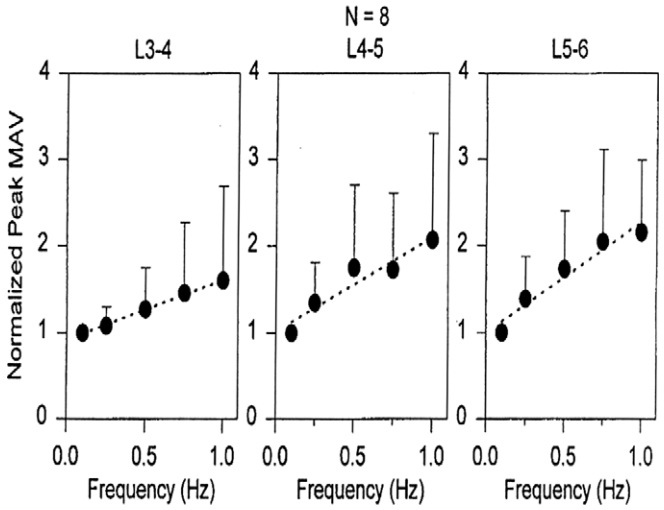

Fig. 10. The mean (±SD) of the peak MAV of the EMG is shown as a function of frequency, demonstrating that progressively stronger muscle contraction was associated with increasing cycle frequency.

Finally, when the ligament was exposed to continuous sinusoidal stretch-relaxation cycling, the reflex trigger thresholds increased and the termination threshold increased as well. The peak EMG amplitude decreased. In essence, prolonged exposure of ligaments to cycling stretch results in laxity and hysteresis accompanied with substantial decrease in the duration and magnitude of the reflexively activated muscular forces, exposing the ligament to increasing potential risk for injury. This was the early sign that prolonged cycling activity of ligaments is associated with risk of injury and/or a neuromuscular disorder, which will be fully addressed later.

6. Ligaments and the flexion-relaxation phenomena

Assessment of spinal function, as it relates to the lumbar region, in flexion-extension requires knowledge and ability to document the flexion-relaxation phenomena. This phenomena consists of active EMG recorded from the paraspinal muscles as anterior flexion begins. The EMG amplitude gradually decreases as flexion progresses and reaches a complete silence at or near 45– 50° flexion. The EMG silence persists through deep flexion and the initial range of extension. At mid-extension the EMG reappears and increases up to full extension (Ahern et al., 1988; Allen, 1948). The current understanding is that the upper body mass, when subjected to the effect of gravity, as it moves into flexion, requires counter resistance from the paraspinal muscles to prevent free collapse forward. As flexion progresses, the posterior ligaments (supraspinous, intraspinous, posterior longitudinal, and dorsolumbar fascia) elongate and develop tension. At some angle, in mid-flexion, the tension developed in the posterior ligaments exceeds the required counter force, allowing the muscles to relax. Further flexion is associated with contraction of abdominal muscles to overcome the increasing forces in

the posterior ligaments. Overall, the process is a load-sharing phenomena between posterior muscles, posterior ligaments, and abdominal muscles.

Since during flexion the posterior ligaments stretch, one would expect that the mechano-receptors within these tissues will be stimulated and trigger paraspinal muscles contraction to reduce the load in the ligaments. In fact, the opposite occurs; increased stretch in the ligaments during deeper flexion is associated with EMG silence. This immediately points out that perhaps the inhibitory component of the ligamento-muscular reflex is active in the flexion-relaxation process.

We conducted a series of experiments to assess the role and function of the ligamento-muscular reflex in the flexion-relaxation phenomena (Olson et al., 2004, in press, submitted for publication). In order to offset the effect of gravity, the same subject group was assesses while performing flexion-extension from erect posture and from the supine position (e.g. sit-ups). The results demonstrated that in the sit-up position, the flexion-relaxation in the paraspinal muscles disappeared and a similar pattern of activity (initial EMG activity and silence about the $\pm 90°$) was observed in the abdominal muscles. The conceptual conclusions point out the demand for dealing with the internal moments (generated by body mass and its orientation to the gravity vector) dictates the pattern of muscular activity in strength, timing and which muscles. From the reflexive standpoint, this is the first indication that the ligamento-muscular reflex is substantially modulated by the spinal and possible higher sensory and motor neurons of different systems (proprioceptive, vestibular, etc.) to yield excitatory or inhibitory responses. The mechanical requirements to execute the intended movement, therefore, are governing the ligamento-muscular reflex response pattern.

In the latest report (Olson et al., submitted for publication), passive flexion extension was executed with the aide of an active dynamometer. The dynamometer supported the body mass throughout the movement. Surprisingly, muscular activity was not observed in any of the anterior or posterior muscles. The results support the assertion made in the previous paragraph, e.g. there was no need to support internal or external moments (since the dynamometer took care of all movements), and the reflex did not trigger any muscular activity.

A tentative, and very fascinating, conclusion is that the ligamento-muscular reflex is much more complex than a hard-wired neurological process which triggers or suppresses muscles responses upon stretch of the ligaments. The reflex is governed by a complex neural network taking into account joint stability, internal mass and its implication in light of movement velocity and acceleration, orientation to gravity, etc.

Evidently, much is left to study on the interactions of the various components and internal or external factors associated with the ligamento-muscular reflex. It is not a simple reflex by any stretch of the imagination.

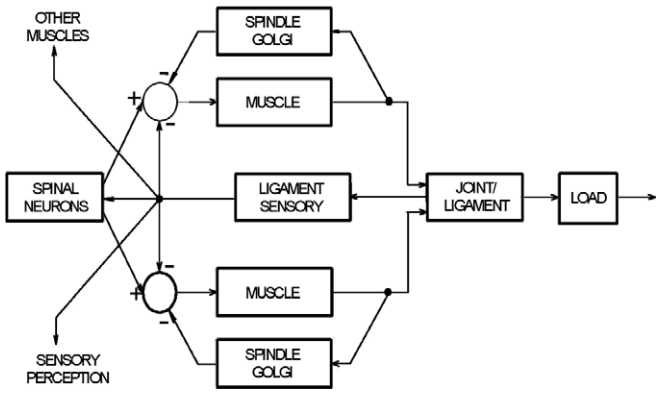

Fig. 11. A control diagram of the forward and feedback components of a joint including the muscles, ligaments, and spinal projections.

From the system viewpoint, one can draw the simplified diagram of Fig. 11 representing the interaction of ligaments and the motor control of a joint.

Reconsidering the mechanical properties of the ligaments; e.g. creep, tension–relaxation, hysteresis, etc. one can predict from the control diagram of Fig. 11 that several types of neuromuscular disorders can develop with time when performing occupational and sports activities. Similarly, an injury or rupture of a ligament could be assessed as a cause for a neuromuscular syndrome.

7. Clinical implications

Indeed, in the early 1980s, a large number of patients with anterior cruciate ligament (ACL) rupture underwent a surgical repair with a synthetic or autograft from part of the patellar tendon. In both cases, the initial results were encouraging, demonstrating a measure of restored stability in the knee. Overtime, however, it was observed that the implanted ligament became lax; that the quadriceps tended to atrophy in many patients; that muscular desynchronization due to the rupture could be restored with physical therapy, and that with time, the patients developed osteoarthritic knees. Overall, conflicting and misunderstood responses were accumulating, indicating that ACL injury is not an isolated deficit but most likely a complex syndrome.

With the help of Fig. 11, one can attempt to gain insight to the logical chain of events that were observed clinically.

1. Rupture of the ACL, even if repaired surgically, can leave a sensory perceptive (kinesthetic) deficit since the afferents in the ligaments are not functioning (ruptured or surgically removed). Indeed, Skinner and Barrack (1991) demonstrated that patients with ACL rupture demonstrated deficiency in kinesthetic perception; e.g. perception of the knee angle was deficient. Such a sensory deficit can be a harbinger of additional damage/injury to the knee when going up or down stairs, playing sports and performing occupational activities. Indeed,

many ACL deficient patients of that time were reporting with secondary knee injury incurred during demanding daily activity.

2. Quadriceps atrophy was commonly observed in ACL deficient patients. The natural response of orthopaedic surgeons and physical therapists was to subject the patient to a quadriceps strengthening program for several weeks to reverse the degeneration. Often, the patients with the now more powerful quadriceps were subjected to additional injury or increased episodes of instability.

   A part of the syndrome, quadriceps muscles at their normal strength can generate forces that increase anterior tibial translation and with the absence of an ACL also cause an anterior knee subluxation (Hirokawa et al., 1991, 1992). It seems that while the ligamento-muscular reflex in normal subjects excites the hamstrings in the range of motion from 60° flexion to full extension, it also inhibits the quadriceps muscles from exerting very large forces, preventing subluxation. The concept of muscular inhibition attracted little attention in the motor control field, but its implications are highly significant for joint stability. The quadriceps is apparently inhibited, in the normal subject, from generating its true maximal forces such that knee stability and overloaded ACL are prevented. In the ACL deficient patient the inhibition is substantially larger since the sensory ACL function is missing. In such conditions, even moderate quadriceps force in the range of 65° to full extension can subluxate the tibia. The weighted control of the ACL reflex seems to inhibit the quadriceps as necessary for the performance of the movement at hand. With its absence, however, deep inhibition occurs, probably via spinal networks. One can conclude that in addition to the excitatory reflex from ligaments to muscles, there is also an inhibitory ligamento-muscular reflex and that was shown in human subjects by Dyhre-Poulsen and Krogsgaard (2000), Solomonow and Krogsgaard (2001), Williams and Brance (2004), and Voigt et al. (1998). The overall objective of the inhibitory and excitatory ligamento-muscular reflex is to provide a stable and safe joint motion.

   The quadriceps strengthening program implemented in the period prior to 1987 was a contraindication as it increased the risk of sublaxation and the potential of new injury. In our report of 1987 (Solomonow et al., 1987), we concluded that hamstring strengthening is most beneficial in the early phase of ACL deficient patients rehabilitation, as it will increase the co-contraction level from the hamstrings, improve knee stability and allow increased force production from the quadriceps later on (Solomonow et al., 1989).

3. Muscular balance of the hamstrings and quadriceps, agonist and its antagonist, is therefore, one of the most important aspects in maintaining knee stability and preservation of the healthy, functional ACL. One important component in balancing an antagonist muscle pair of a joint is the sensory role of ligaments via their inputs to the spinal motor units in an excitatory and/or inhibitory mode.Indeed several groups managed to demonstrate that with an appropriate physical therapy program, advocating muscle re-education, ACL deficient patients could be successfully rehabilitated with conservative treatment (Giove et al., 1983; Steiner et al., 1986).

4. The implications of muscular imbalance or synchronization on the gait of patients with ACL damage was repeatedly reported in the literature (Hasan et al., 1991; Sinkjaer and Arendt-Nielsen, 1991), and increased quadriceps activity was observed in our research with normal subjects whose ACL was statically stretched and developed creep (Chu et al., 2003; Sbriccoli et al., 2005).

   In such circumstances, the ACL was intact, yet the laxity developed due to the creep prevented the mechanoreceptor within the ligament from properly firing at the appropriate threshold and inhibiting the quadriceps during maximal voluntary extension. It seems that rupture of the ACL, for example, can increase the inhibition imposed on a muscle, whereas stretched or lax ACL decreases the inhibition. The exact neural mechanism of the two phenomena may need further study, yet it is clear that the sensory-motor functions of the ligament plays a major role in both phenomena.

8. Neuromuscular disorders associated with ligaments

So far, neuro-muscular disorders associated with a complete rupture of a ligament: e.g. desynchronization of agonist – antagonist activity, changes in the natural inhibition of muscles, muscular atrophy, deficient kinesthetic perception and deficient gait were delineated.

In recent years we embarked on the assessment of neuromuscular disorders associated with an intact ligament, yet subjected to continuous activity such as found in many occupational and athletic environments. Indeed, in the occupational field, non-specific low back disorders/pain is one of the most common medical problems and is a costly problem from the standpoint of the loss of work, medical treatment, and cost to government and industry, etc. The diagnosis and treatment of such non-specific low back disorder or as it is also known as Cumulative Trauma Disorder (CTD) are poorly developed and/or understood (NAS, 2001).

The epidemiology, however, clearly establishes the relationship between static and repetitive (cyclic) work activities and CTD. Biomechanical or physiological validation of the epidemiology is lacking especially experimental validation.

A set of experiments imposing alternating periods of static and/or cyclic load on the lumbar supraspinous ligaments yielded a wealth of new information (Claude et al., 2003; Courville et al., 2005; Gedalia et al., 1999; Solomo-

now et al., 1999; Jackson et al., 2001; LaBry et al., 2004; Lu et al., 2004; Navar et al., in press; Sbriccoli et al., 2004a,b, 2005, in press; Solomonow et al., 2003a,b,c; Williams et al., 2000):

A. Substantial creep developed in the ligament within six periods of 10 min of load spaced by 10 min of rest. A continuous rest period of up to 7–8 h after the six work and rest sessions are not sufficient for the ligament to recover its original length and stress-strain condition. As seen in Fig. 12, the work periods display gradual decrease of reflexive EMG, spasms and cumulative creep. The long rest periods is characterized with initial hyperexcitability in muscle activity and very long recovery of the creep towards the return of the ligament to its original resting length and normal length–tension relationship. Several important issues should be addressed:
   - As the creep causes laxity in the ligament, the thresholds at which the ligamento-muscular reflex is triggered as well as kinesthetic perception change. The feedback signal (see Fig. 11), therefore, is corrupted and results in false perception and lower level activation of the muscles.
   - False kinesthetic or proprioceptive perception introduces errors in the precision of movements and may result in an accident or injury.
   - The decrease in muscular activity elicited by the ligamentous reflex also decreases the normal stiffness and stability of the lumbar spine, exposing it to increasing risk of injury.
   - The long recovery period (over 24 h) required to restore normal ligament operation renders the lumbar spine to prolonged function with decreased protective capacity and increased exposure to injury.

Therefore, an acute or transient neuromuscular disorder exists after a moderate work period during which an increased exposure to injury is present due to ligament laxity, reduced muscular activity and false sensory perception. The origin of this acute/transient disorder is in the creep/laxity of the ligament and its sensory-motor (neuromuscular) implications are due to the corrupt feedback signals from the sensory receptors within the ligaments.

B. It was also shown that several loading components have a critical impact on the development of an acute inflammation in the ligament.
   - Decreasing the rest period between each 10 min work session from 10 min to 5 min.
   - Increasing the number of repetitions from six to nine sessions.
   - Increasing the load from low or moderate to high load within the physiological range.
   - Increasing the work/load duration to sustained periods over 30 min.

All of the above factors elicit an acute inflammation in the ligament (Solomonow et al., 2003a). The neuromuscular component of the acute inflammation phase, observed 2–3 h after the load/rest session is a significant hyperexcitability of the musculature lasting for several hours. Since workers are required to return the work the next day, the

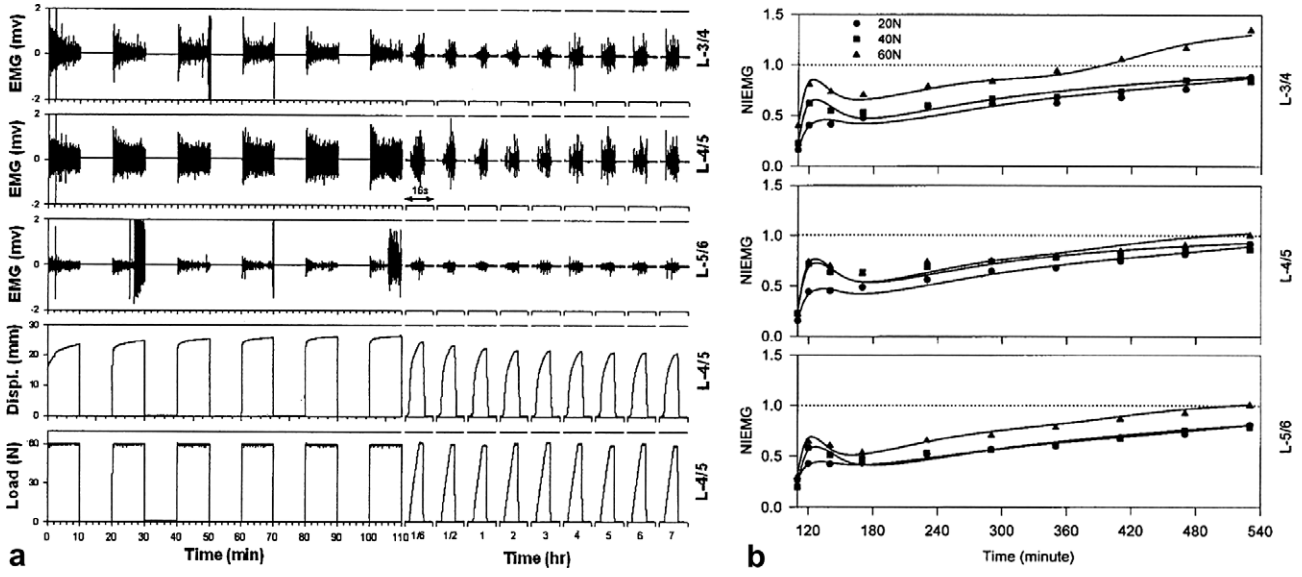

Fig. 12. (a) A typical recording of EMG from the L-3/4, L-4/5, and L-5/6 level (top three rows) as well as lumbar displacement and static load (bottom) recorded from one preparation subjected to a 60-N load. Note the large-amplitude spasms that are superimposed on the gradually decreasing EMG during different 10-minute static load periods. The time axis marked in units of hr. indicates the 7 h recovery period during which short samples of 12 s loading was applied to assess recovery of creep and EMG. (b) The mean NIEMG data and the developed models for the 7 h recovery period are shown superimposed for 20-, 40-, and 60-N loads. Note that the EMG for the 60-N load exceeds unity, indicating hyperexcitability development.

acute inflammation does not have sufficient rest period to heal the damage (micro-ruptures in the collagen fibers), the tissue is exposed to additional stretching and damage, and with continued exposure, develops chronic inflammation. In Fig. 13, samples of ligaments with inflammatory symptoms as evidenced by wide spread of neutrophils is compared to a control sample with few spontaneous neutrophils. The presence of neutrophils infusion in the ligament was always associated with a delayed hyperexcitability.

Chronic inflammation is not a medically treatable injury, is degenerative (results in conversion of ligament fibers to fibrous tissue) and is associated with pain, loss of muscular force (weakness), reduced range of motion of a joint and muscle spasms (Leadbetter, 1990). CTD is an overuse injury where the ligamentous tissues become chronically inflamed resulting in permanent disability (Leadbetter, 1990; Solomonow et al., 2003a).

Additional important observations were made. The work to rest ratio of 1:1 was observed to be a good rule to follow in order to prevent or attenuate the development of acute inflammation. This ratio, however, remained limited to durations of work and load up to 30 min (e.g. 10 min work: 10 min rest, 20 min work: 20 min rest, and 30 min work: 30 min rest). Tests at 60 min work and 60 min rest resulted in acute inflammation. Long work periods cannot be implemented without avoiding damage even if equal duration rest is allowed.

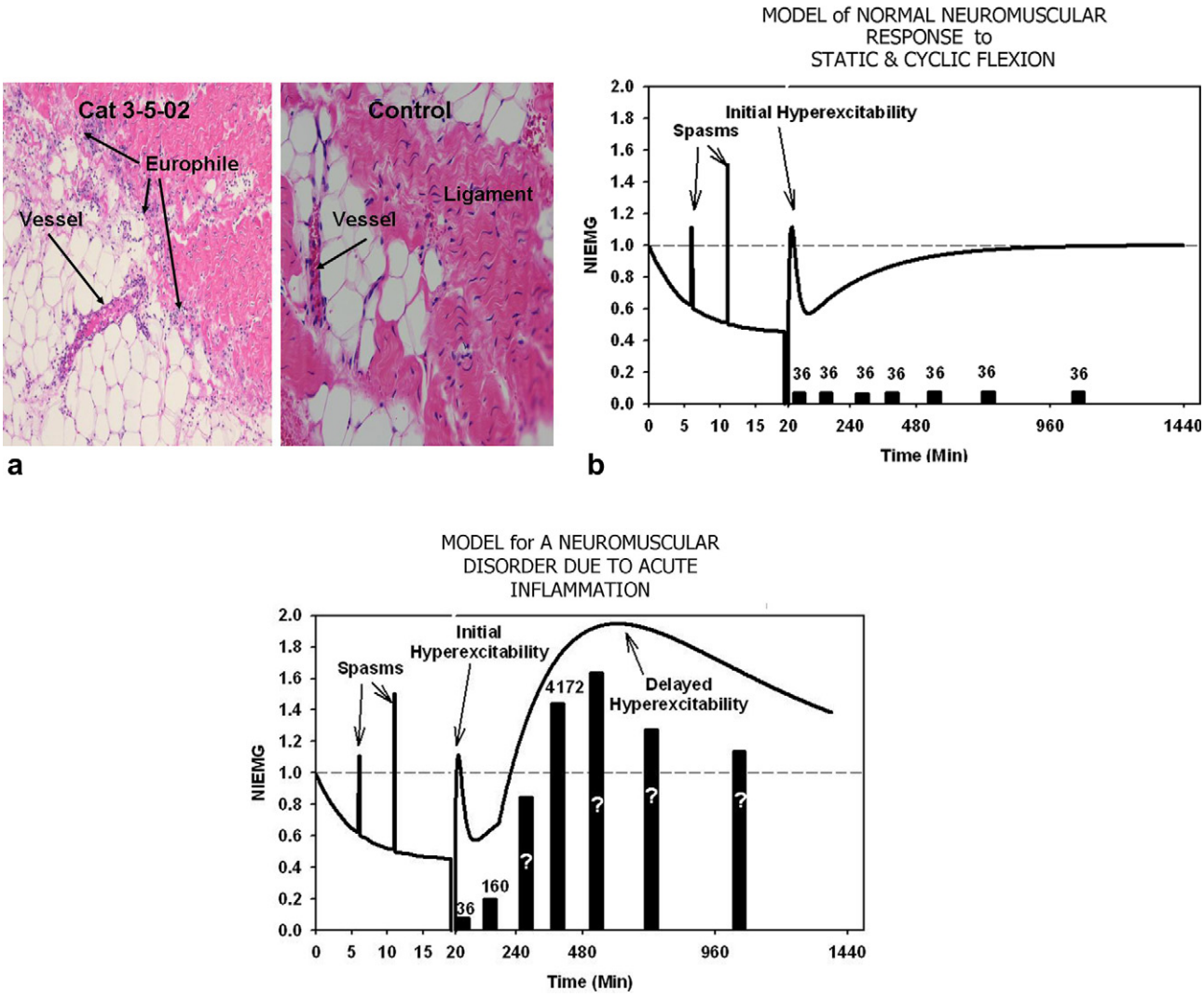

Fig. 13. (a) On the right is a slide showing the density of neutrophils in a ligament from the control group, not subjected to creep. Only spontaneous neutrophils appear. On the left is a slide showing the neutrophil density in a ligament subjected to overstimulation. The density is over 4000/mm^2 as opposed to 36/mm^2 in the control ligament. Note the higher magnification on the right slide. (b) A graphical presentation of the neuromuscular disorders model in a case where the risk factors load, load duration, load to rest ratio and repetitions were below the risk level. Note that during the recovery phase the NIEMG slowly recovers to its normal while the neutrophil density remains low and steady. (c) A graphical presentation of the neuromuscular disorder in a case where the risk factors exceeded the risk threshold triggering a delayed hyperexcitability associated with acute inflammation as expressed by the simultaneously rising neutrophil density in the ligaments. The question marks indicate time segments for which data is collected currently whereas the completed data is given by the number of neutrophils per mm^2.

An acute neuromuscular disorder associated with the creep of the ligament over time is therefore present and consists of reduced muscular activity as work goes on (and decreased spinal stability), development of spasms and the micro-fractures in the collagen fibers increase, significant increase in muscular activity 6–7 h after the work is completed and its association with acute inflammation. Such an acute neuromuscular disorder is the first step leading to chronic inflammation, and this phase should be avoided in any work or sports activity where a few days rest cannot be allowed. The long-term implications of inflammation and the associated neuromuscular disability are currently under intense investigations in our laboratory.

9. Model of neuromuscular disorder

Based on the large number of experiments on the spinal ligamento-muscular response to static and cyclic loading (or flexion-extension) we developed a model that can predict the neuromuscular response to a set of work and rest sequences. From the model, a determination could be made if a delayed hyperexcitability is present and in turn an acute inflammation. The model, therefore, can be useful in the assessment of risk factors (load magnitude, load duration, rest duration, load to rest duration ratio and loading repetitions) or their absence in a given work protocol. Safe work protocols could be designed also using the model.

The choice of the model was based on the physiological and biomechanical properties of the tissue in question, e.g. the ligament. It is well established as a viscoelastic element with responses accurately estimated by exponential equations. During lumbar flexion-extension or knee flexion-extension, the overall response is not that of a single ligament but that of several ligaments, the cartilage, capsule and in the spine also the discs and facet capsules. These different collagen tissues are all viscoelastic, yet the proportion of viscosity and elasticity is different in each one. The disc, for example, contains gel, a fluid, in its internal space, and therefore is more viscous than the supraspinous ligament or the longitudinal ligaments. A good model, therefore, should include bi or tri exponential components to describe the viscoelasticity of each of the various collagen tissues in order to provide accurate output (Solomonow et al., 2000).

The original model (Solomonow et al., 2000), therefore, included bi-exponential description of the displacement of the lumbar spine due to static or cyclic flexion. One component was utilized to describe the exponential elongation/deformation due to fibrous collagen tissues such as ligaments, facet capsule, dorsolumbar fascia, etc. whereas the second component was used to describe the exponential deformation of the lumbar discs which contain significantly more viscosity. The two components are exponential, yet the time constants and coefficients are largely different. The constructed model was successfully used to describe experimental data with high accuracy.

Furthermore, since the reflexive EMG was elicited by the deformation of the viscoelastic tissues, it was assumed to follow its deformation pattern; e.g. exponential decrease. That was executed, also with high accuracy. However, one issue that deteriorated the accuracy of the EMG model was the spontaneous, unpredictable spasms that occurred during the loading periods and also during the following recovery. Since the spasms varied widely in their amplitude and appeared at any time during loading without any predictable pattern, it is impossible to model this phenomenon. The spasms being superimposed on the predictable decrease of reflexive EMG due to viscoelastic deformation introduced an unavoidable inaccuracy in the model, yet allowed the general pattern of the EMG to emerge fairly clearly.

Therefore, the model developed provides good estimates of the deformation of the viscoelastic tissues during the development of creep and its recovery with rest. Similarly, the reflexive muscular activity was estimated well during the loading and rest periods. The spasms, however, should be distinctly noted but lacked representation in the model.

In our model, we simplified the equation in order to obtain a general conceptual behavior of the ligamento – neuromuscular responses. Yet, the accuracy can simply be optimized if one wishes, just by adding additional components representing the tissues at hand.

Model: The model considered is based on our previous work where continuous 20-minute static load was followed by a 7-hour recover period (Solomonow et al., 2000, 2003d; LaBry et al., 2004; Courville et al., 2005; Claude et al., 2003).

The Normalized Integrated EMG (NIEMG) during the cyclic loading period was described by Eq. (1) as follows:

$$\mathrm{NIEMG}(t) = A\mathrm{e}^{-t/T_1} + \mathrm{NIEMG}_{ss} \tag{1}$$

where NIEMG_{ss} is the steady state amplitude, A the amplitude of the exponential component, T_1 the time constant of the exponential component, and t is the time.

Correspondingly, the NIEMG during the long-term recovery was modeled by the following equation as:

$$\mathrm{NIEMG}(t) = tB\mathrm{e}^{-t/T_2} + E(1-\mathrm{e}^{-t/T_3}) + C(t-T_\mathrm{d})\mathrm{e}^{-(t-T_\mathrm{d})/T_4} + \mathrm{NIEMG}_{ss} \tag{2}$$

where B, C, and E are the amplitudes of the three terms; $tB\mathrm{e}^{-t/T_2}$ represents the initial hyperexcitability, which decays within one hour while reaching its peak in the first 10 min; $C(t-T_\mathrm{d})\mathrm{e}^{-(t-T_\mathrm{d})/T_4}$ represents the delayed hyperexcitability; this term is initiated during the rest period, mostly after the second hour of rest, with no effect in the first 2 h; $E(1-\mathrm{e}^{-t/T_3})$ represents the steady state recovery; this term is a slowly rising exponential throughout the rest period; T_d the time delay associated with the initiation of the delayed hyperexcitability; and NIEMG_{ss} is the steady state amplitude as defined in Eq. (1).

In order to convert Eqs. (1) and (2) to describe a series of work periods spaced by rest periods; two new components are defined:

T_W is the time period over which load was applied to the spine.

T_R is the period of rest between any two work periods (T_W).

n is the number of work periods.

Eq. (1) describing the NIEMG behavior during each of the work periods is rewritten as Eq. (3):

$$\mathrm{NIEMG}(t) = A_n \mathrm{e}^{\frac{-[t-n(T_W+T_R)]}{T_{n_1}}} \Bigg|_{n(T_W+T_R)}^{(n+1)T_W+T_R} + \mathrm{NIEMG}_{ss} \quad (3)$$

It was assumed that A and $\mathrm{NIEMG}_{ss}$are not constant throughout the work/rest periods and are changing from one work period to the next.

Furthermore, it was assumed that T_1 might not be the same for all the work periods.

Since this study uses only 10 min of rest, the first transient component of Eq. (2) will be dominant and the steady state component contribution as well as the delayed hyperexcitability term could be neglected for this particular case. During the rest periods, therefore, the modified Eq. (4) is as follow:

$$\mathrm{NIEMG}(t) = (t-[(n-1)T_W+nT_R]) \times B_n \mathrm{e}^{\frac{t-[(n+1)T_W+T_R]}{T_{n2}}} \Bigg|_{(n+1)(T_W+nT_R)}^{(n+1)(T_W+T_R)} + \mathrm{NIEMG}_{ss} \quad (4)$$

It was also assumed that the amplitudes of NIEMG_{ss} and B will vary from one rest period to the next and that T_2 may vary as well. The graphical representation of the model after being subject to non-inflammatory and inflammatory workloads is shown in Fig. 13b and c, respectively.

Similarly, the equation describing the development of displacement, a reflection of creep of the viscoelastic tissue, during a series of work periods spaced by rest periods is given by the following equation:

$$\mathrm{DISP}(t) = \left[D_{0n} + D_{Ln}\left(1-\mathrm{e}^{-\frac{[t-n(T_W+T_R)]}{T_{n5}}}\right)\right] \Bigg|_{n(T_W+T_R)}^{(n+1)T_W+nT_R} \quad (5)$$

where DISP(t) is the displacement as a function of time, D_{0n} the elastic component of amplitude, D_{Ln} the viscoelastic component of amplitude, and T_{n5} is the time constant governing the development of creep during flexion.

The recovery of the displacement during the rest periods is described by the following equation:

$$\mathrm{DISP}(t) = \left[D_{0n} + R_n + (D_{Ln}-R_n)\mathrm{e}^{-\frac{t-[(n+1)T_W+nT_R]}{T_{n6}}}\right] \times \Bigg|_{(n+1)T_W+nT_R}^{(n+1)(T_W+T_R)} \quad (6)$$

Such that R is the residual creep at the end of each rest period and T_{n6} is the time constant governing the recovery of creep in each rest period.

Again, D_0, D_L, and R were assumed to be a variable from one work/rest session to the next. T_{n5} and T_{n6} were also assumed to vary from one session to the next.

The long-term recovery after the work/rest session was modeled by Eq. (2).

Once the mean ± SD of the experimental data were calculated, attempts were made to generate the best fit models described above using the Marquardt–Levenberg non-linear regression algorithm; in some cases, the algorithm failed to converge satisfactorily; in these cases, initial and/or final values were arrived at by sequential recursive iteration, optimizing for regression coefficient.

10. Verification in human subjects

The research conducted on CTD development was carried out on the feline. Two distinct projects were conducted using human subjects in order to confirm that such neuromuscular disorders can be elicited in humans from the same or similar mechanical inputs (e.g. high loads, high number of repetitions, short rest, etc.). One project examined the responses of the lumbar paraspinal muscles to periods of static and cyclic flexion (Solomonow et al., 2003a; Olson et al., in press). The second project assessed the response of the ACL of human subjects to static and cyclic loads (Chu et al., 2003; Sbriccoli et al., 2005).

Spasms in the muscles and significant changes in muscular synchronization was observed after static and cyclic activity of the spine and the knee (see Figs. 14 and 15) confirming the development of an acute disorder. For safety purposes, the work or load was limited to mild exertion or short duration, yet it is evident that adverse functional changes are elicited.

The results in both projects reveal that similar response to those obtained in the feline are observed from normal, healthy subjects subjected to mild static or cyclic (repetitive) activity. Furthermore, similar behavior could be obtained from the ligaments of the lumbar spine and the ACL of the knee.

Recently, additional confirmation that static and cyclic lumbar flexion in humans elicits a neuromuscular disorder similar to those depicted in the feline model were reported by Granata et al. (2005), Rogers and Granata (2006), Dickey et al. (2003), Kang et al. (2002), McGill and Brown (1992), and Shultz et al. (2004).

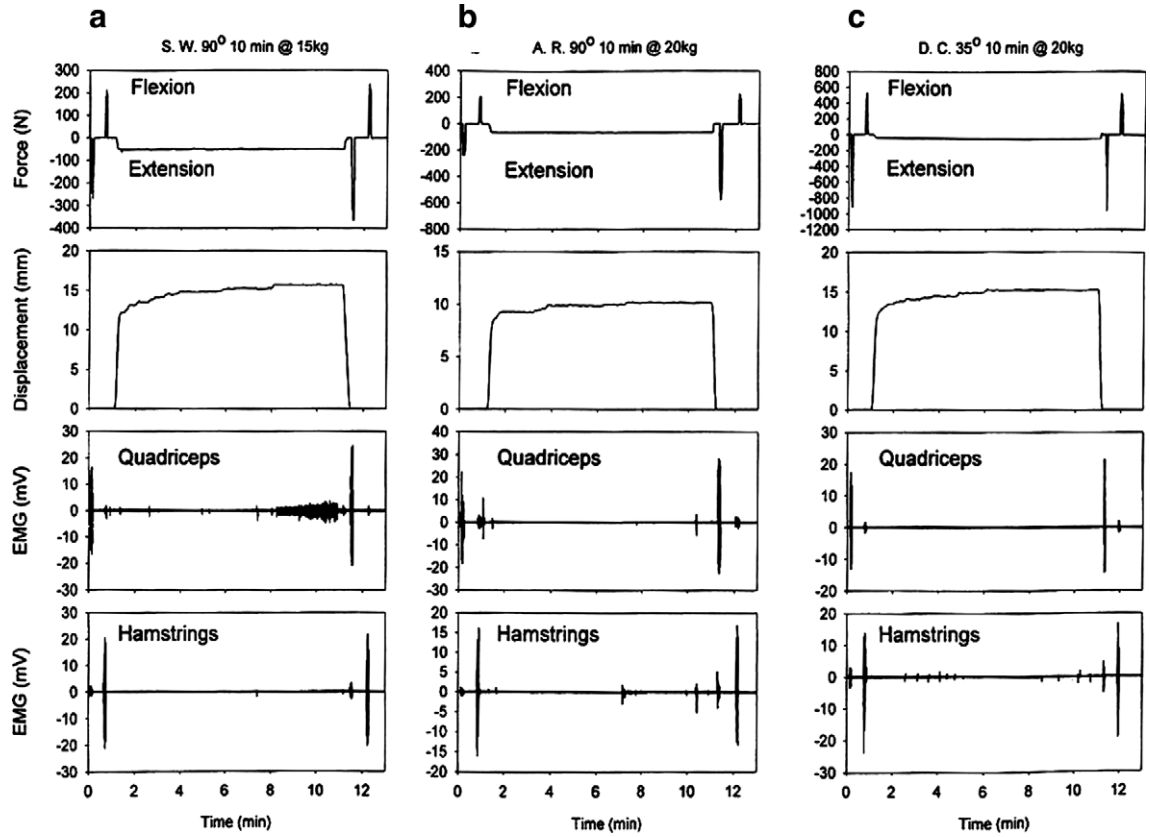

Fig. 14. (a–c) Three typical recordings from three different subjects at 90° and 35° knee angle showing the extension and flexion MVC forces before and after the 10 min loading session (top trace), the anterior displacement of the tibia during the 10 min loading period (second trace from top), quadriceps EMG (third trace) and hamstring EMG (bottom trace). Note the strong continuous burst of spasms in the quadriceps EMG trace of (a) from the 8th minute to the 11th minute. Similarly, in (b), two bursts of spasms are seen, one at about the 7th minute and the second just after the 10th minute, with a corresponding spasm in the quadriceps. IN (c) short bursts of spasms are seen in the hamstrings EMG throughout the 10 min loading period. Note the large increase in quadriceps force at MVC (negative peak) after the 10-minute period of loading the ACL.

11. Translational research – clinical applications

As most research, the ultimate benefit of many years of wondering in the different highways and alleyways of basic and applied medical investigations is some modicum of practical improvement of medical care offered to the patient population, and the associated improvement of the patients lifestyle. Preventive measures are also significant and beneficial.

The lesson we learned so far tells us that in order to maintain knee stability, weighted posteriorly directed force has to be applied to the tibia in the appropriate range of motion. Such a force comes from the ACL in the intact human in the range of motion of 60° flexion to near full extension. Furthermore, such force is not coming exclusively from the ACL, but also from the hamstrings via the ACL-hamstrings reflex. In the ACL deficient patient, the ACL tension is absent and so is the contribution of the hamstrings. In order to allow as close a function to normal as possible, any external device, e.g. orthosis, needs to supply such forces.

In 1983, we surveyed the available knee braces to ACL deficient patients as well as the literature evaluating them. It was clear that most braces consisted of thigh/calf uprights and a knee joint with some connecting members or straps. A posteriorly directed force in the appropriate range of motion was not provided by the braces and the literature evaluating the braces confirmed that they had little impact, if any, on knee stability as required.

We developed a new knee brace (US Patent No. 4,781,180) which incorporated mechanical programmable bilateral levers connected to an anterior retaining strap placed over the proximal tibia as shown in Fig. 16a. The mechanical programming was provided by the knee joint such that at near 60° flexion the levers were activated and developed a constant or gradually increasing posteriorly directed force to the proximal tibia throughout full extension. This ''Smart Brace'', therefore, provided the knee with a similar function of the absent ACL.

In its commercial phase, the ''Smart Brace'' was available from the Bledsoe Brace System (Grand Prarie, Texas) and was consequently evaluated by Acierno et al. (1995). It was found, as shown in Fig. 16b, that ACL deficient patients could generate isokinetic maximal voluntary extension effort throughout the full range of motion with significantly increased quadriceps activation and without

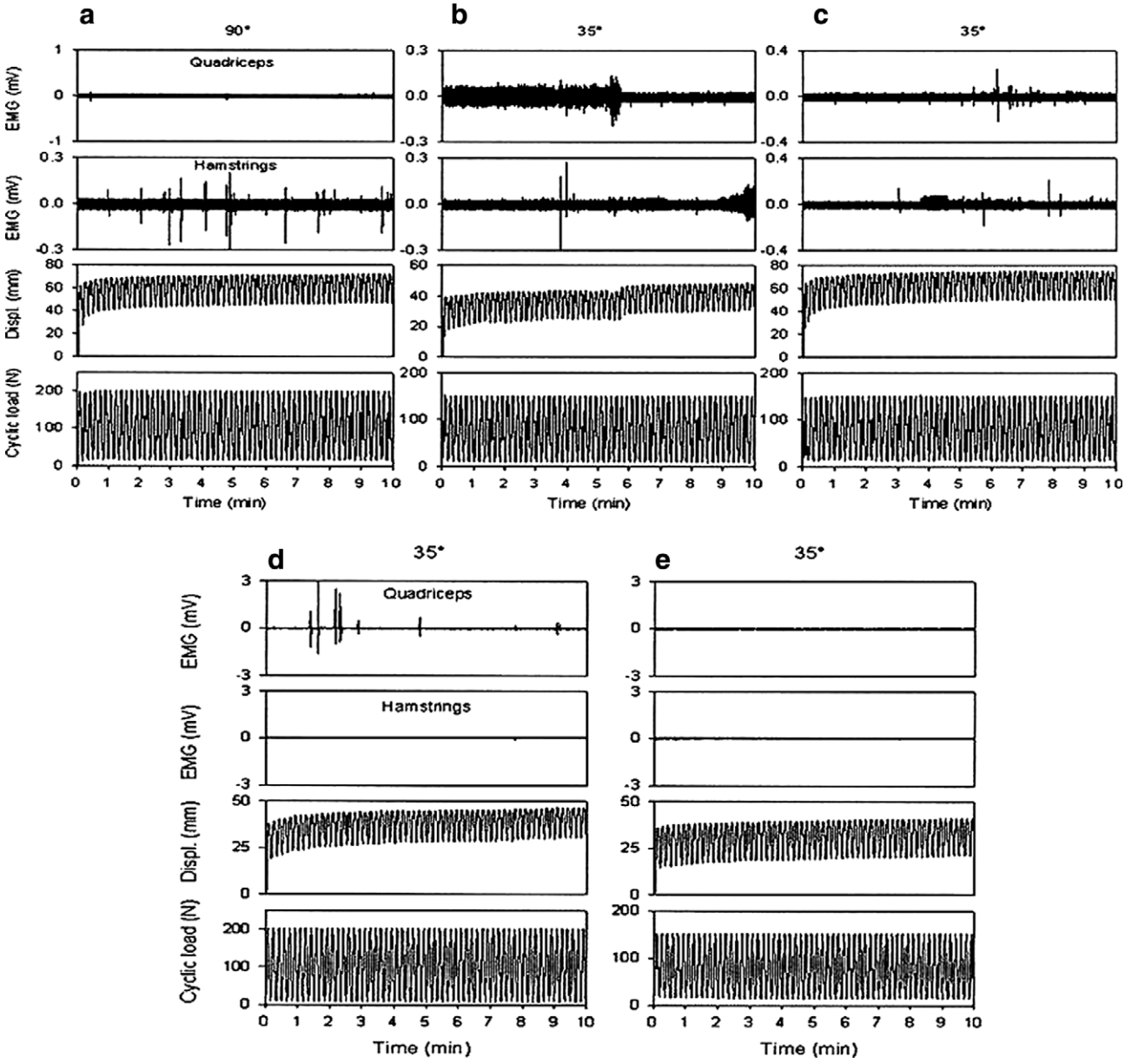

Fig. 15. (a–e) Five typical recordings from five different subjects exposed to cyclic loading of the ACL for 10 min at 90° and 35°. IN the top 2 traces, the EMG recordings from quadriceps and hamstrings during the 10-minute cycle are shown. The two bottom traces represent the anterior tibial displacement and the cyclic load, respectively. Note the presence of EMG spasms in both the quadriceps and hamstrings (a–d). An example with no reflex EMG activity is also reported (e). Displ, displacement.

episodes of knee subluxation. A noticeable decrease in hamstrings co-activation was also noted, as it was not required. The "Smart Brace" found wide acceptance in clinics around the world and performed well, especially in the post-injury period and in daily life of patients with chronic episodes of knee subluxation secondary to ACL rupture.

One of the limitations of knee braces made of metal, plastic or composite materials is that their weight is applied to an inverted cone, the thigh. During activity, gravity tends to cause gradual migration of the brace to the lower leg and reduction in its effectiveness. One approach to prevent this problem is the tightening of the attachment straps to the limb. This, however, applied excessive pressure to the skin and occluded circulation resulting in discomfort and pain within a short duration of use.

A second generation of the "Smart Brace", an electronic version, was consequently developed and applied (US Patent No. 5,628,722). The new version consisted of a light weight elastic sleeve worn over the knee. A miniature electronic sensor monitored knee angle and triggered a muscle stimulator to deliver weighted activation of the hamstrings via surface electrodes incorporated in the elastic sleeve. The posteriorly directed force to the proximal tibia was delivered this time by the hamstrings which were activated in the desired range of motion. The results to date

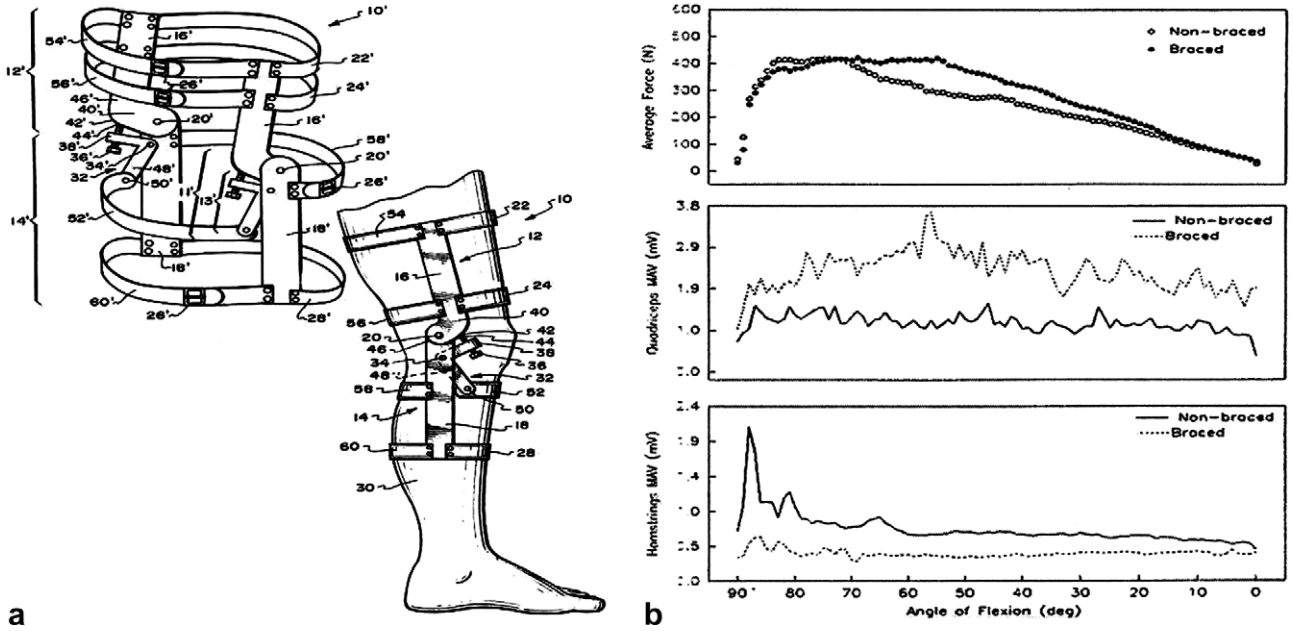

Fig. 16. (a) A schematic of a "Smart Brace" which generates a function similar to that of the ACL in the proper range of motion. (b) Average results from four trials for a symptomatic subject showing average force (top trace), quadriceps MAV, and hamstrings MAV (third trace) also as a function of joint angle. Note the increase in quadriceps MAV and the decreases in hamstring MAV when the brace is worn, demonstrating a return to normal muscle function due to the use of the brace.

demonstrate that the triggered coactivation of the hamstrings could be adjusted as necessary for the condition and convenience of the patient while preventing knee subluxation. An additional finding demonstrated that within a few days of use, a muscle re-learning occurs, with the spontaneous hamstrings coactivation is elevated to prevent subluxation even if the "Smart Brace" is deactivated (Fig. 17).

Similar conditions exist in workers engaged in repetitive (cyclic) or static activities of the lumbar spine. The ligaments and other viscoelastic structures of the lumbar spine become stretched or lax after a period of activity and the afferents within the tissues generate a significantly decreased or corrupted stimulus for activation of the ligamento-muscular reflex. The muscular activity which maintains lumbar stability decreases or becomes absent leaving the spine exposed to injury. A lumbar "Smart Brace" was

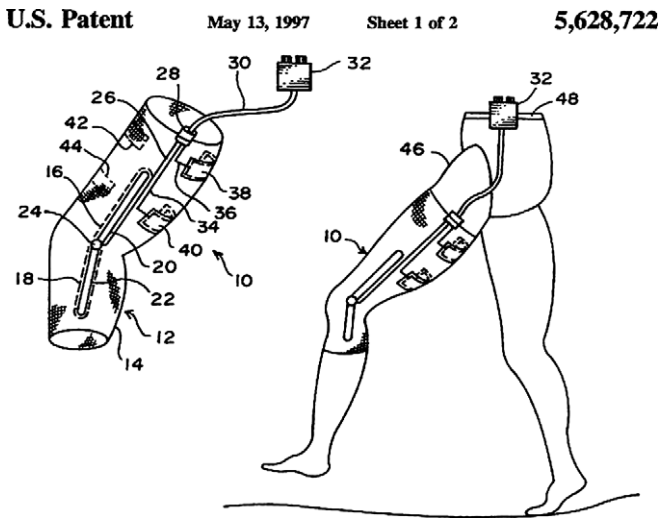

Fig. 17. A schematic diagram of the electronic version of the "Smart ACL Brace" where a sensor about the knee joint triggers surface stimulation of the hamstrings to prevent excessive anterior translation of the tibia and subluxation.

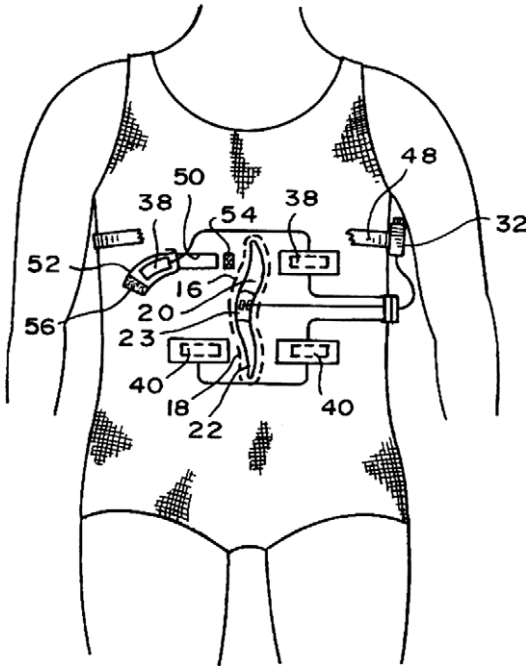

Fig. 18. A schematic of a lumbar electronic "Smart Brace" restoring muscular forces lost due to creep/laxity of the ligaments.

developed (US Patent No. 5,643,329) (see Fig. 18) and is in the stage of evaluation. The brace consists of an elastic garment commonly worn for dance or sport with miniature sensors over the lumbar spine. A muscle stimulator is activated by the sensors and the stimulus delivered via surface electrodes over the bilateral paraspinal muscles. The muscles contract in a weighted mode in the appropriate range of motion as we identified in the studies exploring the flexion-relaxation phenomena (Solomonow et al., 2003a; Olson et al., 2004, in press).

12. Conclusions

Ligaments are not passive tissue. From the sensory standpoint and from their sensory-motor function, ligaments are highly dynamic and non-stationary, yet predictable important organs. The inherent structure of ligaments and their response to static and cyclic loads, as found in work and sports activities, allow us to predict non-stationary behavior as expressed by creep, hysteresis, tension–relaxation, etc. These responses in turn, diminish activity of sensory perception and reflexive coordination of muscular activity such as excitation and inhibition and consequently reflect adversely on joint stability and movement.

The same stimuli or inputs can adversely affect the ligament when applied for long duration, large loads or repetitively without sufficient rest to result in an acute inflammation and its associated acute neuromuscular disorder. The acute disorder is the first stage, if not allowed to resolve with sufficient rest, of a chronic disorder which is devastating and non-reversible, inflicting misery and losses to society.

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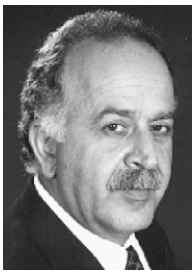

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IDEAS AND TECHNICAL INNOVATIONS

How old is your cervical spine? Cervical spine biological age: a new evaluation scale

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Abstract
Purpose This article aims at presenting a scale that, through the analysis of MRI images, clearly charts the various degenerative stages of the cervical spine and establishes its biological age. We have created this scale by summing together various scores linked to a selection of parameters according to which MRI images are analyzed.
Method We examined 423 cervical spine MRI scans, belonging to patients who had been admitted to the Medical Imaging Service of the Military Hospital of Rome between January 2010 and July 2011. We selected 6 parameters for the analysis of the MRI scans of the cervical spine: (1) the degeneration of the intervertebral discs, (2) the degeneration of the yellow ligaments, (3) the degeneration of the vertebral bodies, (4) the possible presence of spondylolistheses, (5) the presence or absence of foraminal stenosis, and (6) the diameter of the spinal canal. We assigned to each parameter a score system based on a graduated scale. The cervical spine physiological age can be determined by summing up the scores obtained for each parameter.
Results We submitted the data obtained from the study to a statistical enquiry. The results of the enquiry confirmed the suitability of the parameters selected for the evaluation of the aging process of the cervical spine.
Conclusions The effectiveness of the various treatments for cervical spine degenerative disorders is influenced by the overall anatomical conditions of the cervical spine. Up until now there has been no objective criterion for the evaluation of these anatomical conditions. We believe that this scale will be a useful tool to homogenize retrospective studies and to correctly set up prospective studies on the degenerative conditions of the cervical spine and relative treatments.

Keywords Biological aging · Cervical spine · Spinal disease · MRI · Intervertebral disc · Myelopathy

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Introduction

Many scientific papers [1–4] have shown that degenerative cervical spine disorders are closely linked to aging. Lifestyle, hereditary factors, posture, sports, and work-related activities can, however, influence the course of degenerative disorders [5–7]; moreover, in a number of cases, the cervical spine biological age does not match the person's chronological age. In short, aging of the spine appears to be a complex and inhomogeneous process.

In our daily clinical practice, it is not unusual to find individuals whose cervical spine scans show a much

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different result than what would normally be expected taking into account the subjects' chronological age (Fig. 1). In the literature, so far, there are no tools to measure the degree of degeneration of the cervical spine. A scale such as the one presented in this article might prove essential to standardize studies on degenerative pathologies and relative treatments. So far such standardization has not been possible. There is a distinct lack of homogeneity in treatment guidelines, so much so that selection of appropriate treatment is often wholly lead by the preference of the physician; moreover, population samples in clinical studies have been formed mainly according to chronological age [8–11]. As previously mentioned, our study shows that chronological age alone is not a comprehensive and satisfactory parameter when it comes to researching degenerative disorders of the cervical spine.

The decision on whether a patient should be treated surgically or otherwise, and, in the case of surgery, on which type of intervention should be carried out, is taken on the basis of many parameters, such as medical history, the general and neurological conditions of the patient, the presence of osteoporosis and/or osteopenia, as well as the presence or absence of clear signs of myeloradicular compression caused by degenerative pathology of the spine. Given such premise, it is, however, necessary to recognize that the general condition of the cervical spine is an element that influences the effectiveness of treatments and since such condition can greatly vary from person to person even within the same age group, it is not accurate nor helpful to carry out studies that compare tout court groups of patients homogeneous only because sharing the same age range.

This article aims at presenting a scale for the analysis of MRI images that, by clearly charting the various degenerative stages of the cervical spine, can establish with precision the overall state of degeneration of any given cervical spine, or as we prefer to call it, the spine's biological age. The evaluation system created complies with the following requirements: objectivity, comparability, and replicability.

The cervical spine biological age is determined by summing together various scores linked to a selection of parameters according to which MRI images are analyzed.

Materials and methods

For this article, we have examined the MRI scans of the cervical spine belonging to all the patients who were admitted to the Medical Imaging Service of the Military Hospital of Rome between January 2010 and July 2011, for a total of 508 scans. The exclusion criteria applied to this sample were:

- Patients aged under 20,
- MRI scans performed due to recent trauma to the spine,
- MRI scans performed due to neoplastic growths,
- MRI scans performed after surgery to the cervical tract, and
- MRI scans performed due to inflammatory/infectious diseases of the cervical tract.

Following these criteria, our sample was narrowed down to 423 scans.

The MRI scans were performed using a 2010 Release 2.1.5.5 Philips Achieva with gradients between 33 mT/m and 1 slew rate of 150 T/ms; T1 SE sagittal sequences with 400 ms repetition time (TR), 7.4 ms echo time (TE), 90° flip angle with a thickness of 3 mm and 3′. 43″ scanning time as well as T2 FFE sagittal sequences with 3500 ms TR, 120 ms TE, 90° flip angle with a 3 mm thickness and 3′. 44″ scanning time; axial sequences on T2 FFE 3D, 50 ms TR, 12 ms TE, 7° flip angle, 0.5 mm thickness, 3′ scanning time.

For our study, all images were re-elaborated with Osirix software.

The scans were reviewed by two independent teams. Each team included a neuroradiologist with over 15 years of experience, a senior neurosurgeon with over 15 years of

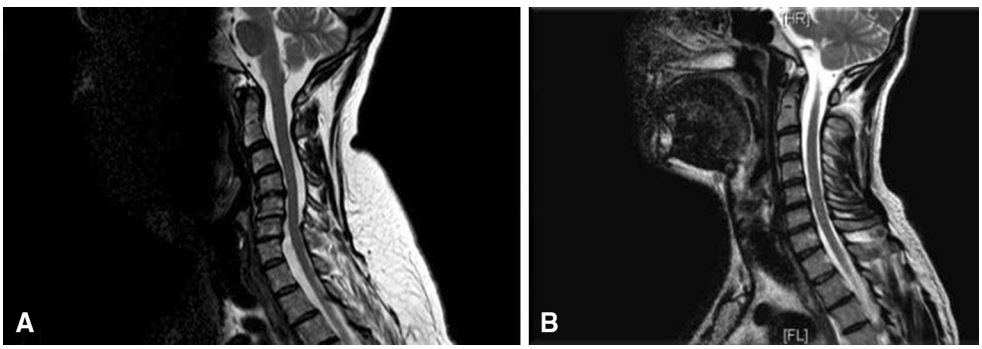

Fig. 1 **a** MRI of a 46 years old man and **b** MRI of an 80 years old man: it seems the opposite

experience in the field of cervical spine and a junior neurosurgeon with less than 15 years of experience.

On the grounds of literature and of our experience, we selected six parameters by which to analyze the sample MRI scans. We assigned to each parameter a score system based on a graduated scale. The cervical spine biological age could then be determined by summing up the scores obtained for each parameter.

The following six parameters were:

1. The degeneration of intervertebral discs,
2. The degeneration of yellow ligaments,
3. The degeneration of vertebral bodies,
4. The possible presence of spondylolistheses,
5. The presence or absence of foraminal stenosis, and
6. The diameter of the spinal canal.

All these factors were evaluated through the use of graduated ordinal scales with incremental scores, whereby each score denoted the state of one of the selected elements as it appeared on the MRI image. Each of these factors was analyzed per single subaxial cervical spine level (C2-D1) as extensively shown by Table 1.

Table 1 The scale

Biological age scale	
(A) Disc (C2–D1 = 6)	Scores between 6 and 30
Normal disc (isointense to CSF on T2-weighted MR images)	1
Dehydrated disc (hypointense to CSF on T2-weighted MR images)	2
Black disc	3
Disc material extrusion and/or anterior and/or posterior osteophytosis	4
Presence of osteophytic bridges	5
(B) Ligaments (C2–D1 = 6)	Scores between 6 and 18
Normal	1
Hypertrophic/with calcification	2
Leaving posterior impression on the canal	3
(C) Vertebral bodies (C2–C7 = 6)	Scores between 6 and 18
Normointense	1
Signal alterations (T1 and/or T2)	2
Presence of Modic changes	3
(D) Segmental alignment (C2–D1 = 6)	Scores between 6 and 12
Normal	1
Misaligned	2
(E) Connecting foramina (C2–D1 = 12)	Scores between 0 and 12
Normal	0
Presenting stenosis	1
(F) Diameter of the canal of the worst level	Scores between 1 and 8
Normal	1
Less than 25 %	2
Between 25 and 50 %	3
Between 50 and 75 %	4
Over 75 %	5
Hyperintense spinal chord at one level	6
Hyperintense spinal chord over several levels	7
Spinal chord atrophy	8
Total	Scores between 25 and 98

Results

Statistical analysis

Initially, the results obtained by the two examining teams underwent the Pearson's test to assess inter-operator dependency: the correlation coefficient equal to 0.891** showed that this scale is not dependent on the operator's subjective view.

We then submitted the data obtained from the study to a statistical enquiry with SPSS v. 18 software.

We first carried out a descriptive statistics analysis; the results of which are displayed in Table 2.

The following variables were added to the six parameters selected:

- Scale total (sum of the individual scores per parameter),
- Chronological age of the subject of the MRI scan,
- The difference between these last two variables.

As it is easily deduced from the table, the average value and standard deviation (SD) of the two variables scale total and chronological age is very similar, indicating a significant super imposability of the two diagrams. The difference of the averages between these two variables is below one point ($N = 423$, $m = -0.929$), while the SD of the difference is once again similar to the SD of the two variables, thus indicating similarity between the dispersion indexes. The Compare Means Test confirmed this observation.

We then carried out on the sample two types of inferential statistics study: Pearson's product-moment correlation coefficient (Table 3) and Factor analysis (Table 4).

The Pearson's product-moment correlation coefficient between the variables, 'chronological age' and 'scale total', was found to be statistically high ($r = 0.726$, $p < 0.01$); as was also the case for all the other scale parameters used as variables, since they too presented a significant positive

Table 2 Descriptive statistics analysis results

	N	Minimum	Maximum	Mean	SD
Interv. disc	423	6.00	29.00	16.5768	4.19525
L. Flavum	423	6.00	18.00	10.0473	3.06759
Soma	423	6.00	17.00	9.1844	2.78010
Listhesis	423	6.00	13.00	6.5768	0.99674
Foramina	423	0.00	10.00	2.6927	2.32850
Canal diameter	423	1.00	8.00	2.2411	1.11793
Total scores	423	26.00	86.00	47.3191	11.39031
Age	423	16.00	90.00	48.2482	12.94748
Variance(age/tot)	423	−29.00	27.00	−0.9291	9.12653
Valid N (list wise)	423				

correlation with the chronological age of the sample subjects ($p < 0.01$).

We then submitted the sample to a Factor analysis (Table 4): a single statistical factor (Fig. 2) was able to determine, in our sample, 56.26 % of variance in the scores obtained using the scale. We hypothesized this factor to be aging.

Discussion

To create our scale we used parameters suggested by the relevant literature on the subject. We examined age in correlation with the following anatomical structures of the cervical spine:

1. Vertebral bodies. In 1988, Modic et al. [12] published the renowned work on MRI scans showing the degeneration of vertebral bodies' bone marrow and of the adjacent endplates. From then on numerous studies were carried out on the subject. We have simplified the analysis of the degeneration of vertebral bodies using a scale with only three base measuring units or degrees:

Score of 1. Absence of non-homogeneity of signal on T1 and T2-weighed images of the vertebral body.
Score of 2. Presence of non-homogeneity.
Score of 3. Presence of any kind of degeneration classified according to the Modic scale.

2. Intervertebral discs. The progressive disc degeneration caused by aging can easily be verified by MRI scan examination. In 2001, Pfirrmann proposed a measuring system for lumbar disc degeneration [13]. For the cervical spine we adopted a similar system with five base measuring units or degrees:

Score of 1. Disc that is hyper or isointense to the cerebrospinal fluid (CSF) on T2-weighted MR images.
Score of 2. Hypointense disc.
Score of 3. Black disc.
Score of 4. Protruded or extruded disc from any side.
Score of 5. Absence of disc space/presence of osteophytic bridges between vertebrae.

3. Intervertebral ligaments. The degeneration of the ligaments is due to changes in the collagen fibers and in calcium content. Numerous articles [14–17] highlight how, with aging, the cervical spine ligaments present a marked tendency toward calcification, in particular toward OPLL (ossification of the posterior longitudinal ligament). We have selected the degeneration of the posterior ligamentous complex (yellow ligament/interspinous ligament), while discounting the remaining ligamentous compartment as it was already included in other parameters (disc, intervertebral foramina, presence of spondylolisthesis, and canal). For this parameter, we established three base measuring units or degrees of progressive degeneration: healthy (score of 1), calcified (score of 2), and projecting into the canal (score of 3).
4. Intervertebral foramina. We can evaluate the degenerative process of the zygapophysial joints and the facet joints by examining the deterioration of connecting foramina [18]. To achieve this, we used the axial sequences for the vertebral bodies studied and the T2-weighed sagittal sequences. On the levels that were not clear, we used 2D reconstruction with Osirix software, thus obtaining the images of the foramina on an orthogonal plane compared to the axis of the foramen in consideration [19]. For each foramen, we established the following base measuring units or degrees: score of 0 if healthy, score of 1 if it presented any form of deterioration [20].
5. Spinal Canal. The degenerative processes of the spine caused by aging provoke a progressive narrowing of the spinal canal with myelopathic signal manifestations in MRI scans [21, 22]. For this reason, we included a parameter to evaluate the AP diameter at the worst level. We adopted the following scale system:

Score of 1. Normal diameter.

Table 3 Pearson's correlation between criteria

	Int. disk	L. Flavum	Soma	Listhesis	Foramina	Canal diameter	Total scores	Age	Variance (age/tot)
Int. disk									
Pearson's correlation	1	0.616**	0.539**	0.444**	0.677**	0.486**	0.891**	0.644**	0.199**
Sig. (2-tailed)		0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
N	423	423	423	423	423	423	423	423	423
L. Flavum									
Pearson's correlation	0.616**	1	0.518**	0.347**	0.558**	0.419**	0.808**	0.605**	0.150**
Sig. (2-tailed)	0.000		0.000	0.000	0.000	0.000	0.000	0.000	0.002
N	423	423	423	423	423	423	423	423	423
Soma									
Pearson's correlation	0.539**	0.518**	1	0.348**	0.512**	0.258**	0.742**	0.549**	0.147**
Sig. (2-tailed)	0.000	0.000		0.000	0.000	0.000	0.000	0.000	0.002
N	423	423	423	423	423	423	423	423	423
Listhesis									
Pearson's correlation	0.444**	0.347**	0.348**	1	0.441**	0.355**	0.554**	0.412**	0.108(*)
Sig. (2-tailed)	0.000	0.000	0.000		0.000	0.000	0.000	0.000	0.027
N	423	423	423	423	423	423	423	423	423
Foramina									
Pearson's correlation	0.677**	0.558**	0.512**	0.441**	1	0.500**	0.817**	0.574**	0.205**
Sig. (2-tailed)	0.000	0.000	0.000	0.000		0.000	0.000	0.000	0.000
N	423	423	423	423	423	423	423	423	423
Canal Diameter									
Pearson's correlation	0.486**	0.419**	0.258**	0.355**	0.500**	1	0.586**	0.390**	0.178**
Sig. (2-tailed)	0.000	0.000	0.000	0.000	0.000		0.000	0.000	0.000
N	423	423	423	423	423	423	423	423	423
Total score									
Pearson's correlation	0.891**	0.808**	0.742**	0.554**	0.817**	0.586**	1	0.726**	0.218**
Sig. (2-tailed)	0.000	0.000	0.000	0.000	0.000	0.000		0.000	0.000
N	423	423	423	423	423	423	423	423	423
Age									
Pearson's correlation	0.644**	0.605**	0.549**	0.412**	0.574**	0.390**	0.726**	1	−0.513**
Sig. (2-tailed)	0.000	0.000	0.000	0.000	0.000	0.000	0.000		0.000
N	423	423	423	423	423	423	423	423	423
Variance (Age/Tot)									
Pearson's correlation	0.199**	0.150**	0.147**	0.108*	0.205**	0.178**	0.218**	−0.513**	1
Sig. (2-tailed)	0.000	0.002	0.002	0.027	0.000	0.000	0.000	0.000	
N	423	423	423	423	423	423	423	423	423

Asterisks indicate significant correlations

Score of 2. Reduction up to 25 % compared to a normal adjacent space.

Score of 3. Reduction between 25 and 50 %.

Score of 4. Reduction between 50 and 75 %.

Score of 5. Reduction above 75 %.

Table 4 Factor analysis

Component	Initial eigenvalues			Extraction sums of squared loadings		
	Total	% of variance	Cumulative %	Total	% of variance	Cumulative %
1	3.376	56.262	56.262	3.376	56.262	56.262
2	0.767	12.778	69.041			
3	0.679	11.310	80.350			
4	0.442	7.371	87.721			
5	0.424	7.061	94.782			
6	0.313	5.218	100.000			

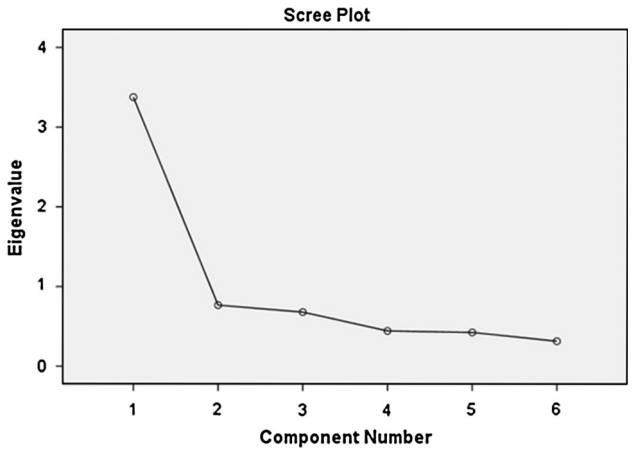

Fig. 2 A single statistical factor was able to determine, in our sample, 56.26 % of variance in the scores obtained using the scale

Score of 6. Presence of myelopathic signal on T2 at single level.
Score of 7. Presence of myelopathic signal over more levels.
Score of 8. Presence of spinal cord atrophy.

The last three degrees do not refer to the diameter of the spinal canal, but to pathologies of the spinal cord that occur in very serious anatomical conditions; in these instances, the walls of the spinal canal no longer represent the element that contains and protects the spinal cord, but they actually become the cause for pathologies of the nervous tissue.

6. Alignment or misalignment between two vertebrae. Degenerative spondylolistheses, which has long been known in the lumbar region, has been studied at cervical level only since 1986 [23]. Its presence increases with aging and it has been found to be high in people over 50 [24]. This is why we chose to include this parameter in our scale by simply acknowledging its absence (score of 0) or presence (score of 1) for each vertebral unit under consideration.

We have not included osteoporosis among the parameters under observation, even though it is an element that needs to always be kept in mind for the selection of treatment for the spine, because osteoporosis represents a very clear pathology of the bone, which is not derived from the degenerative process [25–27].

The results of the statistical analysis show that to evaluate the cervical spine aging process, the choice of the aforementioned parameters has been correct. Since the degeneration caused by aging is not in itself a pathology but an unavoidable physiological occurrence for everyone without exception, whether symptoms are present or not [28], we did not consider it necessary to gather data from a "healthy" sample. Any spine expert is aware that the radiological appearance of the spine does not always correlate with the clinical picture; thus, a patient with spine degeneration may not show any symptoms and, therefore, not require treatment.

The effectiveness of the various medical, physiatrical, and surgical treatments for cervical spine degenerative disorders is influenced by the overall anatomical conditions of the cervical spine. Up until now there has been no objective criterion for the evaluation of these conditions. Moreover, as already stated, the aging processes of the spine are not always homogeneous per age band. These factors contribute to the extreme difficulty in achieving any sort of objective comparison among therapeutic strategies. We believe that this scale will be useful to homogenize retrospective studies and to correctly set up prospective studies on the degenerative disorders of the cervical spine and the relative treatments; it is effective and simple tool for the objective classification and staging of degenerative processes and for the measurement of the cervical spine's biological age; our team has been using it for over a year and found it extremely helpful to determine the appropriate therapy for each patient. In fact, recently, we have begun a prospective study on the choice, in relation to patients' age, of either the artificial disc or the cage as prosthesis during anterior surgery of myeloradiculopathy caused by disk herniation or by cervical spondylosis. This study involves two groups of patients. The choice of prosthesis for the first group will rely solely on the subjects' chronological age, which is currently common practice; while for the other group, the choice will be based on the spine's biological

age, calculated according to our scale. Early data shows that all the patients who were given a disc prosthesis having scored 50 or below on our scale, irrespective of their actual age, even after two years have had no signs of prosthesis' fusion and the consequent lessening of mobility; whereas the only two patients who were given an artificial disk because younger than 50 years old, but whose score was above 50, both showed an early prosthesis fusion process.

In conclusion, our work means to contribute, through a statistical model, to the standardization and simplification of the complex phenomenon that is cervical spine aging, and thus it offers a tool for the greater homogenization of studies concerning the treatments of pathologies linked to spinal degeneration. The sample we chose to build the scale from is statistically sufficient [29, 30]; however, the topic we chose is so varied, vast, and complex that it certainly deserves a larger sample as well as a different approach to the research. In conclusion, we consider ours a pilot study that may lead to a larger multicenter study.

Conflict of interest None.

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biologically to their mechanical environment and to mechanical damage, and these responses may mask the essentially mechanical origin of 'degenerative' changes within them. Section 6 explains why certain individuals develop low back disorders while others, who may subject their backs to more severe mechanical loading, do not. The concept of a 'vulnerable' back is of major medico-legal importance. Section 7 suggests that the manner in which we sit and stand and move can create painful stress concentrations within innervated tissues, even though the tissues remain undamaged. Such 'functional pathology' may explain a great deal of transient back pain. Finally, the summary attempts to piece together all of the available evidence to form a simple and plausible account of the biomechanics of back pain.

1 Functional anatomy of the lumbar spine

Lumbar vertebrae consist of a short weight-bearing vertebral body, and a neural arch which encircles the spinal cord in a ring of bone (Figure 1). Vertebral bodies resist most of the compressive force acting down the long axis of the spine, whereas the neural arch protects the spinal cord and provides attachment points for muscles and ligaments. Adjacent vertebral bodies are separated by intervertebral discs, which comprise a soft deformable nucleus pulposus surrounded by the tough concentric layers (lamellae) of the annulus fibrosus. Intervertebral discs allow small movements between vertebrae, and distribute compressive loading evenly on to the vertebral bodies. The nucleus behaves like a pressurised fluid, and generates tensile 'hoop' stresses on the annulus so that excessive compressive loading of the spine can lead to tensile failure in the annulus.[4] Spinal stability is aided by the apophyseal joints which join adjacent neural arches, and which have cartilage-covered articular surfaces orientated more vertically than horizontally. These joints resist horizontal forces acting on the spine, and protect the lumbar discs from excessive shear and torsion.[3] In lordotic postures, the neural arches can resist more than half of the compressive force acting on the spine, especially following sustained loading at constant force or disc degeneration, both of which narrow the discs and bring the neural arches closer together.[5] Various intervertebral

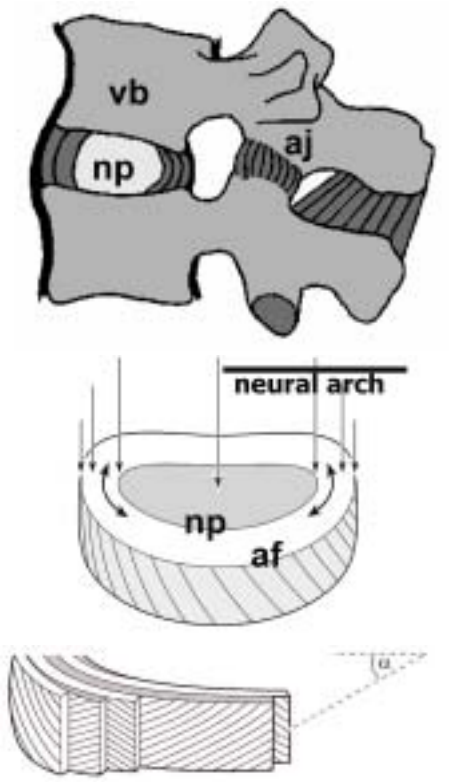

Figure 1 Upper image shows a lumbar 'motion segment' consisting of two vertebrae and the intervening disc and ligaments. (vb – vertebral body; af – annulus fibrosus; np – nucleus pulposus; aj – apophyseal joints; pll – posterior longitudinal ligament.) The middle image shows the direction of 'hoop stresses' (T) in the annulus fibrosus of the intervertebral disc. The lower image shows part of the annulus 'exploded' to show its lamellar structure.

ligaments span adjacent vertebrae, and mostly serve to limit bending movements of the spine.[3] Fibres of the interspinous and capsular ligaments vary in length and orientation, and appear to be deployed specifically to resist flexion movements.[3]

2 Where does back pain come from?

This fundamental question is difficult to answer, because the spine is such a deep structure that it is not amenable to close observation or palpation. It is widely suspected that many transient episodes of back pain arise from the back muscles, perhaps in the region of their musculotendinous junctions, but there is no reliable proof of this. Recent research has, however, made progress in identifying the sources of severe and chronic back pain.

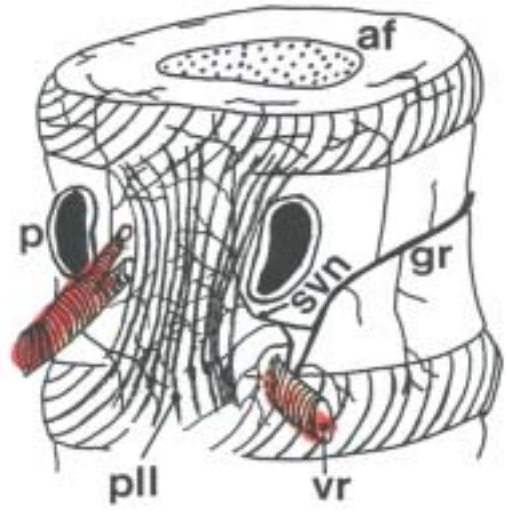

Figure 2 Posterior view of a motion segment with the neural arch removed at the pedicles (p). The mixed sinuvertebral nerve (svn) contains fibres from the grey rami communicantes (gr) and from the ventral ramus (vr) of the somatic nerve root. It forms a dense plexus within the posterior longitudinal ligament (pll), and some fibres penetrate the peripheral annulus fibrosus (af). (Adapted from Bogduk N. The innervation of the intervertebral discs. In Grieve's Modern Manual Therapy, Edinburgh: Churchill Livingstone; 1994, with permission from Elsevier).

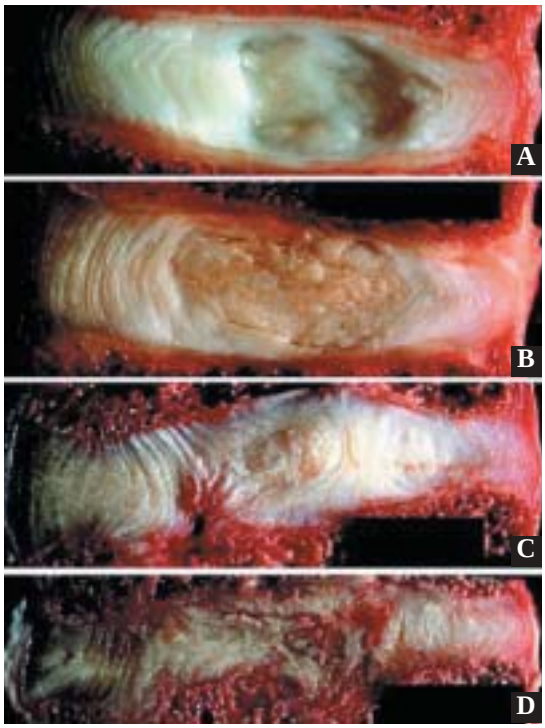

Figure 3 Mid-sagittal sections through four intervertebral discs (anterior on left) are shown. A: young 'grade one' disc. B: mature 'grade two' disc. C: young degenerated 'grade three' disc. Note the inwards-bulging lamellae and disrupted endplate. D: young severely degenerated 'grade four' disc. (Reproduced from an original colour print in Adams MA, Bogduk N, Burton K, Dolan T. The Biomechanics of Back Pain. Edinburgh: Churchill Livingstone; 2002, with permission from Elsevier).

Anatomical evidence

The innervation of most spinal structures is uncontroversial and has been summarised recently by Bogduk and Twomey.[6] The dorsal rami of each spinal nerve divides into three branches: the lateral, the intermediate and the medial. Lateral branches supply the iliocostalis lumborum muscle and the skin; intermediate branches supply the longissimus muscle and the apophyseal joints; and medial branches supply the apophyseal joints, the interspinous and multifidus muscles, and the interspinous ligament. Each medial branch supplies the apophyseal joints at its own level and the one below. Vertebral body endplates have sensory innervation and so they also have the potential to be painful.[7] The posterior longitudinal ligament contains an extensive plexus of nerve fibres with free and encapsulated endings.[8]

The innervation of intervertebral discs has long been controversial, with negative findings being taken at face value, or attributed to technical failure. However, it is now widely accepted that the grey rami communicantes, which arise from the lumbar sympathetic trunks, join the ventral rami of the lumbar spinal nerves to form a mixed nerve, the sinuvertebral nerve, which then supplies the posterior and posterolateral annulus fibrosus, and the posterior longitudinal ligament,[6;8] as shown in Figure 2. Within healthy discs, free nerve endings of various types have been identified in the outermost few millimetres of the annulus fibrosus, coinciding with the collagen-rich tensile region of the outer annulus which exhibits little or no compressive stress (Figure 3). Nerves fibres, or the capillaries upon which they depend, may be unable to withstand the high hydrostatic pressure in the inner annulus and nucleus. Nerve endings and capillaries can grow in towards the centre of

degenerated and painful discs,[9] which generally do not exhibit high hydrostatic pressures (Figure 3).

Pain-provocation studies

A large study on conscious patients undergoing surgery for herniated disc or spinal stenosis showed that leg pain could be reproduced only from an inflamed or mechanically compromised nerve root, and that the posterior annulus was 'exquisitely tender' in one third of patients, 'moderately tender' in another third, and insensitive in the rest.[10] Back pain produced from the annulus was similar to that suffered pre-operatively. The facet joint capsule produced some sharp, localised pain in approximately 30% of patients, but the ligaments, fascia and muscles were relatively insensitive. The importance of the apophyseal joints in producing low back pain was investigated further by Schwarzer et al,[11] who injected local anaesthetic into several facet joints in each patient, and found that 15% of them obtained considerable pain relief from the same joint on more than one occasion. The authors concluded that the apophyseal joints are frequently a cause of pain, but questioned the existence of a specific 'facet syndrome'. Similar techniques have shown that the sacro-iliac joints are a major source of symptoms in approximately 30% of patients with chronic back pain below the level of L5-S1.[12]

Psycho-social factors

Questionnaires can be used to quantify a variety of personal characteristics such as depressive tendencies, attitudes towards health and health professionals, and interactions with work colleagues. These questionnaire scores in turn are important predictors of all aspects of back pain behaviour including the recognition of discomfort as 'pain', the decision to report it, to take time off work, to become disabled, to develop chronic pain, and to respond (or not) to treatment. Recognition of the importance of these factors has been termed a 'Back Pain Revolution' by the author of a book of that name,[13] because it represents a radical departure from a simple 'injury model' of back pain. Nevertheless, it remains true that psychosocial factors are not important predictors of who will develop back pain in the first place, and what back pain they do predict tends to be relatively trivial.[14;15]

3 Ageing, degeneration and pain in lumbar intervertebral discs

It is important to distinguish between ageing and degeneration in the spine, because only the latter is likely to be painful. As discussed previously,[3] 'ageing' should include only those changes which occur inevitably and which are predominantly biochemical in nature, as described in section 7. Degeneration, on the other hand, implies a degradation of structure and/or function that is superimposed on top of the normal ageing process.

Adams et al have attempted to distinguish between ageing and degeneration in cadaveric lumbar discs (Figure 4), using gross structure and mechanical (dys)function as the main criterion.[4] Disc function was assessed by pulling a miniature pressure transducer through the loaded disc. Transducer output is approximately equal to the average compressive stress acting perpendicular to its membrane,[16] and the resulting 'stress profiles' show that young and healthy ('grade one') discs exhibit a constant hydrostatic pressure throughout the nucleus and inner annulus (Figure 4A). The disc behaves like a water bed. Older discs which show no signs of structural disruption ('grade two') exhibit a smaller hydrostatic nucleus, and a thicker annulus which can sustain small stress concentrations in the annulus, usually posterior to the nucleus (Figure 4B). Moderately degenerated discs ('grade three') show evidence of structural disruption in the annulus or endplate, and these changes are accompanied by high stress concentrations in the annulus, and a decompressed nucleus (Figure 4C). Severely degenerated ('grade four') discs are so disrupted that they are often difficult to pass a transducer through, but when measurements can be made, they show very irregular stress distributions, and evidence that compressive load-bearing is being transferred to the neural arch.[5] Evidently severe disc narrowing brings the neural arches close together, and they can then resist up to 90% of the compressive force acting on the spine.[5]

Certain general conclusions can be drawn from these experiments. Firstly, disc mechanical function is affected more by structural disruption

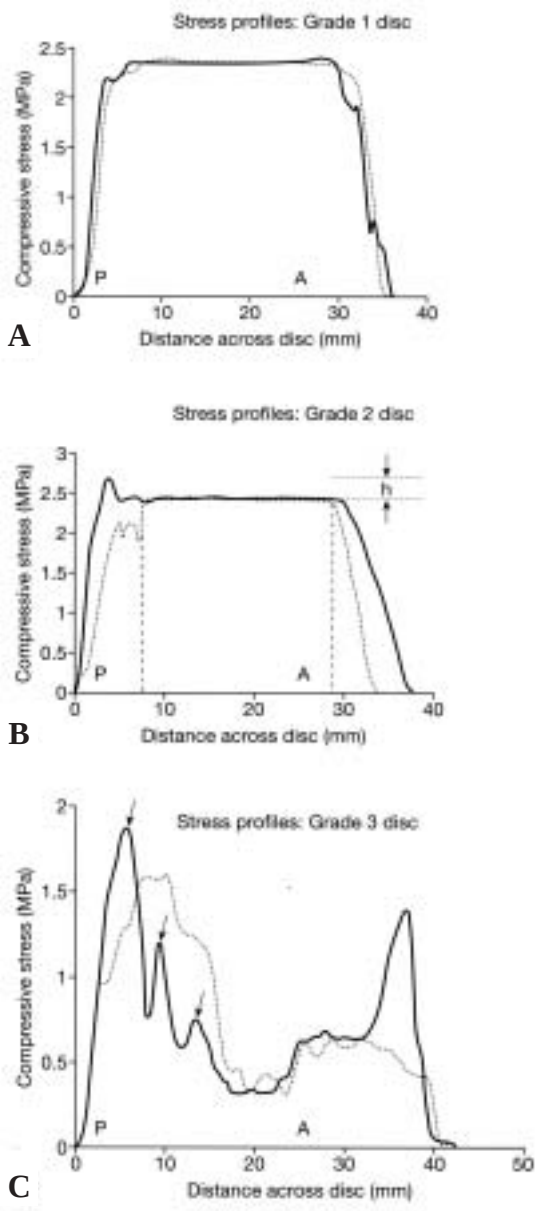

Figure 4 'Stress profiles' showing the distribution of compressive stress across the mid-sagittal diameter of lumbar intervertebral discs. A: 'grade one' disc. B: 'grade two' disc. C: 'grade three' disc. Compare with Figure 3. (Adapted from Adams MA, Bogduk N, Burton K, Dolan T. The Biomechanics of Back Pain. Edinburgh: Churchill Livingstone; 2002, with permission from Elsevier).

than by the biochemical changes of ageing. Secondly, structural disruption prevents a disc from equalising load on the vertebrae, and regions of very high and very low stress are created within the tissue. These stress concentrations occur in (or close to) regions of the annulus which are innervated, and there is some evidence from clinical studies that they can indeed be painful.[17] Epidemiological studies also show that back pain is associated with evidence of disc disruption, such as radial fissures, disc prolapse, endplate fracture, or a collapse in disc height, but not with the age-related biochemical changes which manifest on MRI scans as a 'dark disc'.[18;19] So, there is growing evidence that pain arises from disrupted degenerated discs, but not from old dehydrated discs. However, even the most severe degenerative changes can sometimes be observed in people who have no back pain, suggesting that pain perception depends on biochemical pain-sensitisation mechanisms which are not yet fully understood,[20] as well as on stress concentrations. It is also possible that some individuals with degenerated and narrowed discs escape pain because much of the load-bearing has been transferred to the neural arch.

4 Mechanisms of injury to the lumbar spine

Experiments on cadaveric spines have shown how specific types of mechanical loading can cause characteristic injuries to spinal tissues. These mechanisms have been extensively reviewed by the author,[3;21] and the applicability of such experiments to living people has been considered at length.[22] Only a brief summary is provided here.

Compression

'Compressive' loading acts down the long axis of the spine, perpendicular to the discs, and mainly arises from tension in the longitudinal muscles of the back and abdomen.[23] The vertebral body is the spine's 'weak link' in compression, and always fails before the intervertebral discs, even if the latter are injured before loading commences.[24] Damage is mostly located in the end-plate or in the trabeculae just behind it, and is presumably caused by the nucleus pulposus of the adjacent disc bulging into the vertebra. Compressive damage arising from repetitive loading is probably a common event in life, because micro-fractures and healing trabeculae are found in most cadaveric vertebral bodies. Vertebral body damage decompresses the adjacent disc,[25] and subsequently leads to internal disc disruption,[25;26] and further degenerative changes.[27]

Many old people suffer a characteristic anterior wedge fracture of one or more thora-columbar vertebrae, which can leave them with a kyphotic deformity sometimes referred to as 'dowager's hump'. This is a typical manifestation of osteoporosis, or generalised bone weakening secondary to hormonal changes, but local mechanical factors are also important. Severe disc degeneration and narrowing can cause the neural arch to 'stress shield' the anterior region of the vertebral body to such an extent that it loses bone mineral. This weakened region of bone is then heavily loaded when the person bends forwards, perhaps to pick something up, and fracture can result.[28]

Bending

Anterior bending (flexion) of the lumbar spine is resisted by the ligaments of the neural arch, with the supraspinous and interspinous ligaments being the first to fail when physiological limits are exceeded. Further flexion will tear the apophyseal joint capsular ligaments, and extreme hyper-flexion can tear the posterior annulus, or cause it to pull a chip of bone off the vertebral body.[29] In living people, flexion is limited by the back muscles, but muscle protection can be lost following sustained or repeated bending movements, probably because creep deformation in spinal receptors effectively knocks out the protective muscle reflex.[30] Backwards bending (extension) of the lumbar spine is resisted by compaction of the adjacent neural arches, and the first structures to be damaged are probably the apophyseal joints,[31] or the joint capsules.[32] Alternating full flexion and extension movements cause the neural arches of lumbar vertebrae to bend downwards and upwards, respectively, and the alternating compressive and tensile stresses acting on the pars interarticularis probably contribute to the characteristic defect known as spondylolysis.[33] Not surprisingly, young gymnasts and fast bowlers at cricket are most often affected. Bending of the spine in the frontal plane has received little attention, but if taken to extremes would probably injure an apophyseal joint.

Axial rotation

In the lumbar spine, the orientation of the apophyseal joints leads to bony compaction after only 1-3° of axial rotation before the inter-vertebral ligaments are substantially stretched.[3] Consequently, activities such as over-exuberant discus throwing may injure these joints, and possibly also the anterior regions of the intervertebral disc which lie furthest from the centre of axial rotation in the posterior annulus. In the thoracic spine, the more antero-posterior orientation of the apophyseal joints allows much more axial rotation, and it is possible that the disc could be damaged before the neural arch.

Bending and compression

If bending and compression are applied simultaneously to the lumbar spine (as they would be in life when someone lifts weights from the floor) then failure can sometimes occur by a posterior prolapse of the intervertebral disc.[25;34] For prolapse to occur in a single loading cycle, either the compression or bending must exceed normal limits, and this explains why we do not all suffer this injury. In the laboratory, prolapse occurs most readily in 'grade two' discs from the lower lumbar spine of cadavers aged 40 to 50 years (Figure 5). The mechanism is illustrated in Figure 6. Repetitive application of bending and compression can cause radial fissures to grow into a postero-lateral corner of a disc, resulting in the gradual expulsion of nucleus pulposus.[35]

5 Biological responses to injury

For more than 50 years, conventional wisdom dictated that intervertebral discs could prolapse

Figure 5 Mid-sagittal section through a 'grade two' intervertebral disc which has been induced to prolapse in the laboratory. Some nucleus pulposus has herniated through a radial fissure in the posterior annulus (right) and lies under the posterior longitudinal ligament. (Reproduced from an original colour print in Adams MA, Bogduk N, Burton K, Dolan T. The Biomechanics of Back Pain. Edinburgh: Churchill Livingstone; 2002, with permission from Elsevier.)

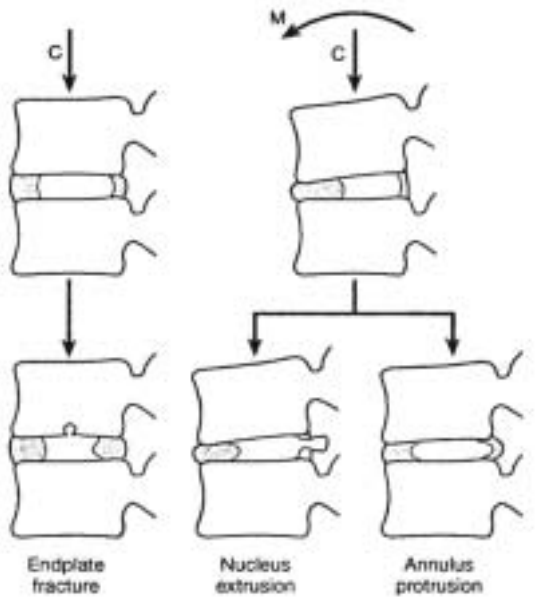

Figure 6 The mechanism of disc prolapse. Left: compressive loading (C) always fractures the vertebral body endplate before damaging the disc. Right: the addition of bending (M) serves to stretch and weaken the posterior annulus, so that failure can occur by the extrusion of nucleus pulposus, or the outwards collapse (protrusion) of the annulus. (Reproduced from Adams MA, Bogduk N, Burton K, Dolan T. The Biomechanics of Back Pain. Edinburgh: Churchill Livingstone; 2002, with permission from Elsevier).

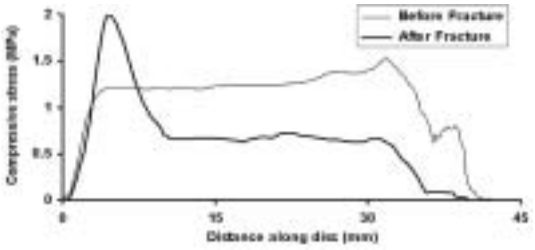

Figure 7 'Stress profiles' (see Figure 4) showing how fracture of a vertebral body endplate reduces compressive stresses in the anterior and central regions of the adjacent disc, and generates a stress concentration in the posterior annulus (left).

only when they were degenerated, but the only evidence supporting this dogma was that disc tissue removed at surgery was seldom 'normal'. We now know that degenerative changes can also follow injury, as the tissues' cells adapt to their altered mechanical (and sometimes nutritional) environment. Thus, an artificial scalpel injury to the annulus or endplate will cause disc degeneration in a range of animals, with a time span of weeks or months depending on the animal's size.[27;36;37] Furthermore, a small study on human teenagers has found that significant disc degeneration occurs several years after an injury to a vertebral endplate.[38]

The mechanism responsible for injury-induced degeneration appears to be that structural damage to a disc or endplate creates regions of high and low stress within the disc,[25] as shown in Figure 7. Tissue culture experiments show that disc cell metabolism is inhibited by exceptionally low and high pressures,[39] and that high pressures also stimulate the production of matrix degrading enzymes.[40] Consequently, injury leads to impaired disc cell metabolism at precisely the time when increased metabolic activity is required to repair the damaged tissue. Degeneration is the result. Other tissues might be similarly affected by physical disruption, with the essential problem being that cells tend to respond to their local mechanical environment, rather than to the requirements of the whole tissue or structure.

Tissue injury could instigate degenerative changes by other means. For example, injury could kill cells directly, or disrupt blood vessels and thereby impair metabolite transport, or break down barriers and allow an inflammatory or autoimmune reaction to occur within the tissue.[6]

6 Predisposition to injury: 'vulnerable' tissues

It is common experience that some people have stronger backs than others, and can perform tasks that their colleagues would not dare attempt. Cadaveric experimentation confirms that there are large inter-individual differences in the strength of skeletal tissues, and that these differences are partly attributable to size, and partly to quality, or strength per unit size. A number of factors explain why some backs are particularly strong, while others are more vulnerable to injury.

Genetic inheritance

Recent studies on identical twins have shown that 70% of intervertebral disc degeneration can be

attributed, in a statistical sense, to genetic inheritance rather than to the (mechanical) environment.[41] Some of the genes responsible have been identified, such as those which code for vitamin D receptors,[42] collagen Type IX,[43] and proteoglycans.[44] However, most of the genetic influence remains to be explained, and it is possible that genes for structural, mechanical, biochemical or metabolic factors could all be involved. Perhaps even neurological influences may render some people injury prone? What is clear already is that the genetic predisposition to disc degeneration involves many genes, and that it is not possible to distinguish between a minority of people with 'vulnerable' backs and a majority with 'normal' backs. Tissue vulnerability appears to be a continuous variable. This is of considerable medico-legal importance.

Ageing

Typical biochemical changes occur in ageing articular cartilage and intervertebral discs. The large proteoglycan molecules that bind water into the tissue become increasingly fragmented, and some fragments are lost, so that the tissue becomes increasingly dehydrated.[45] This process is particularly marked in the nucleus, which becomes steadily more fibrous as proteoglycans are replaced by fibrous proteins including collagen. Loss of water from a disc reduces its ability to equalise loading on the vertebrae, so that the main functional consequence of age-related water loss is a decompressed nucleus, and stress concentrations in the annulus.[46]

Ageing also affects the collagen fibres which provide the tensile stiffness and strength of cartilage. Cross-links between collagen molecules slowly 'mature', creating thicker and stronger collagen fibres which cannot readily be degraded or remodelled when they become damaged. This increased stability of collagen allows additional cross-links to form, some of which involve glucose. The gradual and uncontrolled process of 'non-enzymatic glycation' steadily increases cross-linking between fibres, with the result that they becomes excessively stiff, unable to absorb energy when loaded quickly, and more vulnerable to injury. In effect, the tissue behaves like a woollen jumper that has become 'matted' during a hot wash! A side-effect of non-enzymatic glycation is that cartilage takes on the yellow-brown appearance associated with ageing tissues.

As far as disc prolapse is concerned, it appears that the most vulnerable discs are 'grade two' discs from middle aged people. These are old enough to have a weakened annulus, but young enough to have a hydrated nucleus capable of bursting through it.[34]

Loading history

Repetitive loading can create microscopic damage within a material or tissue which gradually builds up until gross failure occurs. This phenomenon of 'fatigue failure' explains why vibrations can eventually cause aeroplane wings to fall off (unless the microdamage is monitored!) and why over-training can sometimes cause a 'stress fracture' in athletes. In living tissues, the process of damage accumulation is opposed by the process of adaptive remodelling, in which the tissue's cells attempt to strengthen the extracellular matrix so that it can meet the mechanical demands placed upon it (Figure 8). The situation is aptly summed

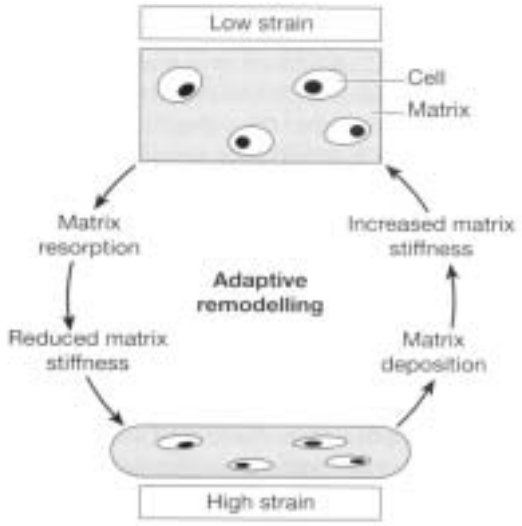

Figure 8 In adaptive remodelling, connective tissue cells respond to low strain (deformation) by resorbing matrix, so that the matrix is less stiff and so deforms more (left). Similarly, the cells respond to high strain by stiffening the matrix and reducing strain to normal levels. (Reproduced from Adams MA, Bogduk N, Burton K, Dolan T. The Biomechanics of Back Pain. Edinburgh: Churchill Livingstone; 2002, with permission from Elsevier).

up by Nietzsche's maxim: "That which does not kill me makes me stronger." Effectively there is a race between strengthening and weakening processes which can leave the tissue either hypertrophied, or injured. Microscopic damage would accumulate most rapidly in tissues such as disc or tendons which are loaded severely, and yet which have a poor blood supply and a low metabolic rate. Similar reasoning would suggest that loading history may lead to injury when an individual increases his level of physical activity suddenly, so that poorly vascularised tissues would be struggling to strengthen as fast as the adjacent bones and muscles.[47]

Impaired nutrition

Intervertebral discs are the largest avascular tissues in the body, and their small cell population receives a barely-adequate supply of nutrients. Any factor which impaired this already-precarious supply of nutrients may lead to cell death and degenerative changes. Cell culture studies have confirmed that disc cells deprived of oxygen have a greatly reduced metabolic rate, and that a prolonged shortage of glucose can kill them.[48] This may explain why disc degeneration is associated with smoking.[49] However, a recent animal model suggests that links between impaired metabolite transport and disc degeneration are not straightforward.[50]

7 'Functional pathology': pain without tissue damage

It is conceivable that stress concentrations in innervated tissues could give rise to pain, even if the stresses were not severe enough to cause damage. (A small stone in your shoe would demonstrate the mechanism nicely.) Experiments on living people have shown that spinal loading depends very much on the precise manner in which a person moves,[23] and experiments on cadaveric spines have shown that the distribution of forces within and between spinal tissues is sensitive to the relative orientation of vertebrae (ie posture),[28;51] and to the speed and duration of loading.[46;52;53] It follows that the manner in which a person uses their back may well be responsible for the presence or absence of back pain, even when imaging studies reveal no spinal pathology to attribute symptoms to. This concept of 'functional pathology' fits in with conventional advice on 'good' and 'bad' posture, and appears to be little more than common sense, and yet it is very difficult to prove. If back ache did indeed arise this way, it would probably be as transient and reversible as the postures and habits that caused it.

Summary

Spinal tissues can age biochemically without becoming degenerated or painful. However a combination of genetic inheritance, ageing and loading history can make some tissues more vulnerable to injury or repetitive loading so that they become disrupted. Degenerative changes follow as cells respond to an unfavourable mechanical and nutritional environment, and a vicious circle of tissue weakening and further injury can develop, particularly within the intervertebral discs. Disrupted tissues give rise to localised stress concentrations which can be painful, but links between degenerative changes and pain are complicated by factors such as stress-shielding and pain sensitisation. Psychosocial factors largely determine subsequent pain behaviour.

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Pain Generation in Lumbar and Cervical Facet Joints

By John M. Cavanaugh, MD, Ying Lu, MS, Chaoyang Chen, MD, and Srinivasu Kallakuri, MS

Facet joints are implicated as a major source of neck and low-back pain. Both cervical and lumbar facet syndromes have been described in the medical literature. Biomechanical studies have shown that lumbar and cervical facet-joint capsules can undergo high strains during spine-loading. Neuroanatomic studies have demonstrated free and encapsulated nerve endings in facet joints as well as nerves containing substance P and calcitonin gene-related peptide. Neurophysiologic studies have shown that facet-joint capsules contain low-threshold mechanoreceptors, mechanically sensitive nociceptors, and silent nociceptors. Inflammation leads to decreased thresholds of nerve endings in facet capsules as well as elevated baseline discharge rates. Recent biomechanical studies suggest that rear-end motor-vehicle impacts give rise to excessive deformation of the capsules of lower cervical facet joints. Still unresolved is whether this stretch is sufficient to activate nociceptors in the joint capsule.

To answer this question, recent studies indicate that low stretch levels activate proprioceptors in the facet-joint capsule. Excessive capsule stretch activates nociceptors, leads to prolonged neural afterdischarges, and can cause damage to the capsule and to axons in the capsule. In instances in which a whiplash event is severe enough to injure the joint capsule, facet capsule overstretch is a possible cause of persistent neck pain.

Lumbar Facet Pain

In a review of the lumbar facet syndrome, Mooney and Robertson[1] noted that the etiology of persistent pain arising from this joint remained elusive and pointed out that there appeared to be no conclusion as to why degenerative joints can be asymptomatic while normal-appearing joints can be painful. Schwarzer et al.[2] injected the lumbar facet joints of 176 patients who had nonspecific low-back pain and no definitive radiologic findings. Of these patients, 15% had pain relief with a shorter-acting anesthetic (lignocaine) and ≥50% improvement in pain with a longer-acting anesthetic (bupivacaine).

Biomechanical studies have confirmed or shown the contribution of the facets to load transmission in the spine and have indicated the possibility of facet overload. Yang and King[3] showed that the lumbar facet superior articular process bottoms out on the lamina below when forces replicating the spinal extensor muscles are used to resist flexion loads. This loading also caused high strains to the facet-joint capsule[4].

In a neurophysiologic study with use of a rabbit model, thirty mechanosensitive units were identified at the lumbar facet joint and twenty-seven were identified in the muscles and tendons near their insertion into the facet[5]. The facet joint contained a much higher proportion of high-threshold, low-conduction velocity units than muscle did. It is these latter units—nociceptors—that are likely to transmit pain. In rabbit facet joints injected with Type-II carrageenan, the multiunit background discharge rate showed an increase that can be divided into two phases—a first phase from zero to thirty minutes, and a second phase from forty-five to 150 minutes[6]. Units that were previously silent appeared in the first fifteen minutes and persisted beyond seventy-five minutes. Thresholds of the characterized units ranged from 1.23 g to >30 g and decreased with time. Histologic examination revealed inflammatory changes in carrageenan-injected tissues, vasodilatation and edema in the capsule, and leukocyte infiltration in the perivascular space within surrounding muscle tissue. In another study, after the injection of substance P (10 μg) into rabbit lumbar facet-joint receptive fields, 54.2% of the units showed immediate onset and 29.2% of the units showed slow onset of the excitation[7]. One-third of the units showed decreased von Frey threshold responses after the application of substance P. These neurophysiologic studies reveal the following in support of lumbar facet pain of capsular origin: (1) a population of high-threshold, small-diameter sensory neurons in the capsule, (2) sensitization and increased discharge of facet-joint neurons in the presence of inflammation, and (3) demonstration of the effects of substance P on these neurons. In addition, Beaman et al.[8] demonstrated substance P-containing nerves in subchondral bone in osteoarthritic facet joints, which suggests that facet pain of subchondral origin may also occur in cases of joint degeneration.

Cervical Facet Pain

Whiplash-associated disorders are among the most common injuries associated with motor-vehicle accidents. In the United States, more than 59% of insurance claimants for motor-vehicle injury reported neck injuries in 1997[9]. Studies of the natural history of whiplash-associated disorders have suggested that chronic pain with continued symptoms develops in

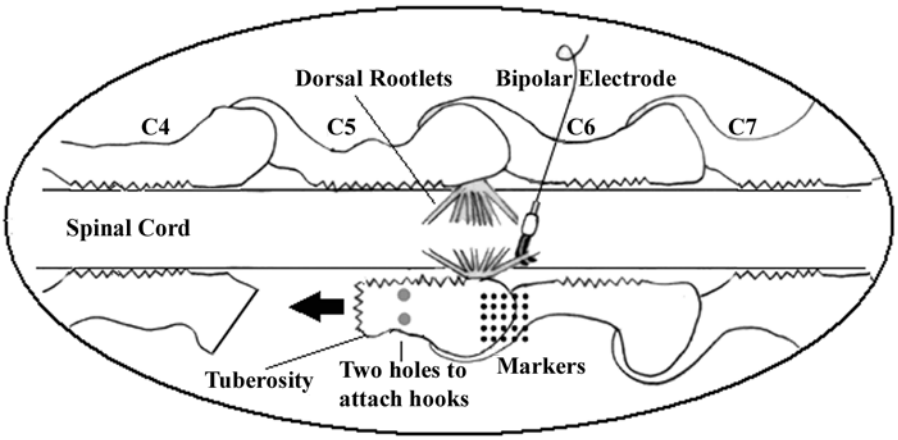

Fig. 1-A

Surgical preparation and positioning of capsule markers. Two holes are shown drilled in the rostral end of the freed C5 process to attach it to the actuator via two stainless-steel hooks. (Reproduced, with modification, from: Lu Y, Chen C, Kallakuri S, Patwardhan A, Cavanaugh JM. Neurophysiological and biomechanical characterization of goat cervical facet joint capsules. J Orthop Res. 2005;23:779-87. Reprinted with permission.)

6% to 33% of acutely injured victims[10]. The societal cost of whiplash injury, including medical and legal expenses, is enormous, as high as $29 billion annually in the United States alone[11].

Many research studies have focused on determining the mechanisms of whiplash injury and appropriate countermeasures. Several regions of the cervical spine are postulated to be a source of whiplash injury and pain generation, including facet joints, intervertebral discs, ligaments and muscles, and spinal nerve roots. Dwyer et al.[12] injected the C2-C3 to C6-C7 facet joints and Dreyfuss et al.[13] injected the lateral atlantoaxial and atlanto-occipital joints with contrast medium under fluoroscopic control to determine if they are potential pain generators. Injection into each joint produced pain patterns replicating clinical neck-pain patterns.

The incidence of cervical facet pain appears to be greater than that of lumbar facet pain. In a study reported by Aprill and Bogduk[14], 128 patients with chronic neck pain underwent diagnostic blocks to the cervical facets; eighty-two obtained complete relief of pain. To account for false positives, a second study was performed on fifty consecutive patients[15] with use of lignocaine and bupivacaine. Of thirty-eight patients who completed the study, twenty-seven had pain relief from both injections and longer-duration relief with bupivacaine. The prevalence of cervical facet pain was concluded to be at least 54% (twenty-seven of fifty). A similar study indicated that 55% of patients with chronic, nonspecific cervical spinal pain had pain of facet origin[16].

A chronic pain condition (late whiplash syndrome) without detectable lesions was reported to occur in subjects with a whiplash injury of the neck[17,18]. The facet joint is a potential source of pain in these cases. Percutaneous radiofrequency neurotomy of the dorsal rami branches was shown to offer pain relief by denaturing the nerves that innervate the facet joint at the level of pain[19]. Long-term relief can be maintained by multiple treatments to overcome axon regeneration. Kallakuri et al.[20] demonstrated nerve profiles that were immunoreactive to substance P and calcitonin gene-related peptide in human cervical facet-joint capsules, strongly suggesting that the capsule does contain nerves that can signal pain.

Several facet-joint injury mechanisms have been proposed, including facet-joint impingement, synovial fold pinching, and facet-joint capsule strain injury. Krafft et al.[21] studied crash recorder-equipped cars and noted no neck injury in impacts with peak accelerations of 6 g or less, temporary neck symptoms at 10 g or less, and long-term disability at 13 g and

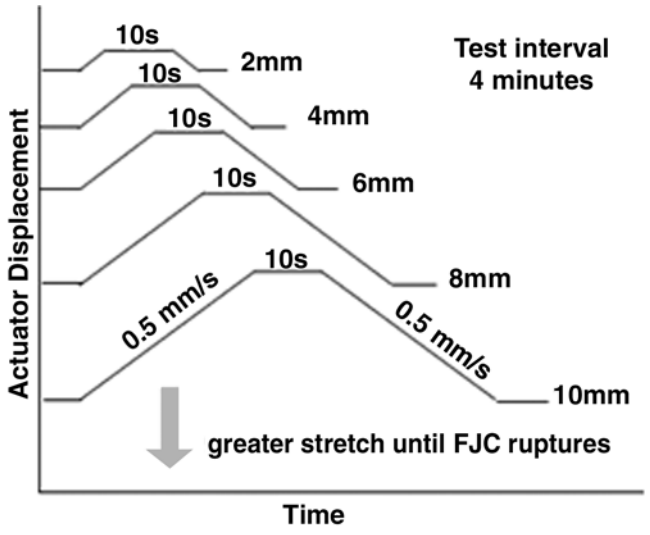

Fig. 1-B

Loading paradigm for quasistatic tests. Tests were run in 2-mm increments with a four-minute rest period between tests. Each load pattern consisted of a 0.5 mm/sec loading ramp, a ten-second hold, and a 0.5 mm/sec unloading ramp. FJC = facet-joint capsule.

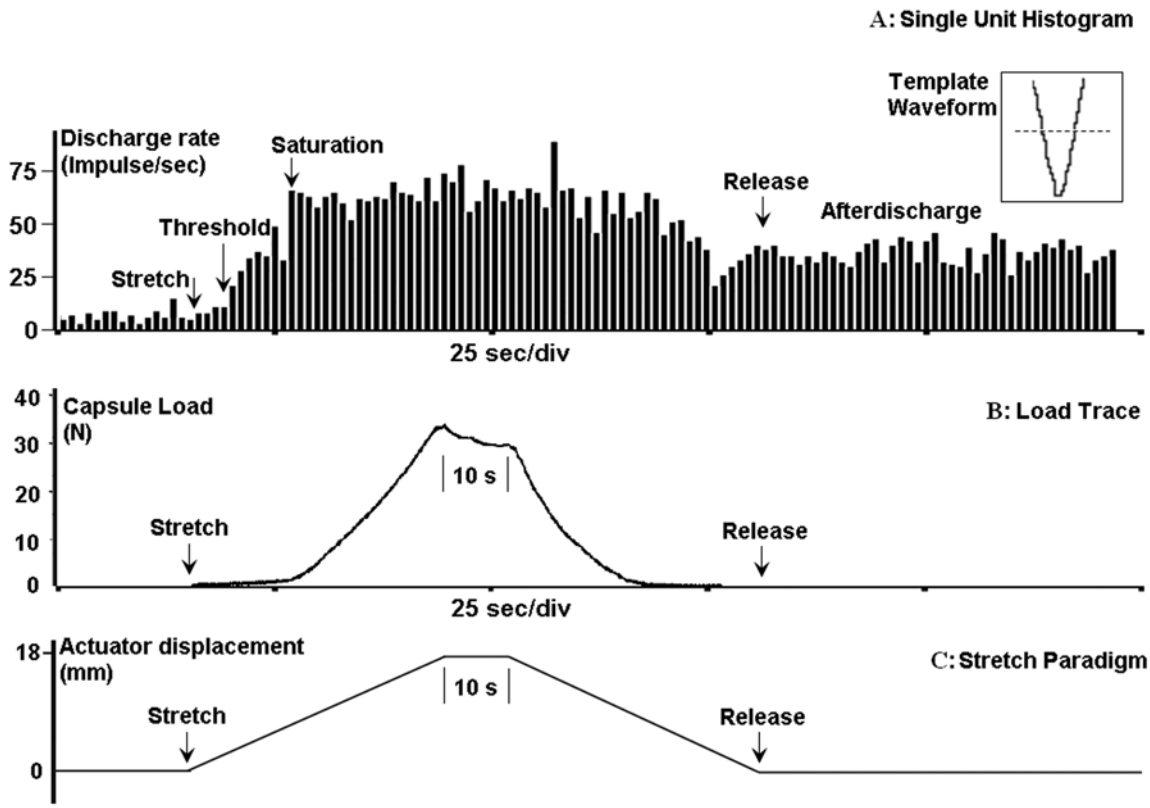

Fig. 2

Neural response of a group-IV unit to 18-mm stretch. (*Top) A:* Single unit histogram. Only the discharges that template-matched the waveform of the unit were counted. The afterdischarge was evident for more than four minutes. Only 125 seconds of the time course is shown here (twenty-five seconds per division). (*Middle) B:* Capsule load. (*Bottom) C:* Actuator displacement scheme. (Reprinted, from: Lu Y, Chen C, Kallakuri S, Patwardhan A, Cavanaugh JM. Neural response of cervical facet joint capsule to stretch: a study of whiplash pain mechanism; with permission of the Stapp Association. Stapp Car Crash J. 2005;49:49-56.)

15 g. The magnitude of facet-joint capsule deformation in these higher "g" whiplash events may possibly result in capsular injury and persistent pain.

Recent Studies Addressing Cervical Facet Pain

To study the possible link between facet capsule stretch and pain generation, our group has developed an in vivo goat model for neurophysiologic and mechanical characterization of facet-joint capsules in the cervical spine[22-25]. These studies are summarized below.

Materials and Methods

Adult LaMancha or Alpine anesthetized female goats (33 to 55 kg) were used. A C4-C7 laminectomy was performed to expose the C6 dorsal rootlets. The spinal cord and roots were immersed in mineral oil at 37°C. The left C5-C6 facet joint was isolated and the C5 inferior articular process was then freed from the pedicle. Two stainless-steel hooks were inserted into holes in this process and connected to an actuator system. A spine fixator, a stereoimaging system, and a computer-controlled actuator coupled with a miniature 50-lb load cell were used to stretch the C5-C6 capsule and measure load and strain[23]. An array of tantalum spheres or acrylic paint targets was applied on the capsule surface (Fig. 1-A) for later strain characterization.

Neural activity of the left C6 dorsal rootlets was recorded with a custom-designed miniature bipolar electrode as described by Chen et al.[22] (Fig. 1-A). Electrical stimuli (0.1 or 0.3 msec duration, 8 or 15 V) were then applied to the capsule at nine locations with a bipolar stimulating electrode. The facet-joint capsule then underwent a series of stretch tests at a loading and unloading rate of 0.5 mm/sec. The first test included 2-mm actuator displacement, followed by increases, in 2-mm increments, for subsequent tests until the capsule sustained rupture (Fig. 1-B).

Waveforms of single sensory units were identified by the action potentials evoked by electrical stimulation. Each waveform was then used as a template by matching the waveform to the individual unit in the multiunit discharge[23]. Image-tracking software was used to track the capsule targets, and linear quadrilateral membrane elements were developed

with use of the target positions as nodes. Digitized marker-displacement history was imposed on the nodes to reconstruct capsule deformation, and finite element strain analysis was performed. The finite elements at the targets were used to describe strain distribution at the nine electrically stimulated areas in which sensory units were identified. Thus, the strain history of a corresponding element was approximated for each unit. An illustration of the data collected from a group-IV unit in an 18-mm stretch test is shown in Figure 2[25].

Results

The following findings are presented in greater detail by Lu et al.[24,25]. Strains of 30% to 41% at the 12-mm stretch test and below did not produce apparent tissue damage. Between the 12-mm stretch and the 22-mm stretch, progressive capsular injury occurred. At the 22-mm stretch, the capsule strains ranged from 41% to 73%, beyond which the capsules typically ruptured. Fifty units were analyzed for their neural properties in relation to strain. These units were categorized by their conduction velocity into thirty-two group-III (thinly myelinated fibers) and eighteen group-IV (unmyelinated C fibers) units. Forty-two units responded to stretch with low-strain thresholds (10.2% ± 4.6%), while eight units responded only to high strains (47.2% ± 9.6%). No significant difference was observed in threshold between groups III and IV. Thirty-five of the forty-two low-strain threshold units displayed discharge saturation at the strains of 44.2% ± 16.7%. No significant difference was seen in saturation threshold between groups.

Twelve low-threshold units and two high-threshold units exhibited afterdischarge. Afterdischarge lasting longer than thirty seconds but less than four minutes occurred after peak strains of 38.5% ± 12.4%; afterdischarge lasting longer than four minutes appeared after 45.0% ± 15.1% strains.

Discussion

Lu et al.[25] demonstrated a quantitative relationship between capsule sensory discharges and applied capsule stretch from cervical facet joints. Their study indicated that capsular strains of 47.2% ± 9.6% are most likely noxious and trigger nociceptive discharges from the capsules, which are transmitted to the central nervous system for pain sensation. Strains that correspond to the onset of nociceptive discharge and to afterdischarge may indicate strain ranges that are injurious or painful in whiplash[26]. In contrast, most of the capsular neural receptors responded in the physiologic range of capsule stretch and fired at strains of 10.2% ± 4.6%.

A majority (83%) of low-threshold units showed saturated responses at high strains of 44.2% ± 16.7%. These responses may play a role in warning the body of potential injury. Similar observations were made in studies in other tissues in which saturation occurred in response to higher-magnitude mechanical stimuli of different modes, including tension, compression, and joint rotation.

This study demonstrated high strain thresholds at 47.2% ± 9.6% for nociception and saturation strains at 44.2% ± 16.7%. These are comparable with the strains that lower cervical facet-joint capsules experienced during whiplash loading, and also fall within the range of partial failure strains in human cadaver facet-joint capsule studies[27,28]. Thus, this study supports a capsule-strain-injury mechanism of whiplash and further provides a neurophysiologic basis for it.

Persistent afterdischarge was observed in this study after capsular strains of 45.0% ± 15.1% and may be related to nerve injury or capsular injury with the release of inflammatory mediators into the surrounding tissue. This peripheral sensitization may lead to central sensitization of pain pathways in the spinal cord. Spinal cord sensitivity can be seen within minutes of tissue injury[29]. More vigorous and longer-lasting afterdischarge may lead to more extensive central sensitization, which may eventually evolve to chronic whiplash pain. Several studies have observed central hypersensitivity to neck stimulation in whiplash patients[30-33].

Our preliminary data demonstrated that axonal swelling and retraction balls (indicators of axonal injury) occurred after capsule strains of 62% to 82%. These axonal changes may lead to hyperexcitability, spontaneous firing, and neuropathic pain[34].

Conclusions

Clinical studies indicate that the facet joint is the origin of a good percentage of lumbar and cervical spinal pain. Studies using diagnostic blocks suggest that the incidence of cervical facet pain is higher than that of lumbar facet pain. Many of these patients have no obvious radiographic abnormalities, and pain may be of capsular origin. Biomechanical studies support overstretch of cervical facet-joint capsules as a possible source of whiplash injury. The neurophysiologic studies reported here support injured facet-joint capsules as a source of the facet syndrome. These latter studies demonstrate high-threshold nociceptors, saturation of mechanoreceptors, and afterdischarges at high strains. Inflammation of the facet joints leads to elevated baseline discharge and decreased thresholds of capsule receptors. High capsular strain may also lead to damaged axons in the capsular tissue, which may then lead to persistent pain. ■

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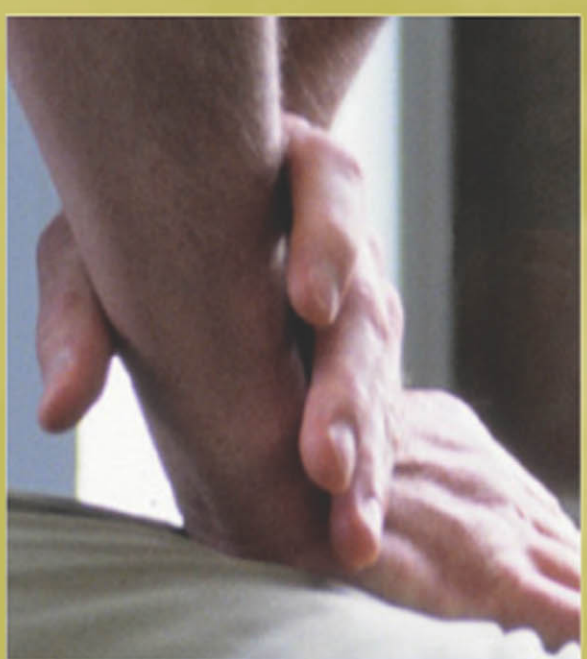

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CHAPTER

32

THE USE OF MEASUREMENT INSTRUMENTS IN CHIROPRACTIC PRACTICE

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OUTLINE

OBJECTIVES

1. To review terminology important to measurement of clinical outcomes, such as reliability, validity, accuracy, precision, sensitivity, specificity, discriminability, responsivity, and clinical utility.
2. To review methods of collecting perceptual outcome measures for pain, disability, satisfaction, and general health.
3. To review functional spine measurements such as spinal stiffness and muscle strength.
4. To review physiological spine measurements such as electromyography and neurodiagnostics.

INTRODUCTION

With the presentation of new patients, clinicians are faced with the challenge of diagnosing their condition, assessing their clinical status, and monitoring their progress. Within this mix of patient management, difficulty arises in objectively measuring patient clinical status. Aside from the primary objective of accurately understanding and describing a patient's clinical status, ever-increasing demands are placed on clinicians from a state and national regulatory standpoint, as well as from the medicolegal arena and third-party reimbursement perspective. Assessing and identifying dysfunction is necessary in the development of objective outcome measures of spinal function. However, if an anatomical diagnosis for low back conditions is impossible 80–90% of the time,[1] being able to differentiate normal spinal function from abnormal is fundamental to creating a diagnosis based on spinal function rather than aberrant anatomy. A diagnosis based on function and tools and techniques to quantify dysfunction provide a means to assess a patient's progress and current condition separate from his or her subjective perception of pain.

The chiropractic encounter has tended to be a high-touch, low-technology health care model with more concern for the person than the disease.[2] Within this realm, *qualitative* assessments have been the predominant feature of clinical assessments in chiropractic, as well as medical, practice. Technological advances over the past few decades, however, have made a number of devices available for clinicians to objectively measure the spine and patient complaints. In addition, outcome assessment instruments have grown in popularity to document the effect a condition has on the patient's activities or quality of life. These advances have begun to bridge the gap between *qualitative* and *quantitative* assessments, serving to raise the bar of objectivity in monitoring patient clinical status.

Building on the knowledge gained from patient history and physical examination, this chapter presents the progression of spinal assessments used in clinical practice. Through a review of the literature, the benefits and shortcomings of popular spine measurement devices are presented with specific emphasis upon usage and *clinical utility.* In this manner, perceptual, structural, functional, and physiological spine measurements are introduced and characterized relevant to patient management. Herein, a rationale is presented for ordering and performing spinal assessments within the context of clinical decision making. As a result of this discussion, new insights will assist the clinician in more effectively managing patients with spinal complaints.

KEY TERMS

Clinical Utility

Prior to discussing spine instrument measures, it is necessary to present several important key terms that will be used throughout this chapter. Because measurements made during the patient encounter provide the clinician with information to describe the patient's health, the usefulness of these measures must be clarified in order to use these tests as a basis for meaningful clinical decisions. Usefulness is known as *utility;* thus, in the realm of clinical practice, the term *clinical utility* applies. Determining the *clinical utility* of a measure is perhaps the most important consideration in test selection. Clinicians must evaluate if a test is able to (a) provide an accurate diagnosis, (b) provide evidence supporting the use of a specific treatment or treatment approach, or (c) enable the clinician to determine the true outcome or effectiveness of the treatment or intervention.[3] To choose the right test for the right patient at the right time is as much an art as it is a science. To assist the clinician in this decision-making process, an introduction of key terms is presented within the context of spine instrument measures.

Qualitative versus Quantitative Measures

Qualitative assessments determine the nature, as opposed to the quantity, of the elements composing a test or measure. Inspection, palpation, and visual observations of patient structure or function are all examples of *qualitative* assessments used by clinicians. Whether the clinician is judging muscle strength by the clinician's kinesthetic sense, visually estimating range or quality of spinal motion through observation, or attempting to define tissue characteristics through palpation, such qualitative assessments can only estimate the clinician's perceived judgment. *Quantitative* assessments, in contrast, express a numerical amount relative to the proportionate quantities of a test or measure. In the context of spine measurements, range of motion can be described in units of degrees, spinal displacements can be described in units of inches or centimeters, and physiological changes can be expressed, for instance, in units of temperature (degrees), electrical signals (volts), or other relevant descriptors. *Quantitative* measures thus allow us to objectify clinical assessments in order to understand and communicate information in absolute terms as opposed to those that are ambiguous. Table 32–1 provides a comparison of commonly used qualitative measures in chiropractic practice and their quantitative counterparts using spine instrument measures.

Reliability

Because *quantitative* assessments use numbers to describe the entity being tested, they tend to be more

TABLE 32–1. Qualitative Clinical Assessments and Their Quantitative Counterparts

Test	Qualitative (Findings)	Quantitative (Units of Measurement)
Perceived pain, disability, and/or functional status	Patients' subjective description (patient demeanor)	Outcomes assessment instruments (numerical score compared to normative values)
Pain threshold or pain tolerance	Palpation for pain (tenderness, grading of trigger points)	Pressure algometry (psi, kg/cm^2, or Pa)
Posture	Visual postural analysis (i.e., head tilt, high shoulder, etc.)	Postural grid photography; surface topographical measures; computer-assisted digitization; diagnostic imaging (x-ray, magnetic resonance imaging, computed tomography) (millimeters or degrees)
Range of motion	Visual estimation (restricted mobility, pain production or reproduction)	Inclinometric measurement; goniometric measurement (degrees)
Intersegmental range of motion	Motion palpation (articular fixation, pain)	Spinal stiffness assessments; static/quasistatic (N/m); dynamic (kg^{-1}, kg, m/Ns, Ns/m, m/N); instantaneous axis of rotation (degrees); instantaneous helical axis (radians)
Muscle strength	Muscle testing (grading 0–5)	Dynamometric measurement (kg or lb) Computerized and digital equipment (kg or lb); load cell or strain gauge types; B200 (kg or lb); electromyelogram (mV)
Muscle endurance	Muscle testing (grading 0–5)	Biering-Sorensen test (time duration, seconds, of task performance); Electromyography (median frequency or wavelet analysis) (Hz)
Muscle spasm	Palpatory myospasm assessment	Surface electromyography (mV)
Nerve function	Orthopedic/neurologic exam (i.e., mechanical tests, stretch tests, deep tendon reflex, dermatomal sensation)	Nerve conduction velocity (ms); needle electromyography (mV); H-reflex (mV); somatosensory evoked potentials (mV); current perception thershold (mV); thermography (degrees C or F)
Pathology	History, inspection, palpation (mass, rubor, calor, dolor)	Diagnostic imaging; laboratory analysis; biopsy

reliable than *qualitative* measures. *Reliability* is the degree of stability exhibited when a measurement is repeated under identical conditions. *Interexaminer reliability,* thus, refers to the agreement between clinicians performing identical tests. Along similar lines, *intraexaminer reliability* concerns the ability of a single examiner to achieve the same results each time a test is performed. Consistencies of results are dependent upon a number of factors, including instrument error, the skill and proficiency of the clinician, patient compliance, and the environment in which the test is performed. These considerations are further discussed in context with the spinal measurements presented in this chapter.

Validity

Reliability, however, must not be confused with validity. Validity is the extent to which a test, measurement, or study measures what it purports to measure. Although a test or measure may be reliable, this does not necessarily mean that it is valid. For example, it would be invalid to use a measure of leg-length inequality to describe a patient's pain because such an assessment isn't intended to quantify pain. Reliability is a necessary but not sufficient condition for validity. For instance, if the dial of the scale were 5 pounds away from zero, one would overreport their weight by 5 pounds. Is the measurement consistent? Yes, but it is consistently wrong. The selection of the appropriate

TABLE 32–2. Types and Definitions of Validity Measurements

Term	Definition
Content validity	The extent to which the content of the test sufficiently covers the area it purports to measure.
Construct validity	The degree to which inferences can legitimately be made from the measure or study.
Concurrent validity	The ability of a measure to indicate an individual's present standing on the criterion variable.
Convergent validity	The degree to which the validity of a measurement correlates to another measurement that is different, but related, and performed at the same time.
Discriminant validity	The ability to correctly discriminate the findings into categories such as positive or negative, normal or abnormal, etc.
External validity	The extent to which the results of a test provide a basis for generalizations to other circumstances.
Face validity	The degree to which a measurement fits with accepted theory.
Internal validity	The approximate truth about inferences regarding cause–effect or causal relationships from the measure or study.
Predictive validity	The extent to which the results of a test are predictive of the future nature of events.

test is thus necessary for validity. The range of interpretations that can be put upon a test is another way to describe validity. Subcategories of validity further dissect the question of validity. Types of validity appear in Table 32–2.

Accuracy and Precision

Also important to consider in test selection are the *accuracy* and *precision* of a measurement device. *Accuracy* is the degree to which a measurement represents the true value of the attribute that is being measured. The *accuracy* of a test is determined, when possible, by comparing results from the test in question with results generated from an established reference method. Weighing an object with a known mass, for example, can assess the accuracy of a weight scale. Consequently, the ability to calibrate a device and regular calibration of equipment are required to maintain *accuracy.* The *accuracy* of an instrument, however, cannot be adjusted beyond its *precision. Precision* is the reproducibility of a quantifiable result or an indication of the random error. To cite an example of the importance of *precision*, consider an inclinometry measure. If an inclinometer system has a standard error of 5 degrees for measuring range of motion, then differences significantly greater than 5 degree must exist to make any judgment about the significance of the results. Both the *precision* and *accuracy* of spine measurement instruments are important considerations when deciphering test results.

Sensitivity and Specificity

Also important in understanding the meaningfulness of spine instrument measures are *sensitivity* and *specificity. Sensitivity* represents the proportion of truly afflicted persons in a screened population who are identified as being afflicted by the test. In other words, *sensitivity* is a measure of the probability of correctly diagnosing a condition, or the true positive rate of a test. Consider, for instance, the *sensitivity* of a magnetic resonance imaging (MRI)-documented disc protrusion among back pain patients. Because disc protrusion is a common finding among asymptomatic individuals,[4] the *sensitivity* of disc protrusion in back pain patients is low. *Specificity,* on the other hand, is the proportion of nonafflicted persons who are so identified by the screening test. It is a measure of the probability of correctly identifying a nonafflicted person, or the true negative rate of a test. Laboratory evaluations commonly have high *specificity* in ruling out a diseased state. Ideally, a test should have 100% *sensitivity* and 100% *specificity.* In other words, the test always correctly identifies the disease state in the population tested. However, instruments used in physical examinations are imperfect and subject to both inherent and human error. Interpretations from physical examination measures thus must be interpreted with caution and correlated with other significant findings.

Discriminability and Responsivity

Finally, clinicians must take into account whether the information gained from an instrument allows

TABLE 32–3. Relationships Between Sensitivity and Specificity Among Tests for Disease States

	Disease State	
Test Result	**Disease**	**No Disease**
Positive	True positive (sensitivity)	False positive
Negative	False negative	True negative (specificity)

the clinician to distinguish between healthy and unhealthy patients. This characteristic, *discrimination,* is determined by making comparisons to a normative database. Further considerations, such as the number of healthy persons that test as diseased (*false positive*) and the number of unhealthy persons who test as negative (*false negative*), additionally assist in determining a measure's *discriminability.* Ideally, a highly discriminating test would have few *false-positive* and few *false-negative* results (Table 32–3). Another term, *responsivity* or *response stability,* refers to the test's ability to provide consistent measurements with repeated use over time. Without this attribute, it is difficult for a clinician to understand the value of a prescribed treatment regimen in pre- and postassessment. Important in assessment of *responsivity* is whether the observed change that occurred is, in fact, reflective of the change that actually occurred. Along these lines, if a measure was found to have a certain range of variability among days of the week, and a test was not performed on the same day, then the variability must be taken into consideration when making any meaningful interpretation from the test comparisons. For the clinician, understanding the benefits and limitations of the instrument measure is of most importance in both test selection and interpreting results in the realm of clinical practice.

CLINICAL CONSIDERATIONS OF THE PAIN PATIENT

Observations made from the moment a patient enters the office can reveal much about his or her condition. Antalgic postures, altered gaits, and guarded movements are examples of presentations that reveal important information. After reviewing the patient history, even more knowledge is gained. Does the patient have pain or paresthesia in a dermatomal distribution suggesting possible nerve root involvement? Conversely, does the patient have local or referred (scleratogenous) type pain possibly arising from somatic structures such as the disc, facet, ligament, muscle, or viscera? While a standard neurological examination may help to confirm the presence of nerve root involvement, the same examination is poor in *discriminating* patients with somatic pain. Even more complex are the uncertainties regarding psychosocial factors and patient motivations to consider when evaluating the pain patient. Within this context, this chapter presents a number of spine instrument measures that are designed to assist the clinician in quantifying patient presentation and outcomes.

In recent years, there have been significant advances in the understanding of the physiologic and biochemical processes that are involved in pain processing at a spinal level. The elucidation of these multifaceted processes has meant a shift away from the conceptualization of pain as a simple "hardwired" system with a pure "stimulus–response" relationship. In fact, many patients report pain in the absence of tissue damage or any likely pathophysiological cause, which may be a result of psychosocial factors,[5] or be related to plastic changes within the nervous system.[6]

The *International Association for the Study of Pain* (IASP) defines pain as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.[5] Naturally, pain is subjective and highly individualistic. Theorists view pain as not simply a sensation, but as a multidimensional phenomenon involving sensory, evaluative, emotional, and response components.[7] Each person learns the meaning of the word *pain* through experiences related to injury in early life,[5] and personal, social, and cultural influences all are thought to play important roles in the pain phenomenon. Because pain, particularly persistent pain, is not often directly tied to specific pathophysiology, but rather is linked to integrated perceptions arising from neurochemical input, cognition, and emotion, the mind greatly influences the intensity of the pain.[8] Moreover, there is a poor association between objective measures of physical pathology and the amount of pain and disability that a patient may express.[9] These factors must be considered in the realm of patient management.

Clinical decision making is based upon securing a working diagnosis from a review of the patient history, physical examination, standard tests, and imaging studies. In the center of this mix lies the patient and the patient's complaints. While this chapter is not intended to provide a comprehensive review of the patient encounter, understanding the role that the patient plays in arriving at a diagnosis is of prime importance. Patient evaluations are not as simple as looking at test results. Comorbid factors such as patient motivation can further influence patient responses on a number of levels—from questionnaire responses to actual test performance. Patients have been known to amplify symptoms or functional status

for a variety of reasons based in the human nature. Anxiety, stress, and emotional disturbances such as depression or hysteria may be responsible for elevated pain scores.[10] In addition, the effects of compensation, litigation, and employment have been named as influences in patient status and outcome.[11] It is clear that comorbid factors exist in patient status and recovery; thus, attentiveness in assessment of the *big picture* is important for clinicians to consider.

A great deal can be learned about a patient through observation. Triano et al. discussed issues surrounding patient motivation in the previous edition of this text.[12] There, it was noted that test results should be interpreted in conjunction with observations made while the test is performed. Observing characteristics such as quality of movements, facial expressions, and performance efforts combined with some standardized approaches to patient evaluation will assist in drawing meaningful conclusions from test results. A common misconception is the assumption that a single measurement is reflective of the patient's legitimate performance capacity. The use of repeated measurements and the use of related tests serve to validate whether test results are reflective of the organic lesion, or are influenced by patient motivation. Such procedures are reviewed in the framework of the spine instrument measures presented in this chapter.

Recent models of spinal pain have been proposed to assist clinicians and researchers in developing useful evaluation and management protocols. Waddell[13] conceptualized the back pain problem as possessing three distinct elements:

- *Pain:* An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.
- *Disability:* Diminished capacity for everyday activities and gainful employment.
- *Impairment:* An anatomical or physiological abnormality leading to loss of normal bodily ability.

While the three elements may be related, it is noteworthy that the strength of the relationship is not perfect and disassociation of the elements can occur.

Another model of disablement has been adapted to the physiotherapy management of low back pain.[14] This model is slightly different than Waddell's because it makes the distinction between a functional limitation and a disability:

- *Functional limitations:* Restrictions in performance at the level of the individual (i.e., the ability to perform a task of daily living).
- *Disability:* Restrictions in the ability to perform socially defined roles and tasks expected of an individual (i.e., inability to work or participate in family social functions).

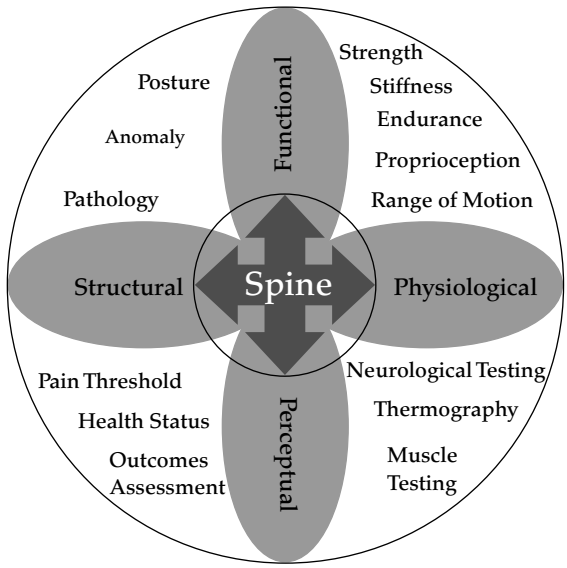

FIGURE 32–1. Categorization of spine instrument measures (perceptual, structural, functional, and physiological) and the associated tests in each category.

The distinction between functional limitations and disability helps to explain why two patients with similar impairments and functional limitations may have very different levels of disability.[14] In common, however, is the fact that clinicians must make decisions based on interpretation of a multitude of test results.

Four kinds of measurements provide relevant information about patient clinical status and/or response to treatment. In general, they are perceptual measurements (i.e., reports of pain severity and pain tolerance), structural measurements (i.e., anomalies, pathology, or posture), functional measurements (i.e., range of motion, strength, stiffness, activities of daily living), and physiologic measurements (i.e., neurologic assessment, laboratory examinations) (Fig. 32–1). The most prevalent complaint among patients presenting to a chiropractic office is musculoskeletal pain.[15] Thus, issues relevant to pain and patient motivations are important in understanding the meaningfulness of spine instrument measures. Research aimed at assessing the quality and effectiveness of health care as measured by the attainment of a specified end result, or outcome, is known as *outcomes assessment.* Such measures include parameters such as improved health, lowered morbidity or mortality, and improvement of abnormal states (perceptual, structural, functional, and/or physiological).

Perceptual Measurements

Patients' perspectives are widely recognized as being essential in making medical decisions and judging the results of treatment.[16] Acknowledging the multifactorial facets of the pain phenomenon, a number of

instruments have been developed to assist the clinician in better understanding patient presentation and monitoring response to treatment. Measurements can be further divided into those tests that are primarily patient-driven (perceptual measurements) and those primarily clinician-driven (structural, functional, and physiological measurements). In this section, two useful perceptual measurements are presented: outcomes assessment and disability questionnaires and algometry. *Perceptual measures* are based upon the conscious mental registration of a sensory stimulus. Thus, results from perceptual measurements are highly dependent on the patient's conscious responses to the question or stimulus.

Outcomes Assessment and Disability Instruments

Outcomes assessment involves the collection and recording of information relative to health processes in an effort to quantify patient status or a change in patient status over time. A variety of questionnaires have been developed to take into account the patients' self-report of their physical function and health. Important properties of any outcomes assessment instrument include practicality (how long it takes to complete; how understandable it is to the patient; acceptability to the population being tested), precision (cross-sectional and test–retest reliability), validity, and responsiveness.[17] Although the field of patient-based outcomes measures is relatively young, the number and types of measures are growing exponentially.[18] Outcomes assessment instruments can be categorized into five classes: general health, pain perception, condition-specific, psychometric, and patient satisfaction.[19]

General Health Outcomes Assessment Instruments General health status measures are designed to broadly assess the concepts of health, disability, and quality of life.[20] One benefit of generic health status instruments is their practicality in terms of use in all patients, regardless of the illness or condition. Although generic health status measures are less responsive to changes in specific conditions than are condition-specific measures, they are important for expansive comparisons of the relative impact of different conditions or treatments on the health of the population.[20] Developed from the Medical Outcomes Study (MOS), the *Health Status Questionnaire.*[21] also known as the short form (*SF-36* or *SF-12,* denoting its number of questions), is a commonly used instrument in managing patients with spinal complaints. A number of other general health assessment instruments are available to clinicians including the *Sickness Impact Profile* (SIP),[22] the *Nottingham Health Profile* (NHP),[23] the *Duke Health Profile* (DUKE),[24] instruments developed out of the *Dartmouth Primary Care Cooperative Information Project* (COOP),[25] and the *Quality of Well-Being Scale.*[26] Table 32–4 describes these general health outcomes assessment instruments.

The SIP, NHP, DUKE, and COOP charts have been used to some extent in the study of patients with

TABLE 32–4. General Health Outcomes Assessment Instruments

Instrument	Description
Health Status Questionnaire (HSQ) (SF-36, Rand-36, MOS-36)	Multipurpose, short-form health survey with 36 questions (shortened version, SF-12, has 12 questions); it yields an eight-scale profile of scores, as well as physical and mental health summary measures
Sickness Index Profile (SIP)	136 items grouped into 12 categories: ambulation; mobility; body care and movement; social interaction; alertness behavior; emotional behavior; communication; sleep and rest; eating; work; home management; and recreation
Nottingham Health Profile (NHP)	38-item questionnaire grouped into six dimensions: physical abilities; pain; sleep; social isolation; emotional reaction; and energy
Duke Health Profile (DUKE)	17 questions grouped into 6 health and 4 dysfunction scores; the health scores are physical health, mental health, social health, perceived health, and self-esteem (physical, mental, and social health scores are further aggregated into a general health summary score); the dysfunction scores are anxiety, depression, pain, and disability.
Dartmouth COOP Chart (COOP)	6 single-item scales including physical fitness, feelings (mental well-being), daily or usual activities, social activities, overall health, and change in health
Quality of Well-Being Scale	Preference-weighted measures of symptoms and functioning to provide a numerical point-in-time expression of well-being, ranging from 0 for death to 1.0 for asymptomatic optimum functioning

back pain and appear to measure similar concepts of health. They have been reasonably well studied in terms of their reliability and validity. Of the available general health outcomes assessment instruments, the Health Status Questionnaire (SF-36) appears to have several advantages over the other generic measures due to its ease of use, acceptability to patients, and its fulfillment of stringent criteria of reliability and validity. McDowell and Newell[27] describe the SF-36 as having a "meteoric rise to prominence." Population and large-group descriptive studies and clinical trials to date demonstrate that the SF-36 is very useful for descriptive purposes, such as documenting differences between sick and well patients and for estimating the relative burden of different medical conditions. In fact, the SF-36 has been used in more than 1000 publications.[28] The usefulness of the SF-36 is illustrated in articles describing more than 130 diseases and conditions. Among the most frequently studied conditions are arthritis, back pain, depression, diabetes, and hypertension, with more than 20 SF-36 publications dedicated to each.[28] The SF-36 appears to strike the best balance between length, reliability, validity, responsiveness, and experience in large populations of patients with back pain.[29] Because it is short, the SF-36 leaves ample room for administration of more precise measures at the same sitting.

Pain Perception Outcomes Assessment Instruments

Pain Intensity This is a quantitative estimate of the severity or magnitude of perceived pain. The three most commonly used methods to assess pain intensity are the *verbal rating scale* (*VRS*); *visual analogue scale* (*VAS*), and *numerical rating scale* (*NRS*).[30] Table 32–5 describes these pain-intensity scales. Positive and negative attributes of the pain-intensity scales are discussed elsewhere.[19,30] VAS and VRS instruments have been found to correlate well, but have differences in the range of categories relative to the VRS.[31] NRS instruments have been found to be easy to administer and score, and thus can be used in a greater variety of patients (e.g., geriatric patients, patients with marked motor difficulties) than is possible with the VAS. Additionally, the validity of the NRS has been well documented in demonstrating positive and significant correlations with other measures of pain intensity.[32] Comparing the VRS, VAS, and 11-point NRS, Bolton et al.[33] further recommended the 11-point NRS for most types of outcomes studies, given the advantages of responsive evaluative measures. Also noteworthy was their finding that asking patients to report their usual pain levels, rather than current levels, enhances the responsiveness of the measures and is a more representative perspective of their pain experience.[33]

TABLE 32–5. Pain-Intensity Scales

Pain-Intensity Instrument	Description
Verbal rating scale (VRS)	Patients read a list of adjectives describing levels of pain intensity and choose the word or phrase that best describes their level of pain (0–3 score; 3 = worst)
Visual analogue scale (VAS)	Patients place a mark on a 10-cm line (on paper or by using a mechanical device), with the ends labeled as the extremes of pain (10 = worst), to denote their level of pain intensity; a quantifiable score is derived from millimetric measurement (0–100)
Numerical rating scale (NRS)	Patients verbally (or by using a pencil) rate their pain from 0–10 (11-point scale), 0–20 (21-point scale), or 0–100 (101-point scale) to rate their pain intensity (highest score = worst)

Pain Affect This is the degree of emotional arousal or change in action readiness caused by the sensory experience of pain. This dimension of pain relates to the distress of an individual and can lead to fear-avoidance behaviors and interference with daily activities. The most widely used measure of pain affect is the affective subscale of the *McGill Pain Questionnaire* (MPQ).[34] The MPQ is a gold standard as a pain-assessment tool because of its established reliability and validity.[30] The MPQ consists of 20 category scales of verbal descriptors of pain categorized in order of severity and grouped into 4 subscales: sensory discrimination, affective, evaluative, and miscellaneous. In this manner, a total score or separate subscores for each subscale can be calculated. A short form of the MPQ has also been studied with positive results.[35] As previously noted, pain is not an independent dimension; rather, it is dependent upon the emotional, motivational, and somatosensory attributes of the patient. Thus, a score on a pain rating scale is not a pure measure of the patient's pain, but is heavily influenced in unknown ways by the patient's emotional and motivational state.[36] Clinicians should take into account the factors that influence pain scores to improve validity. Taking the average of several pain measures across time or across measures can assist in the reduction of erroneous reports of pain.

Pain Location This can give important clues of its etiology or source. The *pain diagram* allows the patient to visually communicate the perception of the location

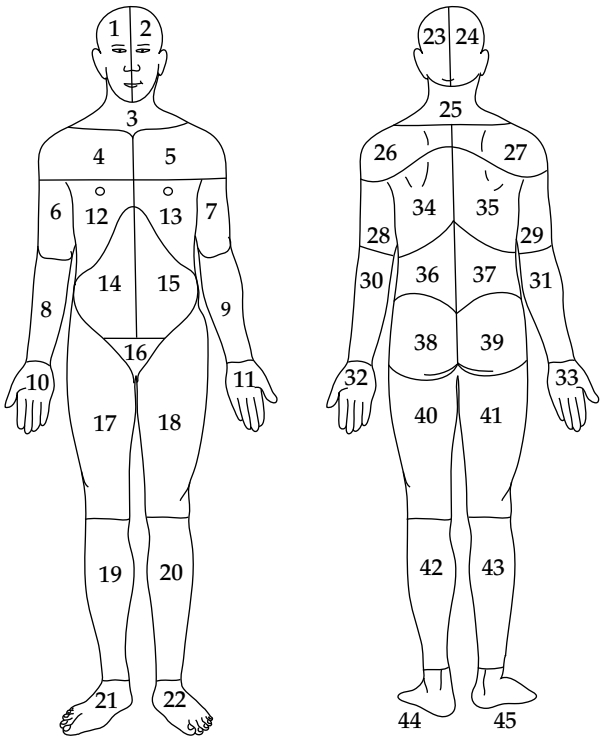

FIGURE 32–2. Pain diagram depicting the body region method of scoring described by Margolis et al. *(Reproduced with permission from Margolis RB, Tait RC, Krause SJ. A rating system for use with patient pain drawings. Pain 1986;24:57–65.)*

and distribution of his or her symptoms pictorially (Fig. 32–2). The pain diagram consists of the front and back outlines of a body on which the patient draws, using different symbols to indicate the quality of pain he or she is experiencing. A score can be derived from points totaled from the number of body regions marked as painful, and the number of different pain qualities reported by the patient. In addition, the size of the painful areas can be quantified. Ohnmeiss[37] studied the repeatability of pain drawings in a chronic low back pain population and found high intraobserver reliability and stability over time. Pain diagrams have also been found to be related to intervertebral disc pathology revealed on diagnostic imaging studies.[38] A number of other studies also demonstrate the reliability and clinical usefulness of the pain diagram in the evaluation and management of patients with musculoskeletal complaints.[39]

Condition-Specific Outcomes Assessment Instruments

While pain quality, intensity, timing, and distribution, reveal important qualities of the patient's condition, the effect of a condition on function, or disability, and activities of daily living is of prime importance. The hallmark of a condition-specific measure is the attribution of symptoms and functional limitations to a specific disease or condition.[40] Unlike items in a generic measure, items in a disease-specific measure assess only those aspects of health that tend to be affected by the disease. The goal is to achieve high relevance and responsiveness of the scales without undue burden to the patient.

A number of instruments specific to the spine or to spine-related complaints have evolved from the need for reliable and valid measures of patient functional status in clinical trials. What have developed are a number of condition-specific instruments for spine-related complaints that are suitable for use in everyday clinical practice (Table 32–6). While it is not the purpose of this chapter to provide a comprehensive review of the numerous condition-specific outcomes assessment questionnaires, some of the most commonly used indices are presented.

Among the many reliable and valid instruments presented in Table 32–6, the following questionnaires are emphasized because of their ease of use and implementation in clinical practice. The *Oswestry Disability Index* (ODI) was developed by Fairbank et al. and later revised.[41] It consists of 10 items assessing the level of pain and interference with several physical activities, sleeping, self-care, sex life, social life, and traveling. The scale is one of the most widely used outcome measures for patients with low back pain. Roland and Morris[44] created a back-specific scale, the *Roland-Morris Disability Questionnaire* (RMDQ), by selecting 24 items from the SIP (e.g., "I avoid heavy jobs around the house," "I sleep less well," "I stay at home") and

TABLE 32–6. Condition-Specific Outcomes Assessment Questionnaires Pertaining to the Spine

Back
Oswestry Disability Index[41,42]
Million Visual Analogue Scale[43]
Roland-Morris Disability Questionnaire[44]
Waddell Disability Index[45]
Low Back Outcome Score[46]
Clinical Back Pain Questionnaire (Aberdeen Low Back Pain Scale)[47,48] (applies to the neck also)
Low Back Pain Rating Scale[49]
Quebec Back Pain Disability Scale[50]
North American Spine Society Lumbar Spine Questionnaire[51]
Resumption of Activities of Daily Living Scale[52]
Bournemouth Questionnaire[53,54]
Functional Rating Index[55] (applies to the neck also)
Neck
Neck Disability Index[56]
Headache Disability Inventory[57]
Copenhagen Neck Functional Disability Scale[58]
Migraine-Specific Quality of Life Questionnaire[59]

adding the phrase "because of my back." The scale has become popular among back pain researchers and has been translated into several languages.[40]

While the RMDQ can be used in chronic back pain patients, often it is the preferred measure for administration to acute low back pain sufferers because its questions appear to be more applicable to those with more recent pain. The RMDQ may be better suited to settings in which patients have mild to moderate disability, and the ODI to situations in which patients may have persistent severe disability.[60] Both the ODI and RMDQ instruments have been recommended by experts as a prime choice for clinicians managing patients with back pain.[29] Similar to the ODI, The *Neck Disability Index* (NDI)[56] consists of 10 items assessing the level of neck pain and inference with activities of daily living. The NDI possesses stable psychometric properties and provides an objective means of assessing the disability of patients suffering from neck pain.[61] For general use, the *Headache Disability Inventory* (HDI)[57] is useful in assessing the impact of headache and its treatment on daily living, although other specific headache questionnaires are available.[59]

Psychometric Outcomes Assessment Instruments Health care providers and researchers alike attest to the importance of the role that psychosocial factors play in influencing the effectiveness of treatment regimens. By definition, psychosocial influences are those issues involving both psychological and social aspects (i.e., age, education, work, marital, and related aspects of a person's history). Such influences can have an effect upon pain perception, adaptation to pain, functional status, and, ultimately, quality of life. In addition, patient motivation (i.e., conscious or subliminal factors of attitude and belief) also affects health-related predicaments.

Depression, anxiety, and personality disorders have been identified as the most frequently occurring psychiatric conditions associated with persistent pain.[19] Incorporation of psychometric outcomes assessment tools may assist in understanding these comorbid factors. With such a variety of instruments available, it is confusing for chiropractors to determine which tool is best for use in their practice. As a general recommendation, the Health Status Questionnaire and the patient history, when used together, may serve as general screening tools for the presence of significant psychosocial factors relating to a patient's condition. Once identified, further assessment of specific conditions or disorders can be conducted with more sensitive indices. Table 32–7 lists several psychometric outcomes assessment instruments available for use in clinical practice.

Patient Satisfaction Outcomes Assessment Instruments The growing regulation of health care has created ever-increasing requirements of accountability from health care providers. Patient satisfaction measures have been developed to assess the health care experience in the eyes of the patient. Common areas of inquiry include the patients' satisfaction with their visit, satisfaction with their overall care, convenience, technical quality of care, and continuity of care, and satisfaction with the financial policies of the office. Because these measures begin to distance themselves from the focus of this chapter, the reader is directed elsewhere for further discussion of patient satisfaction issues. Implementing outcomes assessment tools into clinical practice is as easy as integrating any other procedure into the office environment. Many of the

TABLE 32–7. Selected Psychometric Outcomes Assessment Instruments

Psychometric Instrument	Evaluative Conditions
Beck Depression Inventory	Depression
Modified Zung Depression Index	Depression
Health Status Questionnaire	Depression, health perception
Modified Somatic Perception Questionnaire	Perceived depression
Waddell's Nonorganic Low Back Pain Signs	Nonorganic low back pain
Somatic Amplification Rating Scale	Nonorganic low back pain
Fear Avoidance Beliefs Questionnaire	Chronic pain/ fear avoidance behavior
Anxiety Sensitivity Index	Anxiety
Distress and Risk Assessment Method	Depression, anxiety
Symptom Checklist-90 (SCL-90-R)	Anxiety and depression

Adapted from Yeomans SG. *The clinical application of outcomes assessment.* Table 4–6. Stamford, CT: Appleton & Lange, 2000:33.

questionnaires are easy to use, understand, and implement without compromising valuable time and staffing resources. To gain information on treatment outcomes, it is necessary to administer outcomes assessment instruments before, during, and after a treatment plan.

FUNCTIONAL MEASUREMENTS

Assessment of spinal function across various dimensions of mobility, strength, endurance, and coordination provides a rational approach to clinical assessment, rehabilitation strategies, and determination of return-to-work potential for injured employees.[62] Objective, quantitative measurements of function provide the clinician with a definition of the patient's physical capacity, and succeeding tests document changes in performance with treatment. Understanding the benefits and limitations of the different functional measurements, their clinical utility, and their generalizability serves to assist the clinician in better managing patients.

Spinal Stiffness Assessment

Knowledge of spine segment motion patterns, forces, and stiffness is of fundamental interest to understanding the postural, time-dependent, and dynamic response of the spine, the role of spinal implants in mechanical load sharing, and the response of the extremities (appendicular skeleton) and spine (axial skeleton) to externally applied forces, such as palpatory assessments and chiropractic spinal manipulation. In the course of physical examination, many practitioners assess mechanical responses, such as the amount of stiffness or movement that occurs at different vertebral levels, by palpating the spine. Reliable methods to obtain an adequate understanding of the force-induced displacement response of the spine have long been considered important. In principle, an unstable segment should exhibit increased displacement or decreased stiffness, while a stiffened segment should exhibit decreased displacement when compared to adjacent segments.[63] For assessment of intersegmental mobility, many techniques involve posteroanterior (PA) "springing" of the spine. In this manner, clinicians use their fingers to contact on each side of the spinous process or alternatively impart a force by contacting the spinous process with the heel of their hand and applying an oscillating motion. The examiner thus relies on his or her kinesthetic sense to judge the stiffness or mobility of the spine at the level being tested as compared to adjacent levels and uses this information to formulate clinical diagnoses that direct treatment. This technique is commonly known in chiropractic circles as *motion palpation* and as PA mobilization in the *physiotherapy* arena. Because of the qualitative nature of such assessments, however, many studies have demonstrated that manual motion palpation techniques are not as reliable, specific, or sensitive as previously believed.[64,65] For this reason, mechanical devices have been developed in the hope of improving the reliability and accuracy of spinal stiffness assessment. The quantitative equivalent of motion palpation can be thought of as spinal stiffness assessment.

Static or Quasistatic In the simplest sense, the mechanical responses—force and displacement—are analyzed at a given frequency by means of computerized data analysis interfacing a mechanical stylus containing a potentiometer or load cell that makes contact with the spine. In the evolution of quantitative spinal stiffness assessment a number of devices have been developed using a variety of methodologies. Researchers from Australia developed the *Spinal Physiotherapy Simulator* (SPS),[66] a large table-mounted frame housing a testing head in which a load cell is encased. This device has been found to be reliable in measuring PA spinal displacements in a study of asymptomatic subjects being tested at L3 (intraclass correlation coefficient [ICC] = .88)[66] and accurate in the measurement of a series of elastic beams. In the latter, the system tended to underestimate beam stiffness by less than 1%.[67] This device was found to be highly reliable in the measurement of relative displacement at L3 (ICC = .99) and at L5 (ICC = .95) when a PA force was applied to L4.[68] The SPS has mostly been used in a research setting because of its size. Latimer et al. described an enhancement of the SPS to enable greater portability, thus making the technique more suitable for clinical practice, calling it the *Stiffness Assessment Machine* (SAM)[67] (Fig. 32–3). Edmondston and colleagues also developed a variation

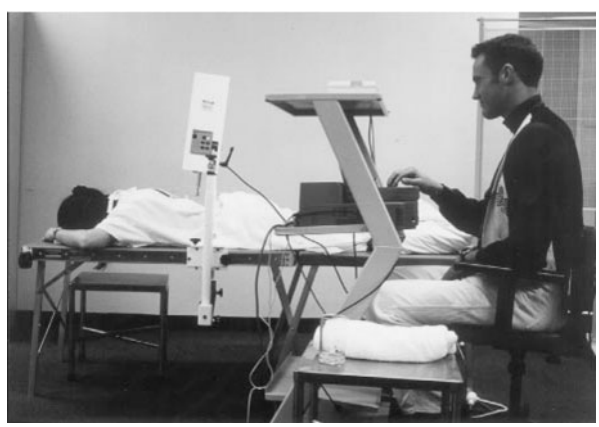

FIGURE 32–3. The Stiffness Assessment Machine (SAM) being used to test posteroanterior stiffness at L3. *(Reproduced with permission from Squires MC, Latimer J, Adams RD, Maher CG. Indenter head area and testing frequency effects on posteroanterior lumbar stiffness and subjects' rated comfort. Manual Ther 2001;6:40–47.)*

TABLE 32–8. Testing Conditions Found to Influence the Posteroanterior Stiffness of the Spine

Study	Testing Variables	% Change in PA Stiffness*
Latimer et al.[71]	Force applied to L3: 80 N vs. 200 N	27% increase
Latimer et al.[72]	Plinth padding: rigid vs. padded at L3	19% decrease
Maher et al.[73]	Plinth padding: rigid vs. padded at L3	22% decrease
Lee and Liversidge[74]	Frequency of PA testing: 0.05 vs. 0.5 Hz	26% decrease
Lee and Svensson[75]	Frequency of PA testing: 0.01 vs. 0.5 Hz	16.5% increase
Squires et al.[70]	Frequency of PA testing: 0.25 vs. 2.0 Hz	9.2% decrease
Squires et al.[70]	Indenter head size: large vs. small	13% decrease
Squires et al.[70]	Indenter head size and PA frequency of PA testing:	21% decrease
Beaumont et al.[76]	Cycle of breathing: FRC vs. Max. Insp.	16% increase
Lee and Liversidge[74]	The vertebrae tested:	
	L4 vs. L5	11% increase
	L3 vs. L4	23% increase
	L3 vs. L5	37% increase
Viner et al.[77]	The vertebrae tested: L1 vs. L5	17% increase
Caling and Lee[78]	The angle of PA vector: neutral vs. 10 degrees cephalad neutral vs.	12% decrease
	10 degrees caudad	11% decrease
Edmondston et al.[69]	Lumbar spine position: neutral vs. flexed	21% increase
Allison et al.[79]	The angle of force application to L5: perpendicular vs. vertical	9% decrease
Lee et al.[80]	Extensor muscle activation: relaxed vs. MVC	317% increase

Key: FRC = functional residual capacity; large indenter = 34 × 46 mm; Max. Insp. = maximum inspiration; MVC = maximal voluntary contraction; small indenter = 12 × 25 mm.

* The results expressed as a percentage (%) change are based upon the variables being tested. The percentage changes were calculated in a standard manner and are expressed as a change from the first to second variable.

Adapted from Squires MC, Latimer J, Adams RD, Maher CG, Indenter head area and testing frequency effects on posteroanterior lumbar stiffness and subjects' rated comfort. *Manual Ther* 2001;6:40–47.

of this device, labeling it the *Spinal Postero Anterior Mobiliser* (SPAM).[69]

What these devices have in common is the desire to minimize testing variables that may affect the measured stiffness values obtained from the spine in order to develop a reliable and valid objective measure of PA spinal stiffness. From a number of published investigations several testing conditions have been found to influence or change the PA stiffness of the spine; they are presented in Table 32–8.

Ultrasonic Indentation Another method of spinal stiffness assessment was developed at the University of Calgary by Kawchuk and colleagues; it uses ultrasound imaging.[81] This technique, referred to as *ultrasonic indentation* (UI), advances a blunt probe housing an ultrasonic sensor mounted to a large frame into the tissue surface and records the ensuing deformation.[82] By obtaining ultrasonic images of a rigid, echogenic target (e.g., spinous or transverse process) at the beginning and end of loading, soft-tissue compression can be quantified by measuring the distance to the target in each image and then subtracting the distance found at maximal indentation from the distance found at preindentation, resulting in a measure of displacement.

Validation studies using UI have resulted in a mean displacement error ranging from 14.37% to 22.05%. Other research with the device has determined its bench-top accuracy and reliability to range between 0.99 and 1.00 (ICC) with error values in force, displacement, and stiffness ranging from 0.81% to 13.62% over varying experimental conditions.[81] Several sources of variation in spinal indentation have also been identified,[83] such as indentation site relocation, intraabdominal pressure, subject movement, muscular response, and stiffness estimation. These variables, which have been unaccounted for in previous indentation studies, might be responsible for the change or lack of change in force-displacement properties between pre- and posttest trials. Ultrasonic indentation has also been put to use, with encouraging results, in investigating experimentally induced degeneration in a porcine model.[84] While ultrasonic indentation appears to be promising in a research setting, its large frame and high cost prohibit its use in a clinical setting, and research has not been done in clinically relevant human subjects. Its

developers are seeking to develop a hand-held device to make the technology available to clinicians in the future.

Dynamic As we have already discussed, the mechanical and physiologic response of the spine to PA forces is dependent upon many factors, including the intensity, direction, duration, and frequency of the applied force. Of these factors, the frequency-response and frequency-dependent stiffness characteristics of the spine to PA dynamic loading are perhaps the least well understood. Efforts to estimate the in vivo stiffness behavior of the spine have mainly consisted of static or quasistatic (low-frequency) mobilization using surface displacement transducers. The spine is a viscoelastic structure that exhibits time-dependent behavior. The dynamic PA frequency-dependent stiffness behavior of the human spine thus reflects its viscoelastic structure, albeit generally more elastic than viscous.

Different structures (ligaments, cartilage, bone, tendons, muscle) will exhibit varying degrees of time-dependent and frequency-dependent viscoelastic behavior. Consequently, the overall structural/vibration response of the spine is modulated by the architecture or structural organization of component tissues, as well as load sharing provided by adjacent structures (e.g., rib cage, sternum, pelvis). When such factors are combined with other considerations, such as spinal curvature, the net effect is a complex structure and frequency-dependent mechanical behavior. As a result, quasistatic loading conditions tend to overestimate the displacement response (underestimating the stiffness) as a consequence of creep deformation of the structure. Evidence of such behavior has been observed in studies reporting the PA motion response of the lumbar spine at different oscillation frequencies.[74,75] In these studies, quasistatic or slow cycling ($\leq$0.1 Hz) PA mobilization is associated with an approximately 15–25% increase in deformation (15–25% reduction in stiffness) in comparison to mobilization at 0.5–1.0 Hz. Another important characteristic of the human lumbar spine is its nonlinear, load-deformation behavior. Inherent nonlinearities in the load-deformation characteristics of the spine result in variations in the measured PA displacement and stiffness that are dependent on the magnitude of the applied force. For example, previous PA mobilization studies have reported a substantial increase in PA stiffness when the peak force applied is increased.[71,85]

Keller et al.[86] validated a modified hand-held adjusting instrument to be used as a mechanical impedance assessment device and later quantified the mobility characteristics (dynamic stiffness and mechanical impedance) of the normal human thoracolumbar spine.[87] The authors found that the thoracolumbar spine typically exhibited an impedance minimum at frequencies ranging between 30 and 50 Hz.[87] Colloca and Keller[88] were the first to simultaneously measure the dynamic stiffness and neuromuscular responses in low back pain patients (Fig. 32–4). The authors observed significantly increased spinal stiffness in those patients with frequent or constant low back pain (LBP) symptoms, in contrast to those patients with only occasional or no LBP symptoms. Patients with increased spinal stiffness were also observed to have larger-magnitude neuromuscular reflex responses corroborating the findings of others who have observed the contributions of the musculature to spine stability.[89] Noteworthy was Colloca and Keller's suggestion that neuromuscular responses be taken into account when assessing spinal stiffness.[88]

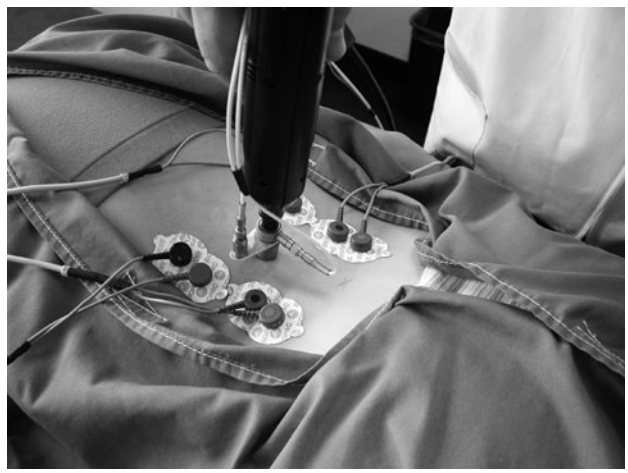

FIGURE 32–4. Dynamic spinal stiffness assessment is performed with a hand-held electromechanical device equipped with an impedance head while simultaneous electromyographic (EMG) measurement is obtained from the adjacent erector spinae muscles. In this manner, the muscular contributions to spinal stiffness can be considered during the neuromechanical assessment.

To further validate dynamic spinal stiffness assessments, Keller, Colloca, and Gunzburg obtained intersegmental motion data in vivo by attaching accelerometers to rigidly affixed bone pins placed into the spinous processes and measuring the resultant motion characteristics to known forces.[90] Fitting original data to a mathematical model, Keller et al. developed a 21-degrees-of-freedom model to describe the motion characteristics of the spine during mobilization assessment procedures and spinal manipulation.[91] Dynamic spinal stiffness assessments show promise in the comprehensive biomechanical analysis of the spine in clinical practice.

Assessment of Muscle Strength

Segmental instability, pathology, or dysfunction is believed to produce abnormal patterns of motion and forces that may play a role in the etiology of musculoskeletal pain. Muscle tension is a function of muscle length and its rate of change and thus can be altered by the level of neural excitation. These relationships are called the length–tension and velocity–tension relationships. The central nervous system excites the muscle, and the generated tension is transferred to the skeletal system by the tendon to cause motion, stabilize the joint, and/or resist the effect of externally applied forces on the body.[62] The ability to quantify spine segment motion, or *kinematics,* together with the concomitant forces, or *kinetics,* is therefore of clinical significance in terms of both diagnosis and treatment of spinal disorders and back pain. Before discussing the use of spine instrument measures in evaluating muscle strength, a review of some key terms provides a better understanding of some of the biomechanical principles in this area.

Manual Testing Qualitative measures of muscle strength include manual muscle testing techniques that rely on grading criteria to clinically assess patients (Table 32–9). Chiropractic clinicians commonly rely on manual muscle testing to evaluate extremity joint injuries, and to grade the motor strength of potential spinal nerve root involvement in patients with radicular symptomatology. Because of the qualitative nature of these assessments, their clinical usefulness is limited as the ability of even skilled clinicians to determine strength differences is rather restricted.[12]

TABLE 32–9. Qualitative Manual Muscle Strength Grading

Grade	Description	% of Deficit
5: Normal	Complete active range of motion against gravity with full resistance	0
4: Good	Complete active range of motion against gravity with some resistance	1–25
3: Fair	Complete active range of motion against gravity only, without resistance	26–50
2: Poor	Complete range of motion with gravity eliminated	51–75
1: Trace	Slight muscle contraction with no joint motion	76–99
0: Zero	No evidence of muscle contraction	100

Adapted from *Guides to the evaluation of permanent impairment,* 5th ed. Chicago: American Medical Association, 2000.

TABLE 32–10. Factors Influencing Trunk Strength

Gender
Age
Body (or body segment) weight
Body position
Exercise and nutrition
Hormonal or genetic factors
Motivation
Motor learning and movement coordination
Physiological factors (i.e., muscle fatigue and muscle co-contraction)
Cross-sectional area of muscle
Type of contraction
Speed of contraction
Duration of contraction
Number of warm-up and learning trials
Rest between trials
Joint limitation (pathology, pain, or dysfunction)

In manual muscle testing performance, relative muscle strength is judged more on the basis of the total force and duration of effort that the examiner uses to overcome the patient than on the actual force generated by the patient. Accuracy in such manual assessment techniques requires differences in strength of 35% or more.[92] Consequently, instruments have been introduced to clinical practice to improve the objectivity of muscle-strength assessments. In general, trunk strength and/or trunk muscle strength has been shown to vary with many different factors as shown in Table 32–10.

Ultimately, the measured force is a function of the individual's motivation, environmental conditions (muscle length, rate of change of muscle length, nature of the external load, metabolic conditions, pH level, temperature, etc.), prior history of activation (fatigue), understanding instruction and description of the tasks to be performed, control strategies and motor programs employed to satisfy the demands of the task, and the biophysical state of the muscles and fitness (fiber composition, physiological cross-sectional area of the muscle, and cardiovascular capability).[62] The complexity of these processes and their interrelationships cannot be overemphasized. Moreover, an individual's strength is reduced by 10–30% when exertions are performed dynamically, as compared to isometric strength.[93]

Dynamometry Researchers and clinicians use many different methods to study trunk strength. No direct measures are available, but intradiscal pressure measurements and intraabdominal pressure

measurements are two in vivo methods of direct measurements used to estimate trunk strength.[94] Two ex vivo, or noninvasive, methods currently used to quantify strength changes are dynamometry and electromyography.

Traditionally, dynamometers are tension-measuring devices in which the stretching of a spring or a strain gauge is used; today, a dynamometer can be defined as any instrument used to measure torque or force. As a whole, dynamometers are clinically convenient and simple, with good reliability as long as positioning is consistent. There are many different kinds of dynamometers used to measure different types of muscle contractions and muscle-induced motions. Some measure only isometric force or torque production; others assess dynamic (i.e., isokinetic or isoinertial) motion as well. Function is usually assessed in one or more of three planes: extension–flexion, rotation, and lateral flexion. Because trunk strength is different at different joint angles, isometric strength test data is normally reported using a "strength curve," a plot showing the force or torque generated by the trunk as a function of the changing angle of the trunk (Fig. 32–5).

Isometric Testing When performing isometric assessments, a sustained effort of 2 seconds has been proposed to meet standardized minimum criteria. Averaging three consecutive tests can also be helpful in identifying insincere efforts. Any variation greater than 10–15% between trials may be suggestive of voluntary holding back in performance. Computer software has been developed to calculate consecutive efforts and further determine a coefficient of variation to indicate whether the test performed was valid.

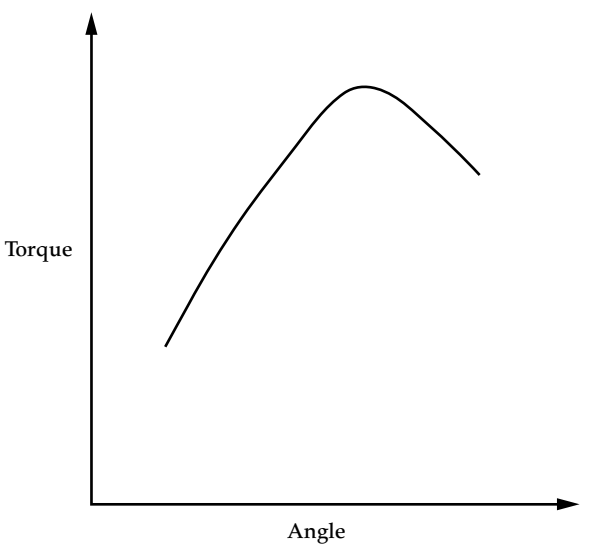

FIGURE 32–5. Strength curve.

Fatigue is another factor that may cause a reduction in strength upon multiple trials; consequently, variations in strength of up to 20% or more are necessary to determine a clinically relevant disparity in muscle strength.[12] JTECH Medical (Salt Lake City, UT) has developed an easy to use hand-held dynamometry system that allows for quantitative manual muscle strength assessment of the extremities (Fig. 32–6) and trunk (Fig. 32–7).

Isokinetic Testing Isokinetic dynamometers measure dynamic force or torque throughout a range of motion at various constant, preset velocities. Isokinetic tests thus require specialized instrumentation that contains either hydraulic or servomotor systems to provide constant velocity. Specific examples of isokinetic dynamometers include Cybex II (Cybex Inc., Ronkonkoma, NY), KIN/COM (Chattecx Corporation, Chattanooga, TN), Biodex (Biodex Corporation, Shirley, NY), and LIDO (Loredan Biomedical Inc., Davis, CA). Triano et al.[12] note that the primary measurement obtained in isokinetic testing is the torque generated during the controlled part of the motion and is only valid during the controlled part of the

FIGURE 32–6. Manual muscle testing of elbow flexion with dynamometry. *(Photograph courtesy of JTECH Medical, a division of Zevex Inc., Salt Lake City, UT.)*

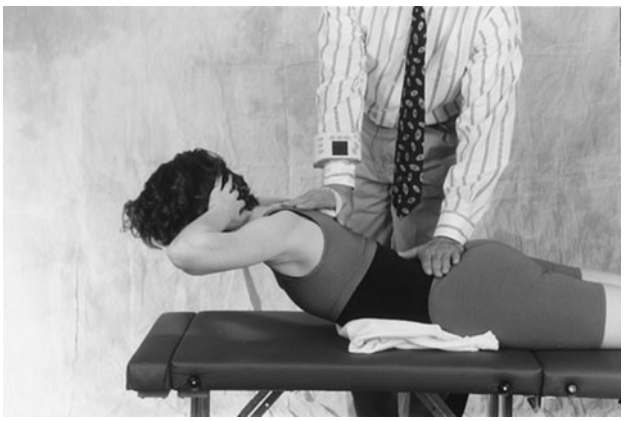

FIGURE 32–7. Manual muscle testing of trunk extension with a hand-held dynamometer. With this particular dynamometer (PowerTrack [JTECH Medical]), maximum force is digitally displayed on a wrist-mounted LCD panel or, alternatively, strength curves are plotted by computerized software. *(Photograph courtesy of JTECH Medical, a division of Zevex Inc., Salt Lake City, UT.)*

motion. In principle, the resistance offered by the machine is equivalent to the applied muscle torque over the entire range of movement. This represents the patient's muscular capacity.[12] Sources of error that should be taken into account with isokinetic testing include inertial error, or the change in limb or trunk orientation through the range of measurement. Inertial error can alter the amount of torque registered by the machine. Torque overshoot is another error that can occur with isokinetic testing, representing a machine artifact that arises from the inertial effect of motion as the preset velocity is achieved.[12] To eliminate these errors, highly specialized machines have been developed.

Isoinertial Testing Isoinertial strength testing requires the control of torque values that the patient will be permitted to use during movement. Isoinertial systems can be made capable of monitoring position, velocity, and torque simultaneously while they independently vary. The B200 Triaxial Isoinertial Dynamometer (B-200) (Isotechnologies, Inc., Hillsborough, NC) is a commercially available isoinertial dynamometer (Fig. 32–8). It measures isoinertial strength against a preset resistance where the subject's velocity varies with the amount of force or torque the subject applies. In other words, the subject's movements (accelerations and decelerations) are made against a constant resistance. If the torque generated by the subject is greater than the machine resistance, the surplus torque will determine acceleration.[95] The B-200 is also unique because movement about all three axes (extension–flexion, rotation, and lateral flexion) can be measured simultaneously by a single machine. Quantifying dynamic motions is important because three-

FIGURE 32–8. The B200 Triaxial Isoinertial Dynamometer (Isotechnologies, Inc., Hillsborough, NC) is used for isoinertial trunk muscle strength testing.

dimensional trunk velocity significantly increases low back pain risk.[96]

The B-200 outputs each subject's trunk position (three-dimensionally), angular velocity, and torque. Position is measured from 0 degrees upright. Sign convention dictates forward flexion as positive (therefore, backward extension is negative). Velocity output is the angular velocity of the upper body, with the axis of rotation considered to be through the hips or L5-S1. Trunk moment (*torque*) output by the B-200 includes the torque of the machine, and must be corrected for the effects of gravity. The B-200 enables measurement of isometric exertions at various trunk postures in addition to its dynamic testing capabilities. Isoinertial trunk strength testing with the B-200 provides reliable measures of torque and velocity parameters, and additional research has identified demographic parameters important to such testing in chronic low back pain patients.[97] In addition, a normative database has been developed to assist in the clinical utility of these measures.[98]

Although somewhat controversial, trunk weakness has often been described as a contributor to low back pain. In fact, several investigations have revealed stronger trunk muscles in asymptomatic subjects as

compared to patients with low back pain.[99,100] In addition to weaker trunk muscles, there also appear to be differences observed in the ratio of flexion-to-extension trunk strength.[95] Other studies using isoinertial techniques have reported that patients with low back pain tend to have slower movements than do normal subjects.[93] Until more evidence is available, however, correlation of trunk strength to other objective measures of trunk function and perceptual measures is necessary to discriminate between symptomatic patients.

PHYSIOLOGICAL MEASUREMENTS

In the presence of clinical findings suggestive of an underlying neurological condition, numerous tests and measures are available to the clinician to further evaluate the patient. Clinicians have become increasingly dependent on neuroimaging studies such as MRI, computed tomography (CT), or bone scans, but more reluctant to order specific physiological tests including electromyography (EMG), nerve conduction velocity (NCV), and evoked potentials studies (Fig. 32–9). The clinician may either not be aware of the precise applications and limitations of these studies, or not be familiar with their use or interpretations. While diagnostic imaging studies are valuable in demonstrating pathology such as disc protrusion, the clinical utility of such studies is limited without clinical correlation. For example, large disc herniation or other structural abnormality may exist without causing nerve compression, and many structural abnormalities are present in asymptomatic individuals.[4] Alternatively, in other situations, a relatively small disc protrusion may result in neurologic deficits and radiating pain. Consequently, the increasing complexity of imaging studies has led to increased necessity for more sophisticated functional tests to look for neurologic deficits.[101]

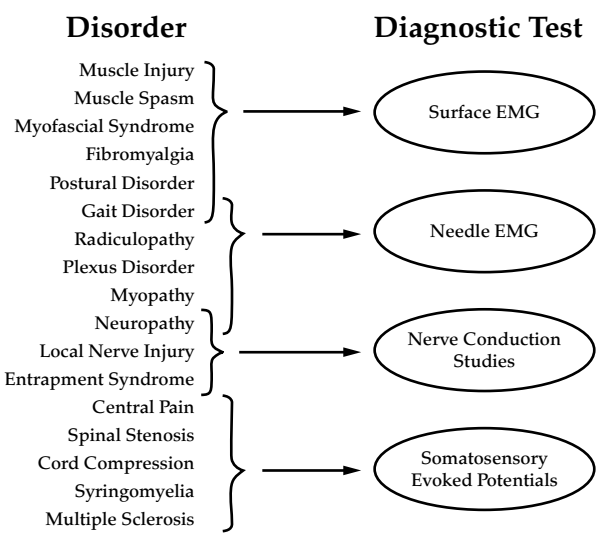

FIGURE 32–9. Neuromusculoskeletal disorders and commonly used corollary diagnostic tests.

Physiological assessments allow the clinician to passively or actively measure resting or functional responses of the body (i.e., electromyography), or evoke responses through monitoring responses of various nerves and muscles to electrical stimuli. Incorporation of specialized testing such as electrodiagnosis substantially alters clinical impressions in a large percentage of patients.[102] The complex relationship between clinical information, the extent of testing, and final diagnostic certainty suggests that specialized medical knowledge is required for accurate physiological assessments. Although this chapter is not intended to provide a comprehensive review of the available spectrum of electrodiagnostic tests and their interpretations, this discussion does provide the clinician with valuable information to assist in understanding the rationale behind some of the more commonly used physiological measurements in clinical practice.

Electromyography

Electromyography (EMG) measures the electrical signals generated by muscle contraction, which are proportional to the degree of neuromuscular activity and therefore also to the strength of muscle contraction. A brief overview of the properties of skeletal muscle will provide important background information of the physiological properties for which electromyography is derived.

The structural unit of skeletal muscle is the muscle cell, also referred to as a muscle fiber. Groups of muscle fibers are termed fasciculi and aggregate to form a whole muscle. A fasciculus can include only a few muscle fibers, as seen in smaller muscles such as the lumbricales, or as many as 150 or more in larger muscles, such as the biceps brachii or gluteus maximus. This unique arrangement of muscle fibers within the fasciculus accommodates independent functioning of the muscle fibers from their respective activation. This is important because the fibers belonging to a motor unit are spread throughout a muscle. A motor unit is defined as a group of homogenous muscle fiber types innervated by a single axon. Activation of a motor unit, therefore, results in the contraction of single muscle fibers within many different fasciculi.

Myofibrils are surrounded by a sarcoplasmic reticulum that plays an essential role in both the storage and release of ionic calcium to signal contractile proteins. The contractile proteins of skeletal muscle are organized into cylindrical organelles, termed myofibrils, each organized into sarcomeres, its fundamental contractile unit. Skeletal muscle is also called striated muscle, resulting from its histological

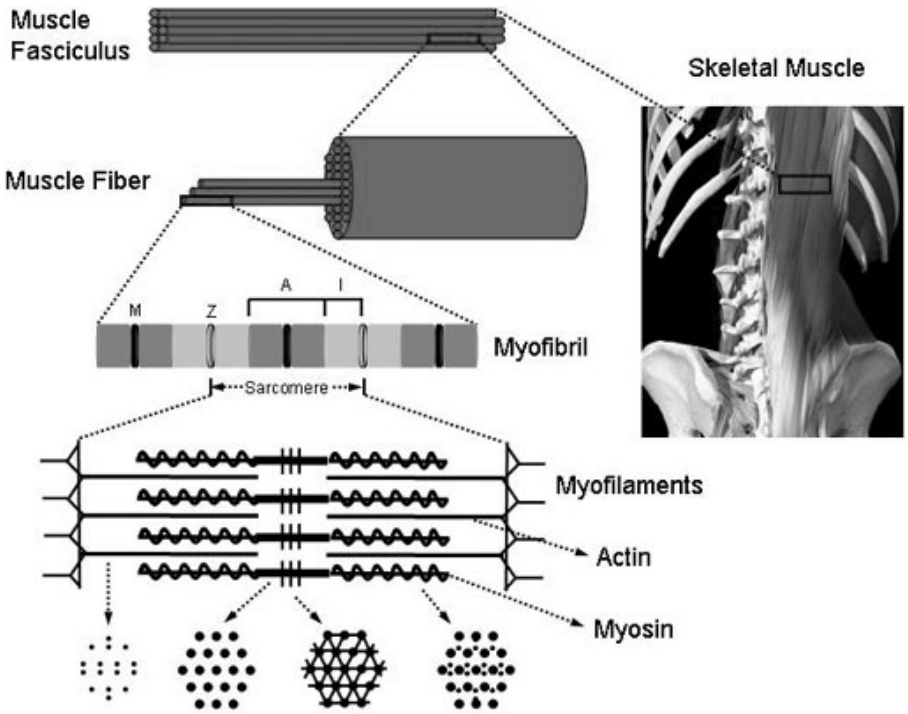

FIGURE 32–10. Gross to molecular skeletal muscle organization. Muscle fasciculi contain muscle fibers comprised of myofibrils, which contain the contractile unit of the muscle, the sarcomere. A = A band; I = I band; Z = Z band. *(Adapted from Bloom W, Fawcett DW. Textbook of histology, 10th ed, Fig. 11–19. Philadelphia: WB Saunders, 1975:309. Skeletal muscle photograph courtesy of Primal Pictures, Ltd., Interactive spine—chiropractic edition, London.)*

appearance from the repetitive series of transverse bands in each sarcomere, the most prominent being the Z, A, and I bands. The distance between two Z bands is defined as the sarcomere, which will vary with the state of contraction or relaxation in the muscle. The dark A bands of the sarcomere are formed by thick myofilaments, termed myosin filaments, and interdigitated thin myofilaments called actin. During contraction the actin filament slides over the myosin. A second set of transverse bridges is the M band, which serves to connect adjacent myofilaments. Huxley[103] demonstrated that thick myofilaments are arranged in a hexagonal lattice and that thin filaments interdigitate with the thick filaments at each trigonal point, producing what is now termed the double hexagonal lattice of myofilaments. Figure 32–10 illustrates the structural organization of skeletal muscle.

Motor units can also be classified.[104] Slow-twitch motor units can fire continuously at low frequencies for long periods of time. Fast-twitch fatigue-resistant units can produce greater forces than slow-twitch motor units, but cannot fire continuously for long periods of time. Fast-twitch fatigable fibers produce the greatest force, but only are capable of doing so for short periods. The force that a muscle produces and the speed of movement are controlled by the type of motor unit found in the muscle, and the motor unit recruitment. Slow-twitch motor unit recruitment is responsible for maintaining posture and slow movements. Slow-twitch fibers are thus recruited first, and the fast-twitch fatigable units are only recruited when a fast powerful movement is required. For each muscle contraction, motor units are recruited at the same force level. During high force demands, after all motor units have been recruited, additional force is generated by increasing the firing frequencies of the motor units. The tension created by a muscle also depends upon the geometric configuration of the muscle fibers, the length of the muscle, and the velocity of the contraction. The inside of a muscle fiber has a resting potential of about –80 mV, which remains in equilibrium until stimulated. A significant stimulus causes a rapid depolarization followed by repolarization, termed an action potential. The temporal and spatial summation of action potentials are responsible for the waveforms observed on oscilloscopes or computers during EMG testing. There are several factors to consider when measuring muscle activity via EMG (Table 32–11), which necessitates a basic understanding of the components involved.[105]

Measurement of Muscle Strength Using EMG Signal Amplitude The relationship between EMG and muscle force naturally arises when viewing an electromyogram. It stands to reason that if there is little to no signal, there will be no active muscle force and, alternatively, the more muscle fibers that are active and the more frequently they fire, the higher the force responsible for the signal. The EMG can be quantified and used to classify the electrical activity level that produces a certain muscular tension based upon changes in amplitude and frequency. In other words, an EMG force measurement seeks to quantify the average

TABLE 32–11. Factors that Influence the Signal Information Content of Electromyography

Factor	Influence
Neuroactivation	The number of motor units recruited; the firing rate of motor unit action potentials; the synchronization of firing
Muscle fiber physiology	The conduction velocity of muscle fibers
Muscle anatomy	The orientation and distribution of muscle fibers of motor units; the total number of motor units; the diameter of muscle fibers
Electrode size and orientation	The number of muscle fibers within the pickup area of the electrode; the number of motor units within the pickup area of the electrode detection surface relative to the muscle fibers
Electrode–electrolyte interface	The material and preparation of electrode and electrode site; the electrode impedance decrease with increasing frequency (high-pass filter)
Electrode configuration	The type of electrode used: needle or surface, monopolar or bipolar; the effect of distance between electrodes and bandwith (band-pass filter); the orientation of electrodes relative to axis of muscle fibers

Adapted from Gerleman DG, Cook TM. Instrumentation. In: Marras WS, ed. *Selected topics in surface electromyography for use in the occupational setting: Expert perspectives.* Washington, DC: US Department of Health and Human Services, 1992:44–68.

number and firing rate of motor units contributing to an actual muscle contraction and to relate the quantity to the actual force produced. The myoelectric signal represents the temporal and spatial summation of all active motor units within the recording area of the electrodes. EMG is thus not a direct assessment of muscle force, but of muscle electrical activity, and other relationships need to be established (calibration of electrical output and force produced) before reasonable muscle force estimates can be made.

The change in the myoelectric signal is based on the motor unit recruitment and firing rate within the muscle. In general, as more force is demanded, more motor units are recruited, and the motor units already firing increase their frequency of firing. Electromyographic measurements thus generally show a relatively monotonic (1:1) relationship between muscle force and trunk muscle activity. However, this relationship varies from muscle to muscle and is linear, curvilinear, or other based on the various roles or responsibilities of different muscles (i.e., posture or locomotion). There is a monotonic relationship between the EMG signal amplitude and muscle force.[106] A quasilinear relationship between EMG and force has been reported for smaller muscles, whereas a nonlinear EMG–force relationship has been determined for larger muscles where the increase in EMG signal is greater than the increase in force.[107] The use of EMG as a biomechanical analysis has been found to reveal impairments that have not been routinely identified with standard clinical tests.[108]

Measuring the EMG activity of trunk musculature has been used in an attempt to assess dysfunction of the lumbar spine. The majority of assessments have focused on quantifying the EMG amplitude differences between low back pain (LBP) patients and control subjects. The rationale behind these investigations is to identify "spasm" or increased muscle activity in LBP populations as a result of muscle splinting or aberrant neural control. The research on this use of EMG as a spinal assessment technique and outcome measure is mixed. This chapter does not go into detail reviewing studies that assessed the discriminant validity of trunk muscle EMG amplitude assessments (see reference 109) but focuses instead on the newer EMG techniques and data collection protocols that may provide a better assessment of spinal function. The use of the erector spinae EMG signal has been researched in an attempt to discern differences between those with low back injury and asymptomatic subjects. Unfortunately, a general consensus on the use of surface EMG in clinical practice is lacking. It is often postulated that those with LBP have an increased level of muscle activity relative to controls. Some studies show no difference between groups,[110] while others show an increase in EMG activity in those suffering LBP.[111]

Flexion-Relaxation Phenomenon There is some support to suggest that differences exist between back pain patients and normal subjects during dynamic flexion tasks at peak flexion[112] and between the ratio of activity during forward flexion and reextension.[113] Several studies have examined the apparent myoelectric silence of the low back extensor musculature during a standing to full flexion maneuver, or the *flexion–relaxation phenomenon*. The electrical silence that occurs in healthy subjects during lumbar spine flexion has been hypothesized to represent the extensor musculature being relieved of its momentary supporting role by the passive tissues, particularly the posterior ligaments.[114] Likewise, a failure of the muscles to relax is thought to be indicative of heightened erector spinae resting potentials or underlying back muscle spasticity (Fig. 32–11).

Watson et al.[115] assessed the test–retest reliability of the flexion–relaxation phenomenon measure in a group of chronic LBP patients (n = 11) and further compared the results between a group of normal healthy controls (n = 20) and a group of chronic LBP patients (n = 70). Repeated measurements over 4 weeks demonstrated between-session reliability of 0.81–0.98 for the dynamic activity. The levels of surface electromyography (sEMG) activity in the fully flexed position were significantly greater in the fully flexed position in the chronic LBP group than in the controls. The flexion:relaxation ratio (FRR), a comparison of the maximal sEMG activity during 1 second of forward flexion with activity in full flexion, demonstrated significantly lower values in the chronic LBP group than in the control group. The combined discriminant validity for the FRR for all four sites resulted in 93% sensitivity and 75% specificity. These results indicate that dynamic sEMG activity of the paraspinal muscles can be reliably measured and is useful in differentiating chronic LBP patients from normal controls. The authors concluded that the FRR clearly discriminated the patients from the healthy controls. Shirado et al.[116] also found that the flexion–relaxation phenomenon could discriminate between chronic back pain patients

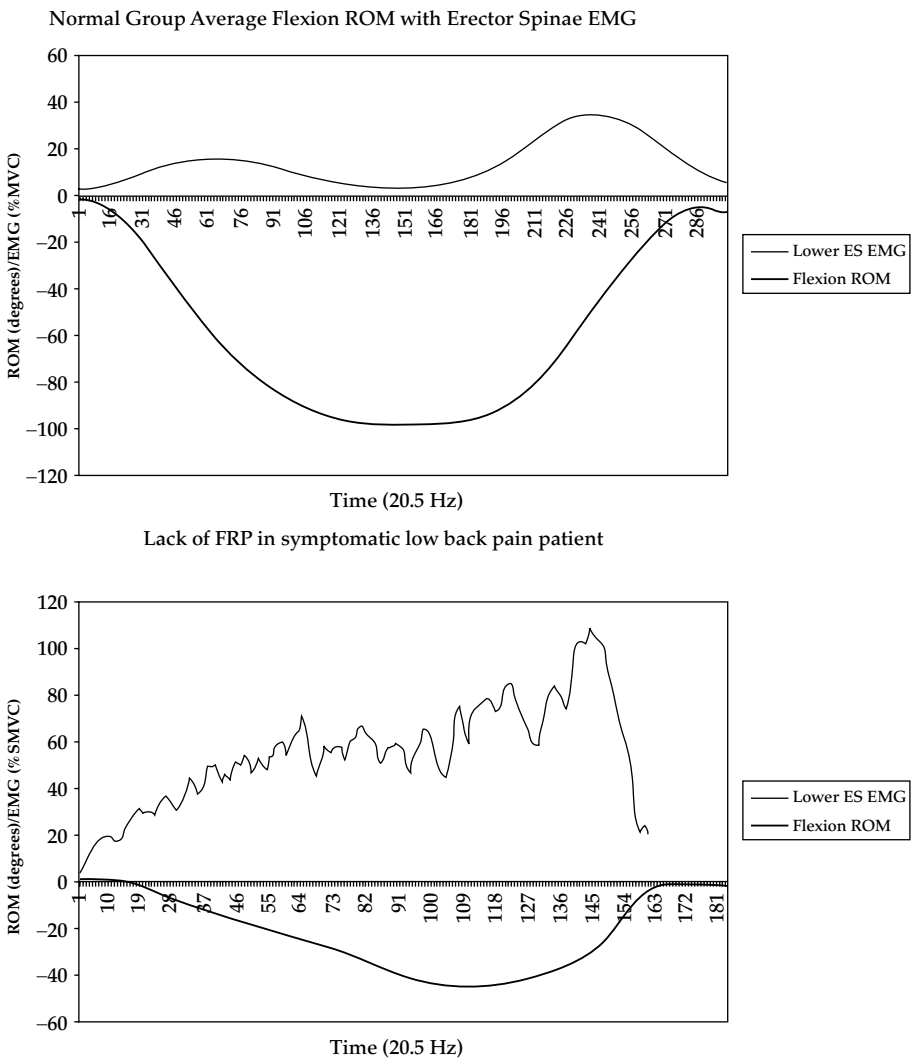

FIGURE 32–11. *Top:* Normal erector spinae muscle activity during flexion–extension. A silence in muscular activity is noted at the peak of flexion, which is indicative of the flexion–relaxation phenomenon. *Bottom:* Lower erector spinae muscle activity during flexion–extension in a patient with chronic low back pain. Note the failure of the erector spinae to silence at the peak of flexion as seen in asymptomatic groups. ROM = range of motion; SMVC = submaximal voluntary contraction.

and normal subjects. In their study of 20 chronic LBP patients, none exhibited the flexion–relaxation phenomenon, as compared to its clear demonstration in 25 healthy subjects prior to maximum flexion. The flexion–relaxation phenomenon has also been investigated in the cervical spine.[117] However, no work has been performed relevant to its ability to discriminate between patients with cervicogenic disorders. Ahern et al. recommended that clinicians pay close attention to qualitative aspects of patient behavior to improve the sensitivity of the physical examination in detecting bona fide impairment when assessing the flexion–relaxation phenomenon.[118]

Paraspinal Muscle Asymmetry It has also been suggested that a difference in the amplitude symmetry between left and right trunk muscles may exist in the LBP population. Again, the research is mixed, with the majority of studies finding no differences between groups,[119] and other studies finding a greater EMG amplitude asymmetry in the LBP group.[120] The inconsistent results reported by studies may be a result of the many factors that modulate measured EMG activity levels that are not related to the level of neural drive. Electrode placement, skin temperature, moisture, cutaneous fat distribution, as well as muscle fiber type and size can all influence measured EMG activity level. Nonhomogeneity in these factors between sides of the body may relegate asymmetry in measured EMG activity to be the norm even though it is possible that bilateral muscles are contracting at equal intensities. With so many factors modulating EMG activity, a large variation in EMG amplitude is seen[121] across subjects. A patient may have an elevated EMG level relative to the patient's normal activation level, whereas the patient's EMG activity level may still be within a range considered normal. Alternatively, not all patients with back pain have a condition that presents with an elevated EMG trunk muscle activity.

One recent study[122] compared the EMG activity of the trunk muscles between normal subjects and chronic LBP patients during standardized trunk movements controlling for the many variables including age, sex, weight, and skin-fold thickness below the attached electrodes. In this study, the EMG amplitude analysis revealed significant differences between groups for some muscles (left lumbar and thoracic erector spinae). The authors further noted that the abnormal (asymmetric) EMG patterns detected among the chronic LBP patients were not explained by postural asymmetries. Other EMG analyses compare the changes in the muscle activation level over time, making it possible to compare the shape of the EMG linear envelope (activation profile) across subjects, or within a subject, to compare bilateral muscle group symmetry. Grabiner[123] found a greater degree of erector spinae bilateral asymmetry in a LBP population (n = 6) than in a control group during an isometric exertion. A similar difference between populations was found by Lehman[124] during dynamic flexion tasks. Lehman's study quantified the symmetry in the bilateral erector spinae (upper T9 and lower L3) EMG linear envelope by using a cross-correlation function that assesses the similarity between the left and right EMG waveforms. They found that the left and right lower erector spinae linear envelopes (activation profile) were less similar (correlated) in LBP sufferers than in normals.

Neurodiagnostics

Conventional electrodiagnostic evaluation, including needle EMG and a variety of nerve stimulation tests, has a proven and long-established place in the evaluation and diagnosis of disorders of muscle and nerve.[125] Ongoing research into more standard electrodiagnostic tests has resulted in the ability to better define the sensitivity, specificity, and theoretical basis of these tests, leading to an improved understanding of how neurodiagnostic testing can influence diagnostic and treatment outcomes.[126] As Table 32–12 shows, numerous neurophysiological tests are available to the clinician managing spinal disorders.

Several questions can be answered by clinical neurophysiologic examination such as whether a neurologic deficit exists, and the extent of its nature, severity, chronicity, and progression. Haldeman and Dvorak[126] have presented the natural progression of tests that add information to the clinical examination (Fig. 32–12). The clinical examination is often capable of accurately defining both the presence and the nature of a neurologic deficit. If motor, sensory, and reflex abnormalities all follow well-defined, consistent patterns, the presence of a particular neurologic deficit can be assumed with a high degree of confidence. Unfortunately, however, in many patients with back pain such findings are not easily discernable. Moreover, no single test has been developed to document all types of neurologic deficit.

Another consideration impacting test selection involves the timing of the condition or injury. EMG measures of denervation and reinnervation are slow, ongoing processes taking 3–4 weeks postinjury for the muscle membrane to react to denervation.[126] Hypersensitive responses in the form of spontaneous electrical activity, as is seen in fibrillation potentials and positive sharp waves, thus are not observed with needle EMG until nearly a month after injury. Direct nerve conduction tests, however, become abnormal immediately after the onset of a neuronal injury.[127]

Needle EMG Needle EMG evaluation appears to be the most useful electrophysiological technique in the

TABLE 32–12. Primary Clinical Neurophysiologic Tests and Their Utilization

EMG	Acute and Chronic Denervation Myopathies
Motor nerve conduction	Peripheral neuropathies
	Entrapment neuropathies
Sensory nerve conduction	Peripheral neuropathies
	Entrapment neuropathies
	Postganglionic nerve injuries
H-reflex	S1 radiculopathies
	Cauda equina lesions
	Sciatic neuropathies
	Peripheral neuropathies
F-responses	Motor neuropathies
	Sciatic neuropathies
	Peripheral neuropathies
Mixed nerve somatosensory evoked potentials (SEPs)	Peripheral and sciatic neuropathies
	Myelopathies
	Brainstem and cortical lesions
Small sensory nerve evoked responses	Sensory radiculopathies
	Sensory peripheral neuropathies
	Myelopathy
Dermatomal SEPs	Root-specific sensory radiculopathies
	Sensory peripheral neuropathies
	Myelopathies
Cortical and nerve root evoked potentials	Myelopathies
	Radiculopathies
Muscle evoked responses	Myospasm
Thermography	Reflex sympathetic dystrophy

Adapted from Haldeman S, Dvorak J. Clinical neurophysiology and electrodiagnostic testing in low back pain. In: Weisel SW, Weinstein JN, Herkowitz HN, Dvorak J, Bell GR, eds. *The lumbar spine*. Philadelphia: WB Saunders, 1996:141–161.

diagnosis of radiculopathy[128] and is used to measure single motor unit potentials. Spontaneous activity is measured during and after the insertion of the electrodes into the muscle to be examined, and again once activity has equilibrated. The patient is also requested to perform varying degrees of muscular contraction intensities. The characteristics of the duration, amplitude, and phases of the action potential are examined for abnormalities associated with disease. Some phenomena associated with neurological disorders include synchronization for motor unit potentials, fibrillation potentials, positive sharp waves, and fasciculations. Myopathies often demonstrate the common characteristic of a diminished mean duration of action potentials. Other findings include spontaneous activity, increased polyphasic potentials, and reduced motor unit field.[12] Needle EMG has proven useful in distinguishing false-positive radiologic studies because normal persons have few, if any, electromyographic abnormalities in the paraspinal muscles.[129] Needle EMG, in particular, can be a sensitive test for radiculopathy and neuronal deficits.[126] Such testing, however, requires a high level of technical experience and expertise.

Nerve Conduction Velocity Nerve conduction velocity (NCV) testing provides information about the speed, or latency, of neural transmission along a known distance of a sensory or motor nerve fiber. By stimulating a nerve at two different points, two latencies can be obtained and a velocity calculated using the following equation: $NCV = D/(L_{proximal} - L_{distal})$. The distance (D) in millimeters between the two electrodes divided by the difference in latency time (L) in milliseconds equals the conduction velocity of the nerve (NCV) in meters per second. Measurements may be made at several points along the nerve to identify the location of a lesion. Nerve conduction velocities can be compared with known values for interpretation.

In understanding nerve stimulation studies, one must remember that a nerve fiber is a cluster of variable-size nerves that will respond to different stimuli. The wave of propagation that results can be *orthodromic* (from proximal to distal) or *antidromic* (from distal to proximal). In this manner, the response of a nerve can be identified using recording electrodes and the relationship between stimulus and response can be displayed and recorded. The applied stimulus is graded as subthreshold, threshold, submaximal, maximal, or supramaximal.

H-Reflex The Hoffman reflex, or H-reflex, is an electrical analogue of the sensory motor monosynaptic stretch reflex that is elicited by selectively stimulating Ia fibers of the posterior tibial or median nerve. Such stimulation can be accomplished by using slow (less than 1 pulse/second), long-duration (0.5–1 msec) submaximal stimuli with gradually increasing stimulation strength that bypass the muscle spindle and directly stimulate the afferent nerves. The H-reflex can be thought of as a controlled version of the classic deep tendon reflex where mechanical stimulation to the tendon containing sensory receptors elicits a subsequent motor response. Studying H-reflex modulation may also provide insight into how the nervous system centrally modulates stretch reflex responses.

In the lower extremity, the H-reflex is traditionally performed by applying the electrical pulse over tibial nerve at the popliteal fossa, which produces a burst of action potentials traveling both orthodromically

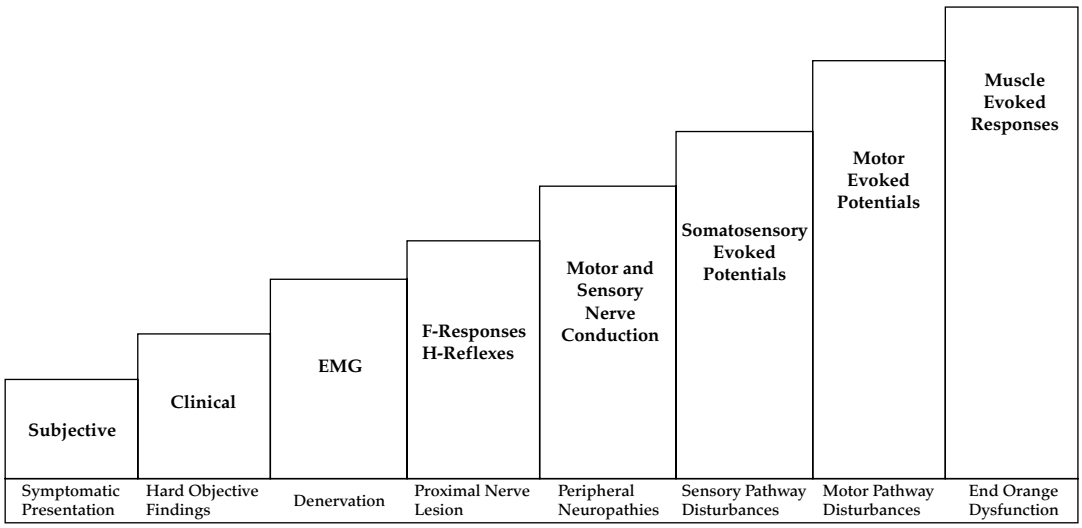

FIGURE 32–12. How each electrodiagnostic family of tests adds information to the clinical examination. *(Adapted from Haldeman S, Dvorak J. Clinical neurophysiology and electrodiagnostic testing in low back pain. In: Weisel SW, Weinstein JN, Herkowitz HN, Dvorak J, Bell GR, eds. The lumbar spine. Philadelphia: WB Saunders, 1996:144.)*

and adromically from the site of stimulation (Fig. 32–13).[130] The first impulses to reach the recording electrodes are a direct motor response termed the M-wave. The H-wave is delayed because of the reflex duration from the time it takes for the stimulus to travel along the Ia fibers, through the dorsal root ganglion, across the spinal cord to the anterior horn cell, which then propagates the impulse along the alpha motor axon to the muscle. H-reflex latency can be determined easily from charts, according to height and sex, or from published normal values.[131] Alternatively, the patient's asymptomatic limb can be used as the normal value because the difference in latency between both sides should not exceed 1 msec.

The H-reflex can be obtained at low stimulation levels without any motor response (M-wave) preceding it. As the stimulation strength is increased, the M-wave appears. With further increases in stimulation strengths, the M-response becomes larger and the H-reflex decreases in amplitude. When the motor response becomes maximal, the H-reflex disappears and is replaced by a small late motor response, the F-wave. The H-reflex can normally be seen in many muscles, but is easily obtained in the soleus muscle (with posterior tibial nerve stimulation at the popliteal fossa), the flexor carpi radialis muscle (with median nerve stimulation at the elbow), and the quadriceps (with femoral nerve stimulation). The H-reflex is useful in the diagnosis of S1 and C7 root lesions, as well as the study of proximal nerve segments in either peripheral or proximal neuropathies. The H-reflex has been shown to have a high correlation with the Achilles tendon reflex and measures the presence or absence of an S1 radiculopathy with a high degree of accuracy.[132] The use of a magnetic stimulator in conducting H-reflex tests allows for the recording from stimulation of nerves at multiple levels from the popliteal fossa to the spine.[133] Dishman et al. have used H-reflex testing protocols in addition to transcranial magnetic stimulation in the investigation of the effects of lumbar spinal manipulation on the excitability of the motor neuron pool[134,135] with encouraging results and applicability to understanding the mechanisms of spinal manipulative therapy.

F-Response The F-response is a long-latency muscle action potential seen after supramaximal stimulation to a nerve. The F-wave results from a centrifugal volley in an alpha motor neuron, following antidromic excitation of the nerve cell body in the ventral horn of the spinal cord. This test is performed by stimulating a motor nerve in the leg or forearm, resulting in an impulse back to the anterior horn in an orthodromic response in the same motor nerve, which, in turn, can be recorded in the muscle to which the nerve travels.[136] Unlike the H-reflex, the F-wave is always preceded by a motor response and its amplitude is rather small, usually in the range of 0.2–0.5 mV. Although it can be elicited in a variety of muscles, it is best obtained in the small foot and hand muscles. The data obtained from the F-wave have been used in many different ways to determine proximal or distal pathology. The normal values can be determined from charts or published data and depend on the height of the patient, the length of the arm or leg tested, and the presence of any peripheral slowing of nerve conduction. In unilateral lesions, the best normal values remain those of the patient's asymptomatic limb. The difference

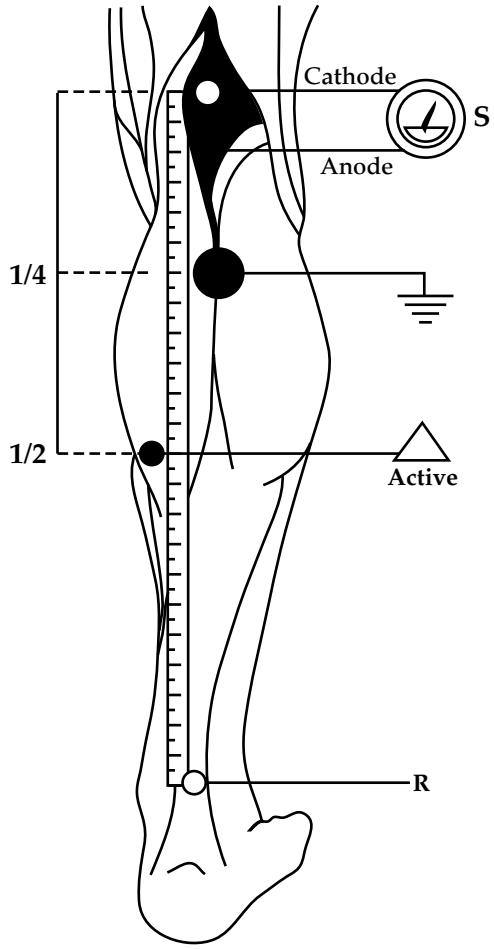

FIGURE 32–13. Location of electrodes for obtaining tibial nerve H-reflex. The active (recording) electrode is placed half the distance between mid-popliteal fossa and apex of the medial malleolus. R = reference electrode is applied over the triceps surae tendon and the ground is placed between the active and stimulating electrodes; S = stimulating electrodes are applied directly over the nerve on the popliteal fossa. *(Drawing courtesy of Dr. J. Donald Dishman and reproduced with permission from Dishman JD, Cunningham BM, Burke J. Comparison of tibial nerve H-reflex excitability after cervical and lumbar spine manipulation. J Manipulative Physiol Ther 2002;25:318–325.)*

between both sides' shortest latencies should not exceed 2–3 msec, depending on the nerve being tested.

Clinical applications of the F-response include conditions such as entrapment neuropathies, root compression syndrome, and estimation of motor neuron excitability. Toyokura et al.[137] evaluated 100 patients with lumbosacral radiculopathy and confirmed disc herniation, and reported a 70% positive response rate to F-response testing. It should be remembered, however, that because this response is independent of the sensory nerve root, F-responses are not sensitive for sensory radiculopathy or neuropathies. Bobinac-Georgijevski et al.[138] performed H- or F-wave latencies of the medial head of the gastrocnemius muscle in 97 patients with suspected S1 radiculopathy with or without additional L5 radiculopathy. Needle EMG of the medial gastrocnemius muscle was supplemented by H- or F-wave latency measurement bilaterally by percutaneous stimulation of the tibial nerve in the cubital fossa. EMG abnormalities indicating S1 radiculopathy were followed by H- or F-wave latency abnormality in 63% of patients. The rest (37% of patients) showed mild EMG abnormalities followed by a normal H- or F-wave. A normal EMG finding was followed by a normal H- or F-wave. Subsequently, a normal EMG finding was followed by normal H- or F-wave in 64% of patients, whether increased latency of the H- or F-wave without EMG abnormalities in gastrocnemius muscle was present in 36% of patients. The results of this study indicated that measurements of H- or F-response latencies provide the objective evidence of S1 radiculopathy, presenting with the unilateral increase of latency or the absence of response. The authors additionally noted that abnormal H-response latencies without EMG abnormality confirm the condition of sensory root affection only.

Evoked Potentials Evoked potentials are electrical signals generated by the nervous system in response to sensory stimuli. Auditory, visual, and somatosensory stimuli are among those often used for clinical evoked potential studies. Somatosensory evoked potentials (SEPs) consist of a series of waves that reflect sequential activation of neural structures along the somatosensory pathways following electrical stimulation of peripheral nerves. SEPs have been used to complement the F-wave response in determining the sensory component of a radiculopathy. The easiest and most commonly used method of eliciting an SEP is by stimulating large mixed nerves, such as the median nerve at the wrist, the common peroneal nerve at the knee, or the posterior tibial nerve at the ankle.[126] Upon stimulation of these nerves, it is possible to obtain a well-defined and reproducible response over both the spinal cord and the scalp through the use of computer averaging of the time-locked potentials. By measuring the latency of these responses and relating them to normative values that account for patient demographics, it is possible to document disturbances in the primary sensory pathways from the point of stimulation to the scalp.[139] SEP abnormalities can reveal a reduced amplitude or impaired morphology of the signal.

SEPs are used for clinical diagnosis in patients with neurologic disease and for intraoperative monitoring during surgeries that potentially compromise the somatosensory pathways.[140] Abnormal SEPs can result

from dysfunction at the level of the peripheral nerve, plexus, spinal root, spinal cord, brainstem, thalamocortical projections, or primary somatosensory cortex, and therefore are very nonspecific regarding the nature of any pathology. Because individuals have multiple parallel afferent somatosensory pathways (i.e., anterior spinothalamic tract or dorsal columns), SEP recordings can be normal even in patients with significant sensory deficits.[139] SEPs are characteristic of the functional integrity of the fast-conducting, large-diameter group Ia muscle afferent fibers and group II cutaneous afferent fibers, which travel in the posterior column of the spinal cord. When a mixed peripheral nerve (containing both sensory and motor fibers) is stimulated, both group Ia muscle afferents and group II cutaneous afferents contribute to the SEP response. SEPs thus provide information concerning the integrity of the pathway through the brain, brainstem, spinal cord, dorsal nerve roots, and peripheral nerves.

SEPs from physical stimuli administered in either the upper or lower extremity are detectable in the brain or the spine simply by placing electrodes over the spinous processes at multiple levels and over the scalp to evaluate the somatosensory pathway.[126] In this manner, it is possible to determine the level within the spinal cord at which a suspected lesion is interfering with the primary sensory pathways. SEPs may be useful in assessing suspected spinal stenosis or pathology proximal to the spinal nerve root,[127] in addition to being helpful with intraoperative monitoring during spinal surgery.[141]

CONCLUSIONS

A wide range of instruments have been developed through the years to assist the clinician in transforming a once qualitative-only practice to one that seeks to obtain quantitative objective findings in patient management. Spine instrument measures include perceptual, structural, functional, and physiological dimensions, with numerous instruments designed to evaluate specific facets of each dimension. Varying degrees of reliability and validity, as well as sensitivity and specificity, exist in many of the measures of each dimension. As noted in the prior edition of this textbook,[12] some measures are generally accepted, well established, and widely used, while others have no proven value or are developmental in nature. The chiropractic clinician should be able to discern which measures best serve the interests of patients from both a utility and financial standpoint. As in many other health care professions, technological advances continue to bring new instruments to the marketplace in chiropractic. The main features of any instrument can be evaluated to ascertain clinical utility and can be evaluated on the basis of discriminability and normative data.[12] Claims of efficacy of any instrument or technology and clinical utility must be soundly based in the peer-reviewed indexed literature and be properly scrutinized to be worthy of use in chiropractic practice to establish a diagnosis, monitor clinical outcomes, and be reimbursable from third-party payers.

SUMMARY

1. The clinical evaluation of a patient is dependent on both qualitative assessments, such as inspection, palpation, and visual observation, and quantitative assessments that use tools to express a numerical value to describe a particular clinical finding. The latter often require the use of complex diagnostic questionnaires or equipment. Any objective test used to measure clinical outcomes must be evaluated for such factors as reliability, validity, accuracy, precision, sensitivity, specificity, discriminability, responsiveness, and clinical utility. These terms all have well-described definitions and scientific methods that are used to describe their value in the clinical encounter.
2. Perceptual measures used to describe the clinical condition of a patient are dependent upon the patient's conscious response to a question or verbal or visual stimulus. Outcomes assessment instruments can be categorized into five classes: (a) general health status of a patient, (b) pain perception including pain intensity, affect, and location, (c) condition-specific instruments that evaluate the effect of a condition such as back pain on a patient's functional capacity, (d) the influence of psychometric or psychosocial factors such as depression and anxiety on a patient's outcome, and (e) patient satisfaction with health care experience.
3. The assessment of spinal function includes the measurement of such factors as mobility, strength, endurance, and coordination. Spinal stiffness, defined as the mechanical responses to force and displacement of spinal tissues during movement can be assessed qualitatively during the clinical examination through various palpation techniques or quantitatively through the use of a number of measurement devices. Spinal stiffness can be assessed as a quasistatic–static function or a dynamic function. Muscle strength can be evaluated either manually or through the use of various dynamometers and can be expressed as either isometric, isokinetic, or inertial strength.
4. Physiological measures of spinal function depend primarily on electrophysiological principles. Electromyography can measure the electrical activity

of muscles using signal amplitude measured over the skin during muscle contraction, changes in muscle electrical activity during flexion and extension of the spine, and asymmetry of paraspinal electrical muscle activity. The research on these measures, however, has had mixed outcomes that make it difficult to determine the clinical usefulness of these tests. Neurological deficits can be documented through the use of needle electromyography, peripheral nerve conduction, H-waves, F-responses, and a number of different methods of recording cortical and spinal evoked potentials. Each of these tests has unique sensitivities and specificities that determine their clinical use.

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QUESTIONS

1. In what percentage of low back pain cases is an accurate anatomic diagnosis not clearly defined?
2. What are the three aspects that a clinician must consider when determining whether a proposed test has clinical utility?
3. What is the difference between pain, disability, and impairment?
4. Name five methods of assessing pain, two methods of assessing disability caused by low back pain, and six ways to assess muscle strength.
5. What are the main differences between needle EMG and NCV?

ANSWERS

1. In 80–90% of low back pain cases an accurate anatomic diagnosis not clearly defined.
2. Clinicians must evaluate if a test is able to (a) provide an accurate diagnosis, (b) provide evidence supporting the use of a specific treatment or treatment approach, or (c) enable the clinician to determine the true outcome or effectiveness of the treatment or intervention.
3. *Pain* is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage; *disability* is diminished capacity for everyday activities and gainful employment; and *impairment* is an anatomical or physiological abnormality leading to loss of normal bodily ability.
4. *Five methods of assessing pain:* (a) verbal rating scale, (b) Visual Analogue Scale, (c) numerical rating scale, (d) McGill Pain Questionnaire, and (e) pain diagram.

   Two methods of assessing disability caused by low back pain: (a) Roland-Morris Disability Questionnaire and (b) Oswestry Disability Index.

   Six methods of assessing muscle strength: (a) manual testing, (b) dynamometer, (c) isometric testing, (d) isokinetic testing, (e) isoinertial testing, and (f) EMG.
5. Needle EMG measures single motor unit potentials, and appears to be the most useful electrophysiological technique in the diagnosis of radiculopathy. Nerve conduction velocity (NCV) measures speed, or latency, of neural transmission along a known distance of a sensory or motor nerve fiber, and is best used to measure neurologic deficit associated with peripheral nerve entrapments.

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Twenty-year Longitudinal Follow-up MRI Study of Asymptomatic Volunteers

The Impact of Cervical Alignment on Disk Degeneration

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Study Design: A 20-year longitudinal study.

Objective: To evaluate the long-term effect of sagittal alignment of the cervical spine on intervertebral disk degeneration in healthy asymptomatic subjects.

Summary of Background Data: This study continues a previous 10-year longitudinal study to determine whether sagittal alignment affects disk degeneration during normal aging.

Materials and Methods: We assessed 90 healthy subjects (30 men and 60 women) from among 497 volunteers who underwent magnetic resonance imaging (MRI) and plain radiographs of the cervical spine between 1994 and 1996 (follow-up rate 18.1%). The mean age at the initial study was 35.5 ± 13.4 years (11–65 y). We compared initial MRIs and follow-up MRIs, conducted at an average of 21.6 years after the initial study, for (1) decreased signal intensity of the intervertebral disks, (2) posterior disk protrusion, and (3) disk-space narrowing from C2–3 to C7–T1. Subjects were grouped by age at follow-up (under 40 vs. 40 y and older) and by a lordotic or nonlordotic cervical sagittal alignment at baseline. We assessed neck pain, stiff shoulders, and upper-arm numbness at follow-up, and examined associations between clinical symptoms and MRI parameters.

Results: Progressive changes during the 20-year period included a decrease in disk signal intensity (84.4% of subjects), posterior disk protrusion (86.7%), and disk-space narrowing (17.8%). No significant association was observed between sagittal alignment and decreased disk signal intensity, posterior disk protrusion, or disk-space narrowing. Among subjects over the age of 40, progressive degenerative changes at C7–T1 were significantly more frequent in nonlordotic subjects (90.9%) compared with those with cervical lordosis (54.2%, $P = 0.032$). The prevalence of clinical symptoms was similar in lordotic and nonlordotic subjects at follow-up.

Conclusions: Nonlordotic cervical alignment was related to the progression of disk degeneration at C7–T1 but not other levels. Cervical alignment did not affect the development of clinical symptoms in healthy subjects.

Level of Evidence: Level III.

Key Words: cervical sagittal alignment, disk degeneration, aging, disk-space narrowing, lordosis, disk degenerative disease

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Degenerative changes in cervical spinal disks lead to neck pain, disk herniation, cervical spondylotic myelopathy, and other degenerative disorders as people age. In 2007, Strine and Hootman[1] estimated that 31% of the population in the United States had neck or back pain, and that neck pain due to disk degenerative disease affected 900 million people, representing a significant burden on society. Risk factors for disk degeneration include smoking,[2] axial load bearing,[3,4] a high-risk occupation,[5] level of education,[6] and genetic factors.[7,8] The sagittal alignment of the cervical spine has also been reported to influence the development of disk degeneration.[9]

Harrison et al[10] suggested that the normal cervical spine is lordotic (16.5–66 degrees), and that a kyphotic alignment is pathologic. Other studies reported nonlordotic alignments, such as straight or S-curve shapes, are frequently found in a normal population.[11,12] Thus, there is no consensus as to whether lordosis should be regarded as the only normal alignment.

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Sagittal alignment is thought to negatively impact clinical outcomes after surgical treatment for cervical degenerative diseases.[13–15] However, few studies have investigated the association of sagittal alignment with the degeneration of cervical intervertebral disks in asymptomatic subjects. In 2009, we reported a 10-year longitudinal study of 113 subjects from among 497 healthy volunteers in a cross-sectional study that evaluated the occurrence of age-related changes in intervertebral disks by magnetic resonance imaging (MRI),[16] and found that the sagittal alignment of the cervical spine influenced the progression of degenerative changes but not the onset of clinical symptoms after 10 years.[9] To our knowledge, this 10-year study is the only longitudinal MRI study to date to investigate sagittal alignment and clinical symptoms.[9]

We recently recruited the original cohort for a 20-year follow-up study focusing on the natural aging of the cervical spine.[17] In the present study, we focused on the impact of sagittal alignment on the progression of intervertebral disk degeneration and the development of clinical symptoms in healthy subjects using volunteers from the original cohort.

MATERIALS AND METHODS

Before starting this longitudinal follow-up study, we obtained approval from the institutional review boards of each participating institution. In the initial cross-sectional study, we obtained MRIs of the cervical spine for 497 asymptomatic healthy volunteers (262 men and 235 women) between 1993 and 1996.[16] The volunteers were recruited for the initial study by mail. None of the volunteers had symptoms obviously related to the cervical spine, and volunteers with known preexisting cervical, thoracic, or lumbar spinal disorders were excluded from the initial study. All subjects provided written informed consent after the purpose and methods of this longitudinal study were explained. Of the 497 volunteers who participated in the original study, 90 (18.1%) responded to the mailed invitation and were included in this 20-year follow-up study. This group consisted of 30 men and 60 women, with a mean age of 35.5 ± 13.4 years (11–65 y) at the time of the initial MRI (Table 1) and a mean interval of 21.6 ± 0.7 years (19.8–23.0 y) between the first and final MRI. The remaining 407 subjects did not participate in the 20-year follow-up due to the following reasons: 103 did not have initial radiographs that were available or of sufficient resolution to detect disk degeneration, we were unable to find addresses for 62 subjects, we received no response from 189 subjects, and 53 subjects declined to participate due to lack of time, health problems, or other reasons. Volunteers who had sustained a neck injury, were surgically treated for neck pain, or were diagnosed with a systemic disease such as rheumatoid arthritis during the follow-up period were also excluded. All subjects filled out a questionnaire about symptoms related to the cervical spine and underwent a physical and neurological examination by spine surgeons before undergoing an MRI of the cervical spine. The previous MRIs used a 1.5-T (Signa, General Electronic, WI) or 0.5-T (Resona, Yokogawa Medical System, Tokyo) superconducting imager following a protocol described in detail in our previous report.[16] All MRIs for the 20-year follow-up were obtained with a fast spin-echo technique using a 1.5-T superconducting imager (Signa Excite HD 1.5 T, General Electric, WI). We obtained T1-weighted sagittal images (TR/TE 380/8.2; echo train length 2; 4 mm slice thickness, spacing 1 mm; FOV 24 cm; matrix size 256×192; NEX 2 times; BW 31.25 kHz), T2-weighted sagittal images (TR/TE 5000/100; echo train length 24; NEX 2; 4 mm slice thickness; spacing 1 mm; FOV 24 cm; BW 31.25 kHz), and T2-weighted axial images (TR/TE 5000/102; 5 mm slice thickness; FOV 16 cm; matrix size 256×192, NEX 2; BW 15.63 kHz).

In the original cross-sectional study, plain radiographs of the cervical spine were obtained with the subjects in a sitting position, gazing forward and relaxed. The film-tube distance was set to 1.5 m. We did not obtain plain radiographs at the 20-year follow-up because of the ethical consideration of avoiding additional radiation.

Subjects were classified according to whether their original cervical sagittal alignment was lordotic or nonlordotic; the latter included straight, sigmoid, and kyphotic shapes as described by Chiba et al.[15] Subjects were also classified by the age at the initial investigation as young (younger than 40 y) or older (40 y and older); this cut-off was decided according to a study by Boden et al[18] on aging in cervical intervertebral disks, and our previous 10-year follow-up study.[9] There were 24 young lordotic (YL) subjects, 31 young nonlordotic (YNL) subjects,

TABLE 1. Subject Sex and Age at the Initial Study

Age (y)	Male	Female
10–19	8	3
20–29	13	12
30–39	3	16
40–49	3	14
50–59	1	12
60–	2	3
Total	30	60

TABLE 2. Grading System for Magnetic Resonance Evaluation by Matsumoto

Decrease in intervertebral disk signal intensity	
Grade 0	As bright as or slightly darker than cerebrospinal fluid
Grade 1	Markedly darker than cerebrospinal fluid
Grade 2	Complete loss of signal
Posterior disk protrusion	
Grade 0	No protrusion
Grade 1	Disk material protruding beyond the posterior margin of the vertebral body without cord compression
Grade 2	Disk material protruding beyond the vertebral body with cord compression
Disk-space narrowing	
Grade 0	100%–75% of the height of the upper healthy disk
Grade 1	75%–50% of the height of the upper healthy disk
Grade 2	< 50% of the height of the upper healthy disk

TABLE 3. Incidence of Progressive Degeneration

	Decrease in Signal Intensity [n/N (%)]		Posterior Disk Protrusion [n/N (%)]		Disk-space Narrowing [n/N (%)]	
Group	**Prevalence**	***P***	**Prevalence**	***P***	**Prevalence**	***P***
Young lordosis	22/24 (91.7)	0.443	22/24 (91.7)	0.271	4/24 (16.7)	0.686
Young nonlordosis	25/31 (80.6)		24/31 (77.4)		3/31 (9.7)	
Older lordosis	20/24 (83.3)	0.629	23/24 (95.8)	0.227	7/24 (29.2)	0.403
Older nonlordosis	9/11 (81.8)		9/11 (81.8)		2/11 (18.2)	

24 older lordotic (OL) subjects, and 11 older nonlordotic (ONL) subjects.

From MR images, we assessed (1) decreases in disk signal intensity, (2) posterior disk protrusion, and (3) disk-space narrowing. Each item was evaluated by Matsumoto's classification[16] with a minor modification described in our previous 10-year follow-up report[9,19] (Table 2). The initial and present MR images were graded independently by an experienced neuroradiologist in a blinded fashion. A change of at least 1 grade in 1 or more intervertebral levels over the follow-up period was regarded as a progression of degeneration, and the percentage of subjects with findings of progression was designated as the rate of progression. We analyzed the progression of disk degeneration between the 2 examinations by χ^2 test to assess relationships between cervical sagittal alignment and the progression of disk degeneration or the onset of symptoms. The interobserver reliability of the MRI grading was tested by calculating kappa scores. A P-value <0.05 was considered significant. SPSS Statistics 22 software (IBM Corp, New York, NY) was used for all statistical analyses.

RESULTS

At the end of the 20-year follow-up period, the most prevalent change was a progression of posterior disk protrusion (86.7%), followed by decreased signal intensity of the disks (84.4%, Table 3). Disk-space narrowing was observed in only 17.8% of the subjects. A progression in decreased signal intensity was observed in a large percentage of subjects in all groups (YL 91.7%, YNL 80.6%, OL 83.3%, and ONL 81.8%). A progression in posterior disk protrusion was also observed frequently in all 4 groups (YL 91.7%, YNL 77.4%, OL 95.8%, and ONL 81.8%). Progressive disk-space narrowing was infrequent in all groups (YL 16.7%, YNL 9.7%, OL 29.2%, and ONL 18.2%). For all 3 items, there was no significant difference between the YL and YNL groups or between the OL group and ONL groups, suggesting that cervical alignment was not associated with degenerative changes when grouped by age.

Progressive disk degeneration was most frequent at C4–5 and C5–6 (both 84.4%, Table 4). Progressive degenerative changes at C7–T1 were significantly more frequent in the ONL group (90.9%) than in the OL group (54.2%, $P = 0.036$). There were no significant differences by sagittal alignment at disk levels other than C7–T1.

In the initial study, none of the subjects had symptoms obviously related to the cervical spine. However, at the 20-year follow-up, 67.8% of the subjects reported clinical symptoms such as neck pain (16.7%), stiff shoulders (47.8%), and numbness in the upper limbs (7.8%). We did not find any significant difference between lordotic or nonlordotic subjects in the onset of clinical symptoms of neck pain, stiff shoulders, or numbness in the upper limbs (Table 5).

Case Presentation

A 47-year-old woman with a kyphotic cervical spine was classified into the ONL group in the initial study (Fig. 1). Although MRIs obtained 21.2 years later showed decreased disk signal intensity and a narrowing of disk spaces, she had no cervical symptoms (Fig. 2).

DISCUSSION

In the present study, we observed a significant progression of degenerative changes at C7–T1 in older subjects (≥ 40 y) with a nonlordotic alignment compared with those with a lordotic alignment. Our previous 10-year follow-up study found that disk degeneration occurred most frequently at C5–6, followed by C6–7.[19] MRIs obtained at the 20-year follow-up revealed disk degeneration at C5–6 and C6–7 in 75%–90% of the subjects in both the lordosis and nonlordosis groups. The C7–T1 intervertebral disk is located at the base of the cervical spine and sustains the weight of the skull and the cervical vertebrae. In 2001,

TABLE 4. Progressive Degenerative Changes by Intervertebral Disk Level

	C2–3 (%)	*P*	C3–4 (%)	*P*	C4–5 (%)	*P*	C5–6 (%)	*P*	C6–7 (%)	*P*	C7–T1 (%)	*P*
Young lordosis	66.7	0.613	83.3	0.208	75.0	0.337	91.7	0.135	76.7	0.255	58.3	0.561
Young nonlordosis	66.7		70.0		83.3		76.7		87.5		60.0	
Older lordosis	29.2	0.285	70.8	0.144	79.2	0.619	91.7	0.372	91.7	0.372	54‘.2	0.036*
Older nonlordosis	45.5		45.5		81.8		81.8		81.8		90.9	

*Statistically significant.

TABLE 5. Incidence of Clinical Symptoms

	Neck Pain [n/N (%)]		Shoulder Stiffness [n/N (%)]		Numbness in the Upper Limbs [n/N (%)]	
Group	**Prevalence**	***P***	**Prevalence**	***P***	**Prevalence**	***P***
Young lordosis	5/24 (32.3)	0.239	13/24 (54.8)	0.536	3/24 (12.5)	0.393
Young nonlordosis	10/31 (5.6)		17/31 (54.2)		2/31 (6.5)	
Older lordosis	1/24 (4.2)	374	8/24 (33.3)	0.374	2/24 (8.3)	0.464
Older nonlordosis	0/11 (0.0)		5/11 (45.5)		0/11 (0.0)	

Harrison et al[20] performed digitized measurements from the lateral cervical radiographs of 4 different types of alignment of the cervical spine and reported that axial load stresses are 6–10 times greater in a kyphotic than in a lordotic alignment. Thus, increased loading stress occurring in the context of a nonlordotic alignment over an extended period of time may accelerate disk degeneration.

This result was consistent with our 10-year follow-up study,[9] in that the progression of posterior disk protrusion was significantly more frequent in subjects over 40 years of age with a nonlordotic cervical alignment. In contrast, Kim et al[21] evaluated cervical lordosis in a cross-sectional study of 104 subjects with adult spinal deformity, and did not find a significant relationship between cervical degeneration and cervical alignment. However, that study evaluated degenerative changes using an EOS 3D imaging system (EOS Imaging, Paris, France) rather than MRI of the cervical spine. Moreover, although the subjects did not have symptoms related to the cervical spine, Furthermore, although subjects were asymptomatic at cervical spine, their background were all adult spinal deformity.

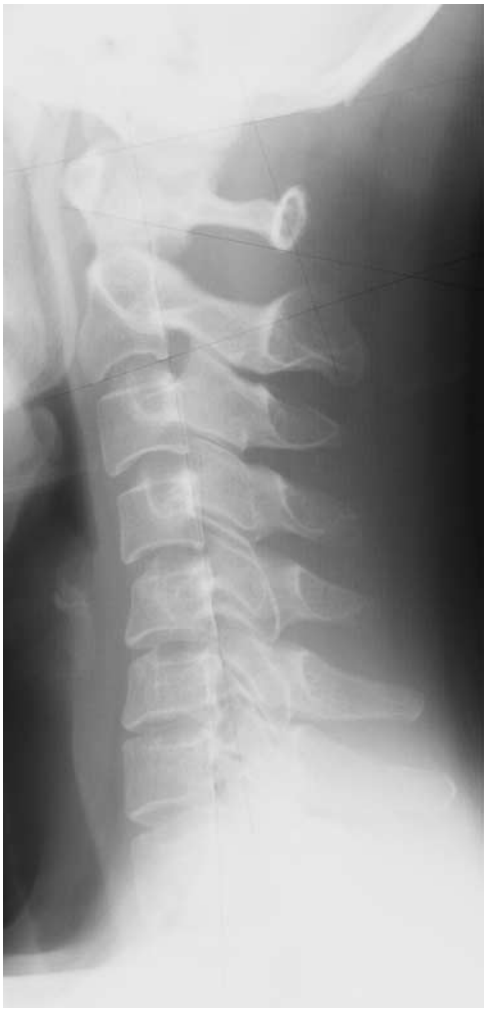

FIGURE 1. Case presentation: lateral radiograph of the cervical spine of a 47-year-old woman who was asymptomatic at the initial study and was classified into the older/nonlordosis group.

Whether sagittal alignment has an impact on the clinical onset of neck symptoms is still controversial. In the present study, there was no significant association between sagittal alignment and the onset of clinical symptoms. In 1993, Gay[12] conducted a systematic literature review and concluded that cervical alignment had little influence on clinical symptoms. In a cross-sectional study, Helliwell et al. analyzed subjects grouped according to posttraumatic neck pain, chronic neck pain, and no pain (asymptomatic control group)[11] and reported that a straight alignment of the cervical spine was most frequent in subjects with no pain (42%), followed by subjects with posttraumatic neck pain (19%) and chronic neck pain (26%). This result indicates that a nonlordotic sagittal alignment is not always pathologic. After investigating radiographs of 762 healthy volunteers, Kumagai et al[22] concluded that the sagittal alignment of the cervical spine was not associated with neck symptoms. Grob examined the association between the presence of neck pain and cervical lordosis and found no significant association between cervical alignment and clinical symptoms.[23] However, some cross-sectional studies[24,25] suggest that neck pain is correlated with sagittal alignment. After studying 216 patients with chronic neck pain, Seong et al[25] concluded that a nonlordotic alignment, such as a straight alignment or sigmoid curve, is significantly associated with the severity of neck pain. The present study revealed that the sagittal alignment of the cervical spine influences disk degeneration only at C7–T1 and is not associated with the future onset of clinical symptoms.

One limitation of this study is the follow-up rate (18.1%) that may cause selection bias between the participating and nonparticipating subjects. A second limitation is that plain radiographs were taken only at the initial study and not at the follow-up to avoid unnecessary radiation exposure, therefore limiting our ability to evaluate changes in cervical spinal alignment during the 20-year follow-up

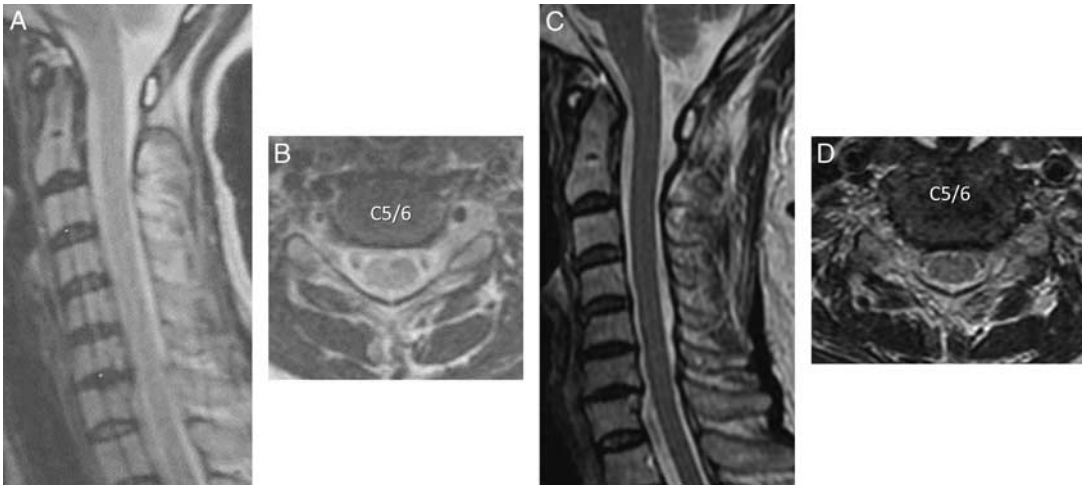

FIGURE 2. Magnetic resonance (MR) images obtained at the follow-up of 21.2 years after the original MR images show decreased signal intensity at C7–T1 and disk-space narrowing at C6–7. However, the subject had no cervical symptoms at the follow-up. MR images include (A) a sagittal T2-weighted MR image and (B) an axial T2-weighted MR image at the C5–6 level, obtained at the initial study, and (C) a sagittal T2-weighted MR image and (D) an axial T2-weighted MR image at the C5–6 level, obtained at the final follow-up.

period. However, to the best of our knowledge, this is the first longitudinal 20-year study evaluating the association between cervical alignment and degenerative changes by MRI, as well as neck-related clinical symptoms. We believe that these results contribute to our understanding of natural aging in the cervical spine in relation to cervical alignment and the occurrence of clinical symptoms.

CONCLUSIONS

This 20-year follow-up study of the cervical spine in healthy subjects showed that, while a nonlordotic cervical alignment may be related to progressive disk degeneration over time, the sagittal alignment of the cervical spine had no impact on the development of clinical symptoms related to the cervical spine.

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ORIGINAL ARTICLE

Does the sagittal alignment of the cervical spine have an impact on disk degeneration? Minimum 10-year follow-up of asymptomatic volunteers

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Abstract There have been few studies that investigated and clarified the relationships between progression of degenerative changes and sagittal alignment of the cervical spine. The objective of the study was to longitudinally evaluate the relationships among progression of degenerative changes of the cervical spine with age, the development of clinical symptoms and sagittal alignment of the cervical spine in healthy subjects. Out of 497 symptom-free volunteers who underwent MRI and plain radiography of the cervical spine between 1994 and 1996, 113 subjects (45 males and 68 females) who responded to our contacts were enrolled. All subjects underwent another MRI at an average of 11.3 years after the initial study. Their mean age at the time of the initial imaging was 36.6 ± 14.5 years (11–65 years). The items evaluated on MRI were (1) decrease in signal intensity of the intervertebral disks, (2) posterior disk protrusion, and (3) disk space narrowing. Each item was evaluated using a numerical grading system. The subjects were divided into four groups according to the age and sagittal alignment of the cervical spine, i.e., subjects under or over the age of 40 years, and subjects with the lordosis or non-lordosis type of sagittal alignment of the cervical spine.

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During the 10-year period, progression of decrease in signal intensity of the disk, posterior disk protrusion, and disk space narrowing were recognized in 64.6, 65.5, and 28.3% of the subjects, respectively. Progression of posterior disk protrusion was significantly more frequent in subjects over 40 years of age with non-lordosis type of sagittal alignment. Logistic regression analysis revealed that stiff shoulder was closely correlated with females ($P = 0.001$), and that numbness of the upper extremity was closely correlated with age ($P = 0.030$) and male ($P = 0.038$). However, no significant correlation between the sagittal alignment of the cervical spine and clinical symptoms was detected. Sagittal alignment of the cervical spine had some impact on the progression of degenerative changes of the cervical spine with aging; however, it had no correlation with the occurrence of future clinical symptoms.

Keywords Cervical spine · Magnetic resonance imaging (MRI) · Sagittal alignment · Aging · Asymptomatic volunteers

Introduction

Disk degeneration occurs with aging [3], leading to structural changes of the intervertebral disks, including posterior bulging of the disks and narrowing of the disk space. Such structural changes in the disks may have influence on the sagittal alignment of the cervical spine [13], while, conversely, malalignment of the cervical spine may render excessive load to the disks, possibly promoting disk degeneration.

Sagittal alignment of the cervical spine is known to vary morphologically with age and gender [9]. Harrison et al. [13] conducted cross-sectional evaluation of the cervical spinal curvature in 72 healthy subjects using plain X-rays, and reported a mean lordosis angle of the cervical spine (C2–C7) of 34°. Nojiri et al. [23], who conducted a similar assessment in 313 healthy Japanese volunteers, reported a mean lordosis angle to be 16.2°. Gore et al. [10] conducted a 10-year longitudinal evaluation of the sagittal alignment of the cervical spine by plain radiography, and reported that the lordosis angle of the cervical spine tended to increase with aging. Thus, it appears that the cervical spine generally shows a lordotic curvature. On the other hand, Matsumoto et al. [21] reported that subjects younger than 40 years of age presented a non-lordotic cervical curvature more frequently than those over 40 years.

It is reported that neck pain is complained by 34.4% of the general population. Similar to low back pain, neck pain is one of the most common musculoskeletal complaints that most humans experience at some time in their lives [2]. However, many reports have shown the absence of any distinct correlation between the sagittal alignment of the cervical spine and the development of neck pain. Grob et al. [11] divided 107 patients with diseases of the lower extremities into groups with and without neck pain, and assessed the correlation between neck pain and the sagittal alignment of the cervical spine on plain lateral radiographs. They found no significant correlation between the sagittal alignment of the cervical spine and the presence of neck pain, and reported that any association between neck pain and the abnormality of the sagittal cervical alignment is purely coincidental.

Thus, previous cross-sectional studies have failed to show any correlation between the sagittal alignment of the cervical spine and the clinical symptoms. However, no long-term longitudinal studies have been undertaken to date to clarify associations among the sagittal alignment, clinical symptoms and the development and progression of degenerative changes of the cervical intervertebral disks.

We conducted a cross-sectional survey of the cervical spine in 497 healthy volunteers using magnetic resonance imaging (MRI), and reported the occurrence of age-related changes of the intervertebral disks in 1998 [22]. In this study, we also obtained plain radiographs of the cervical spine of the subjects.

In the present study, we have obtained MRI of the cervical spine once again in the same cohorts approximately 10 years after the previous MRI study. The objectives of the present study were to evaluate if the degenerative changes of the cervical spine found in the previous study have progressed and to clarify the relationships among the sagittal alignment of the cervical spine, progression of disk degeneration, and the development of clinical symptoms.

Materials and methods

For the present study, we obtained approvals from the institutional review boards of all participating institutions. Four hundred ninety-seven asymptomatic healthy volunteers (262 males and 235 females) underwent MRI of the cervical spine in the initial study between 1993 and 1996. All participants in the previous study had no symptoms related to the cervical spine. The participants in the initial investigation were recruited by oral advertisement from the investigators to the hospital staffs and their acquaintances and to high school students close to the investigators' hospitals. No patient with known preexisting cervical, thoracic, or lumbar spinal disorders was included into the initial investigation. The occupations of the initial participants were as follows: office workers 214; doctors, nurses

and medical coworkers 138; manual workers (construction, farming, etc.) 12; students 75; others (housewives, retired, etc.) 58. Those with a history of neck injury and/or treatments for neck pain, and those with systemic diseases, such as rheumatoid arthritis, were excluded.

We asked the volunteers to participate again in the present survey by mail or telephone. Written informed consent for the participation was obtained from all participants after the explanation of the purpose and contents of the present study. Of the 497 subjects examined in the previous study, 113 subjects whose previous MRI and radiographs were both available participated in the present follow-up study. The reasons for drop-outs of 384 subjects at the follow-up study were as follows: 203 subjects were unable to be located; 71 refused or were unable to participate in the follow-up study; 110 did not have the initial radiographs available.

There were 45 males and 68 females, whose mean age at the time of the initial imaging was 36.6 ± 14.5 years (11–65 years), and the mean interval between the first and second imaging was 11.3 years (9.9–12.8 years) (Table 1). All subjects filled questionnaires regarding clinical symptoms and underwent neurological examination by orthopedic spine surgeons, then underwent MRI of the cervical spine. The previous MRI was conducted using 1.5 Tesla (T) or 0.5 T superconducting imagers, while in the present study, 1.5 T superconducting imagers were used for all subjects.

In the previous imaging, a 1.5-T (Signa, General Electronic, WI, USA) or 0.5 T (Resona, Yokogawa Medical System, Tokyo, Japan) superconducting imager was used. In the present investigation, a 1.5-T superconducting imager was used for all subjects. In the previous imaging, using phased array coils, a fast spin-echo technique was used with following sequences: a T1-weighted sagittal image [repetition time (TR)/echo time (TE), 520/12; echo train length, 4; thickness of slice, 5 mm; field of view (FOV), 24 cm; matrix size, 256 × 192; number of excitation (NEX), 4 times], T2-weighted sagittal image (TR/TE, 5000/102; echo train length, 16; the remaining items were the same as those for T1-weighted sagittal images), and T1- and T2-weighted axial images (FOV, 16 cm; the remaining items were the same as those for T1-weighted sagittal images). When the 0.5-T system was used, images were taken by a spin echo technique using a surface coil for the cervical spine with following sequences: T1-weighted sagittal images (TR/TE, 450-500/25; thickness of slice, 5 or 7 mm; FOV, 25 cm; matrix size, 256 × 256 or 256 × 192; NEX, 4 times), T2-weighted sagittal images (TR/TE, 2000/100; thickness of slice, 5 or 7 mm; FOV, 25 cm; matrix size, 256 × 224 or 256 × 160; NEX, twice), and T1- and T2-weighted axial images (FOV, 20 or 22 cm; NEX, twice or four times; the rest items were the same as those for T1-weighted sagittal images).

In the present investigation, images were taken by a fast spin-echo technique using a 1.5-T superconducting imager (Signa Excite HD 1.5 T, General Electronic, WI, USA) with the following sequences: T1-weighted sagittal images (TR/TE, 380/8.2; echo train length, 2; thickness of slice, 4 mm; FOV, 24 cm; matrix size, 256 × 192; NEX, three times), T2-weighted sagittal images (TR/TE, 5000/100; echo train length, 16; NEX, three times; remaining items were the same as those for T1-weighted sagittal images), and T1- and T2-weighted axial images (TR/TE, 5000/102; thickness of slice, 5 mm; FOV, 16 cm; remaining items were the same as those for T1-weighted sagittal images).

In the previous study, plain radiographs of the cervical spine were obtained with the subjects in a sitting position, gazing forward, and relaxed. The film-tube distance was set to 1.5 m. In the present study, a second X-ray was not obtained because of the ethical consideration to avoid an extra exposure to X-rays.

The sagittal alignment of the cervical spine was classified into two types, lordosis and non-lordosis type, the latter including straight sigmoid and kyphosis according to the classification reported by Chiba et al. [4] (Fig. 1). All participants were divided into four groups by their age (<40 years and ≥40 years) and the sagittal alignment (lordosis and non-lordosis) of the cervical spine: young lordosis (YL) group, $n = 29$; young non-lordosis (YNL) group, $n = 36$; old lordosis (OL) group, $n = 34$; and old non-lordosis (ONL) group, $n = 14$. The cut-off line of the age at 40 years was chosen according to the study reported by Boden et al. [1] regarding aging in the cervical intervertebral disks. The items evaluated on MRI were (1) decrease in signal intensity of disk, (2) posterior disk protrusion, and (3) disk space narrowing. Each item was evaluated using the Matsumoto's [22] classification with a minor modification, which was used in our previous report (Table 2).

All levels from C2–C3 to C7–T1 were evaluated. An increase by at least one grade in any item at one or more intervertebral levels was regarded as progression of

Table 1 Age and gender of study population

Age	No. of males	No. of females
10–19	8	7
20–29	17	11
30–39	8	14
40–49	5	12
50–59	4	22
>60	3	2
Total	45	68

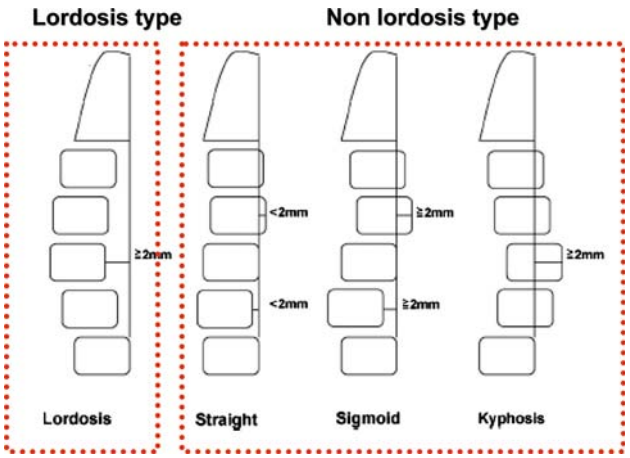

Fig. 1 Sagittal alignment of cervical spine. A line is drawn between the lower posterior corner of the C2 and C7, and this line is defined as "A." Perpendicular lines are drawn from the lower posterior edge of the bodies of C3–C6 to this line, and the length of these lines is defined as a1–a4. If every a1–a4 is anterior to "A" and one of them is more than 2 mm, the curvature is defined as lordosis. If every a1–a4 is posterior to "A" and one of them is more than 2 mm, the curvature is defined as kyphosis. If every a1–a4 is less than 2 mm, the curvature is defined as straight. If a1–a4 exists both anterior and posterior and one of them is more than 2 mm, the curvature is defined as sigmoid

Table 2 Grading system for MR evaluation

1. Decrease in signal intensity of intervertebral disk
Grade 0: as bright as or slightly darker than cerebrospinal fluid
Grade 1: markedly darker than cerebrospinal fluid
Grade 2: complete loss of signal
2. Posterior disk protrusion
Grade 0: no protrusion
Grade 1: disk material protruding beyond posterior margin of vertebral body without cord compression
Grade 2: beyond vertebral body with cord compression
3. Disk space narrowing
Grade 0: 100–75% of height of upper healthy disk
Grade 1: 75–50% of height of upper healthy disk
Grade 2: less than 50% of height of upper healthy disk

degeneration. The present and previous MRI films were graded independently by two experienced neuroradiologists in a blinded fashion. The results were finalized by the one neuroradiologist. The data on the progression of disk degeneration on MRI during the 10-year interval between the two examinations were statistically tested using χ^2 test. Multiple logistic regressions analysis was conducted to analyze the relationship between the sagittal alignment of the cervical spine and the progression of disk degeneration and between the sagittal alignment of the cervical spine and the occurrence of symptoms. The inter-observer reliability of the MRI-grading was tested by calculating kappa scores. A P value less than 0.05 was considered to be statistically significant. Dr. SPSS II for Windows (SPSS Japan Inc., Tokyo, Japan) was used for all analyses.

Results

In the initial MRIs, decrease in signal intensity of the disk was observed in 6 (21%) and 11 (31%) of the subjects in the YL and YNL groups ($P = 0.271$), and 13 (93%), and 28 (82%) of the subjects in the OL and ONL groups, respectively ($P = 0.329$). Posterior disk protrusion was observed in 5 (17%) and 7 (19%) of the subjects in the YL and YNL groups ($P = 0.540$), and 19 (56%) and 5 (36%) of the subjects in the OL and ONL groups ($P = 0.171$). Disk space narrowing was observed in none of the YL and YNL groups, and 8 (24%) and 4 (29%) of the subjects in the OL and ONL groups ($P = 0.489$). Thus, there were no significant differences in the frequency of any of the MRI changes evaluated between the YL and YNL groups or between the OL and ONL groups.

Progression of decrease in signal intensity of the disk, posterior disk protrusion, and disk space narrowing were recognized in 73 (64.6%), 74 (65.5%), and 32 (28.3%), respectively, of all subjects.

No significant difference in the incidence of progression of decrease in signal intensity of the disk or disk space

Table 3 Incidence of progression of each MR finding

	Decrease in signal intensity		Posterior disk protrusion		Disk space narrowing	
	Prevalence (%)	P value	Prevalence (%)	P value	Prevalence (%)	P value
Young lordosis group	17/29 (58.6)	0.521	17/29 (58.6)	0.341	5/29 (17.2)	0.239
Young non-lordosis group	22/36 (61.1)		24/36 (66.7)		3/36 (8.3)	
Old lordosis group	25/34 (73.5)	0.379	20/34 (58.8)	0.020*	15/34 (44.1)	0.171
Old non-lordosis group	9/14 (64.3)		13/14 (92.9)		9/14 (64.3)	

Asterisks indicate statistical significance

Table 4 Logistic regression analyses of MR findings and sagittal alignment of cervical spine

	Decrease in signal intensity		Posterior disk protrusion		Disk space narrowing	
	P value	Odds ratio (95% CI)	*P* value	Odds ratio (95% CI)	*P* value	Odds ratio (95% CI)
Sagittal alignment (non-lordosis)	0.970	0.9846 (0.44–2.33)	0.033*	2.645 (0.15–0.93)	0.785	1.143 (0.34–2.29)
Age (>40 years)	0.116	2.033 (0.84–4.92)	0.082	2.281 (0.90–5.78)	0.000*	8.564 (3.05–24.02)
Sex (male)	0.054	2.349 (0.99–5.60)	0.025*	2.871 (1.14–7.21)	0.336	1.631 (0.60–4.42)

Asterisks indicate statistical significance

95% CI 95% confidence interval

Table 5 Incidence of clinical symptoms

	Neck pain		Shoulder stiffness		Numbness in the upper limbs	
	Prevalence (%)	*P* value	Prevalence (%)	*P* value	Prevalence (%)	*P* value
Young lordosis group	4/29 (13.8)	0.239	7/29 (24.1)	0.230	1/29 (3.4)	0.446
Young non-lordosis group	2/36 (5.6)		5/36 (13.9)		0/36 (0.0)	
Old lordosis group	6/34 (17.6)	0.329	12/34 (35.3)	0.265	1/34 (2.9)	0.069
Old non-lordosis group	1/14 (7.1)		7/14 (50.0)		3/14 (21.4)	

Table 6 Logistic regression analyses of clinical symptoms and sagittal alignment of cervical spine

	Neck pain		Shoulder stiffness		Numbness in the upper limbs	
	P value	Odds ratio (95% CI)	*P* value	Odds ratio (95% CI)	*P* value	Odds ratio (95% CI)
Sagittal alignment (non-lordosis)	0.154	0.365 (0.68–10.94)	0.788	0.872 (0.42–3.12)	0.314	2.786 (0.49–2.63)
Age (>40 years)	0.646	1.348 (0.37–4.82)	0.208	1.898 (0.70–5.15)	0.030*	13.555 (1.29–142.83)
Sex (male)	0.955	1.038 (0.290–3.71)	0.001*	0.720 (0.16–0.325)	0.038*	11.826 (1.15–121.33)

Asterisks indicate statistical significance

95% CI 95% confidence interval

narrowing was observed between the YL and YNL groups or the OL and ONL groups, while incidence of progression of posterior disk protrusion was significantly higher in the ONL than the OL group ($P = 0.020$) (Table 3).

Logistic regression analysis using the sagittal alignment, age, and gender as the covariates revealed that the odds ratio of posterior disk protrusion in the non-lordosis group over the lordosis group was 2.646 ($P = 0.033$). The odds for progression of disk space narrowing was significantly higher in the older group, including OL and ONL groups ($P < 0.001$), and the risk for progression of posterior disk protrusion was significantly higher in the male subjects ($P = 0.025$) (Table 4).

Of all the subjects who used to be asymptomatic at the time of the initial study, 13 subjects (11.5%) had neck pain, 31 (27.4%) stiff shoulder, and five (4.4%) numbness in the upper extremities, at the time of the present study. The inter-group evaluation revealed no statistically significant differences between the YL and YNL groups or between the OL and ONL groups in terms of the frequency of neck pain, stiff shoulder, and numbness of the upper extremities (Table 5).

We then conducted logistic regression analysis using the sagittal alignment, age and gender as the covariates, and the occurrence of clinical symptoms as the dependent variable. The presence of stiff shoulder was closely correlated with the female gender ($P = 0.001$), and that of numbness in the upper extremities was closely correlated with the age ($P = 0.030$) and male gender ($P = 0.038$). However, the sagittal alignment of the cervical spine was not significantly correlated with the development of any symptoms (Table 6).

Regarding the inter-observer reliability of MR grading, the kappa scores for decrease in signal intensity of disks, posterior disk protrusion, and disk space narrowing were 0.60, 0.72, and 0.71, respectively. Thus, the inter-observer reliability of MR reading was favorable.

Case presentation: Figs. 2 and 3.

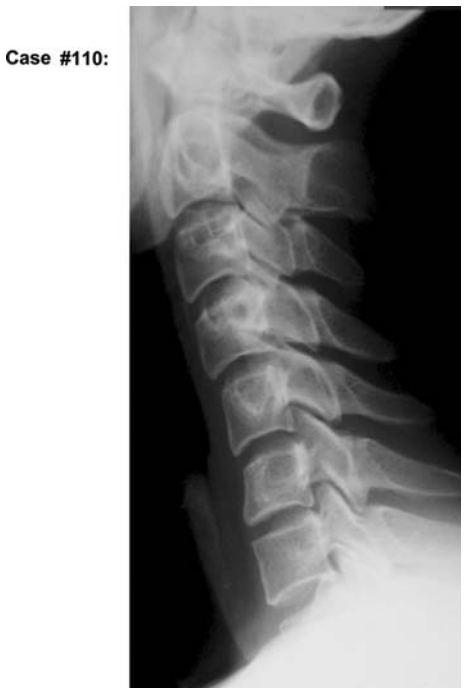

Fig. 2 Case presentation. The 49-year-old male had no clinical symptoms at the time of the previous study and was classified into the old non-lordosis group

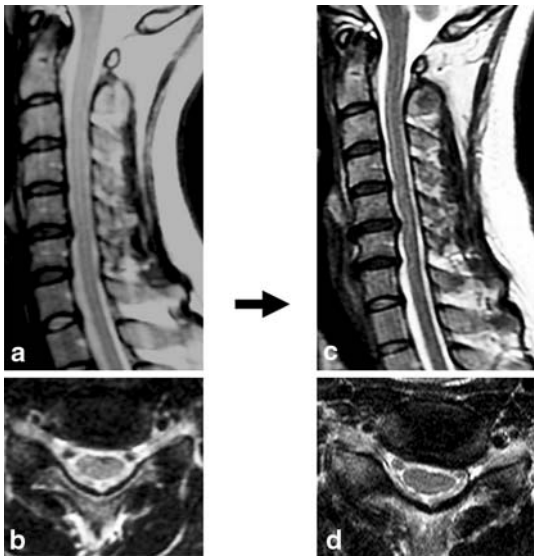

Fig. 3 Case presentation. Twelve years later, progression of decrease in signal intensity, posterior disk protrusion at C5–C6 was demonstrated on the follow-up MR images. However, he still remained free of clinical symptoms related to the cervical spine at the follow-up. **a** Sagittal T2-weighted MR image obtained at the previous study. **b** Axial T2-weighted MR image at C5–C6 level demonstrating posterior disk protrusion of grade 1. **c** Sagittal T2-weighted MR image of the same subject 12 years later showing progression of decrease in signal intensity (grade 1) at C3–C4 to C6–C7 and posterior disk protrusion at C5–C6 (grade 2) and at C6–C7 (grade 1). **d** Axial T2-weighted MR image at C5–C6 at the follow-up demonstrating progression of posterior disk protrusion

Discussion

Previous studies have shown that age-related degenerative changes of the cervical spine occur at a constant rate even in healthy persons. There have been a number of reports on the evaluation of age-related changes of the cervical spine using plain radiography. Freidenburg et al. [8] conducted a plain radiographic evaluation in healthy individuals, and recognized spondylotic changes of the cervical spine in 25 and 75% of the subjects in their fifties and seventies, respectively. With regards to the evaluation by MRI, Boden et al. [1] reported that age-related changes of the cervical spine could be detected in at least 90% of healthy males over the age of 50 and 90% of healthy females over the age of 60.

Matsumoto et al. [21] compared the alignment of the cervical spine in 495 asymptomatic subjects with those in 488 patients with acute whiplash injury. They reported that there was no difference between the asymptomatic and the patient group in terms of the absence of lordosis or presence of local kyphosis. They also reported that there was no correlation between the alignment of the cervical spine and the presence of any clinical symptoms.

Thus, numerous reports published in the literature to date have concluded that there is no direct correlation between age-related changes of the cervical spine and the occurrence of any clinical symptoms [1, 10, 22].

Several reports have shown that some of the factors [5] promoting the progression of degenerative changes of the cervical spine were excessive load on the spine [6, 19], a past history of lumbar vertebral diseases [17], smoking [12], and hemodialysis [20, 25, 27]. Jumah et al. [19] investigated the factors promoting degeneration of the cervical spine in 305 Ghanans and found that 63.6% of the subjects who routinely carried baggage on their head had spondylotic changes of the cervical spine, while only 36.0% of those who did not habitually carry loads showed such changes. These observations indicated that excessive load on the neck is a promoting factor of degenerative changes of the cervical spine.

Although alignment of the cervical spine was frequently studied in cases of cervical myelopathy or radicular pain in relation to surgical outcomes [7, 15, 16, 18, 24, 26], scarce attention has been paid to the cervical alignment in healthy populations, and no study has dealt with the impact of the alignment of the cervical spine on the progression of degenerative changes of the cervical spine.

The results of the present study revealed that the frequency of progression of age-related changes of the cervical disks during 10 years was significantly higher in the non-lordosis and older groups, and in the male subjects. Harrison et al. [14] have reported that the vertical load exerted to the vertebral body of the cervical spine was at least ten times stronger at the apex of kyphosis than that of

lordosis. This biomechanical information may explain the high frequency of posterior disk protrusion in the non-lordosis group in our study.

On the other hand, there was no significant correlation between the sagittal alignment of cervical spine at the time of the first MRI and the occurrence of clinical symptoms over the next 10 years. The occurrence of clinical symptoms was rather more closely correlated with age and gender.

One of the limitations of the present study is the fact that the sagittal alignment of the cervical spine was only evaluated on radiographs taken at the time of the first study because of the ethical consideration against repeated exposures to radiation. We were not able to evaluate the longitudinal changes in the alignment of the cervical spine. Some subjects may have had changes in the alignment during the 10-year period. The sagittal alignment of the cervical spine evaluated on MRI taken in the supine position might not be correlated with those evaluated on sitting radiographs. Another limitation is that, in both studies, superconducting imagers were used and the fast spin echo sequence was mainly used, but the types of MR imagers and softwares were not identical between two studies, which could have led to some difference in the quality of images between the first and second MRI. To minimize the impact of such differences in the image quality, we used the same classification for image grading, e.g., signal intensity of the disk was compared with the intensity of the cerebrospinal fluid at the same level to maintain universality of the results of image assessment. The inter-observer agreement between the two readers on the image evaluation using the kappa score was acceptable. The third limitation is some bias in the patient selection at the initial investigation and at the follow-up. Because, in the initial study, the participants were recruited using oral advertisement by study investigators, medical workers accounted for a large percent of the study population. The bias in participants at the follow-up study was related to the low follow-up rate of the original cohorts due to various reasons as described in "Materials and methods".

Nonetheless, for these limitations, this is the first study of the long-term observation that elucidated the relationship between the alignment of the cervical spine and the progression of disk degeneration in healthy individuals. The present study revealed that the alignment of the cervical spine had some impact on the progression of the degenerative changes of the cervical spine.

Conclusion

The incidence of progression of posterior disk progression was significantly higher in older subjects with non-lordotic alignment than those with lordotic alignment.

Sagittal alignment of the cervical spine was not correlated with the occurrence of future clinical symptoms, but it did have an impact on the progression of degenerative changes of the cervical spine.

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DIAGNOSTICS

Ten-year Longitudinal Follow-up MRI Study of Age-related Changes in Thoracic Intervertebral Discs in Asymptomatic Subjects

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Study Design. Prospective longitudinal study.

Objective. The aim of this study was to evaluate long-term degenerative changes in intervertebral discs in the thoracic spine in healthy asymptomatic subjects.

Summary of Background Data. Longitudinal magnetic resonance imaging (MRI) studies of intervertebral disc degeneration have been reported for the cervical and lumbar but not the thoracic spine.

Methods. In this longitudinal study (average follow-up 10.0 ± 0.6 years), we assessed degenerative changes in the thoracic spine of 103 volunteers (58 men) of 223 healthy volunteers in the initial MRI study of the thoracic spine (follow-up rate 46.2%). The mean age at the initial study was 45.0 ± 11.5 years (24–77 years). Initial and follow-up thoracic-spine MRIs were graded for the following 4 factors of degenerative changes: decrease in signal intensity of intervertebral disc (DSI), posterior disc protrusion (PDP), anterior compression of dura and spinal cord (AC), and disc-space narrowing (DSN) from T1–2 to T12–L1. We assessed associations between changes in MRI grade and demographical factors such as age, sex, body mass index, smoking habits, sports activities, and disc degeneration in the cervical spine.

Results. MRIs revealed that 63.1% of the subjects had degenerative changes in the thoracic intervertebral discs that had progressed at least one grade during the follow-up period. DSI progressed in 44.7% of subjects, PDP in 21.4%, and AC in 18.4% during the 10-year period. No DSN progression was seen. DSI was frequently observed in the upper thoracic spine (T1–2 to T4–5). Disc degeneration was relatively scarce in the lower thoracic spine (T9–10 to T12–L1). PDP was frequently observed in the middle thoracic spine (T5–6 toT8–9). We found significant associations between DSI and cervical-spine degeneration ($P = .004$) and between AC and smoking ($P = .04$).

Conclusion. Progressive thoracic disc degeneration, observed in 63.1% of subjects; was significantly associated with smoking and with cervical-spine degeneration.

Key words: aging, cervical spine, disc degeneration, longitudinal study, magnetic resonance imaging, smoking, thoracic spine.

Level of Evidence: 2

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Intervertebral discs gradually degenerate with age,[1] leading to disc herniation and degenerative disc disease. These conditions create a broad burden on society. Boos *et al*[1] graded the degenerative changes in 180 cadaveric sagittal lumbar-segment slices and reported that the grade of degenerative change was significantly associated with age.

Magnetic resonance imaging (MRI) has been widely used in the past few decades to evaluate musculoskeletal disorders and is one of the best radiographic methods for detecting disc degeneration.[2,3] Several cross-sectional studies have used MRI to elucidate the natural history of human aging and investigate disc degeneration.[4–6] In 1992, Boden *et al* reported that one-third of 67 volunteers who had never

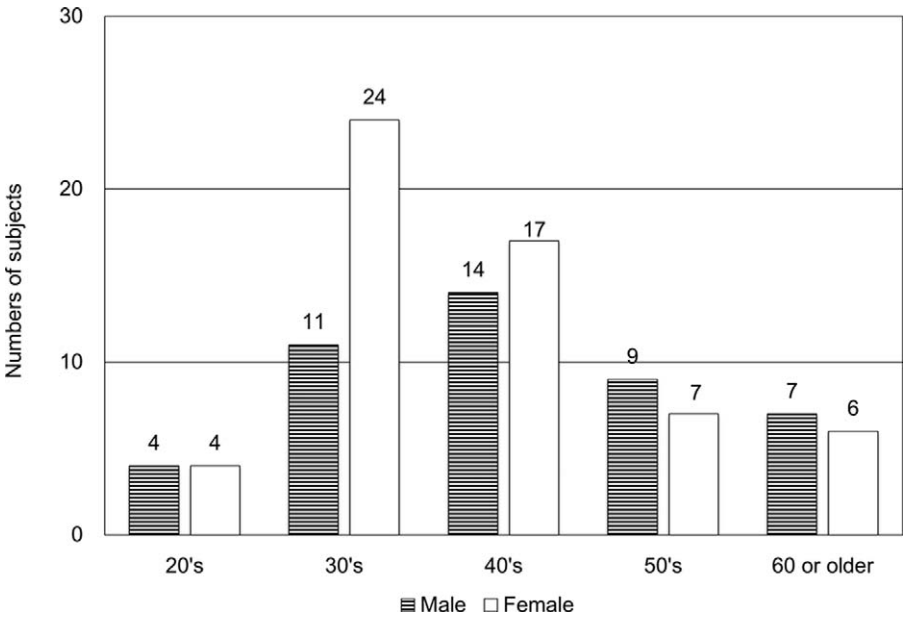

Figure 1. The number and sex of participants according to age group at the time of the initialthoracic-spine magnetic resonance imaging.

complained of low back pain had a substantial abnormality detected by MRI, such as a bulging disc or herniated nucleus pulposus.[5] MRI has also been used in longitudinal studies of the effect of aging on intervertebral discs.[7]

In 2010, in a cross-sectional study of thoracic intervertebral disc degeneration in 94 asymptomatic volunteers, Matsumoto *et al*[8] reported that approximately half of the subjects showed degenerative changes in the thoracic spine on MRI, and that degeneration was related to the factors of age, smoking, and cervical-spine degeneration. In the present longitudinal study, we conducted a 10-year follow-up MRI of the thoracic spine in the same cohort and investigated the progression of thoracic intervertebral disc degeneration on MRI as well as factors related to thoracic disc degeneration in healthy subjects.

MATERIALS AND METHODS

This present study is part of a 20-year follow-up study[7,9,10] that began with MRI studies of the cervical spine in 497 Japanese volunteers between 1993 and 1996.[10] None of the volunteers had symptoms related to the cervical spine, and volunteers with known preexisting cervical, thoracic, or lumbar spinal disorders were excluded from the initial study. Ten years later, 223 of the original volunteers (44.7%) responded to mailed invitations and underwent follow-up MRI studies of the cervical spine, as well as initial studies of the thoracic spine.[7] The present study, conducted as a 10-year follow-up after the initial thoracic-spine MRI studies, included 103 of the 223 subjects who participated in the initial MRI studies of the thoracic spine (follow-up rate 46.2%). These 103 subjects included 58 men and 45 women with a mean age of 45.0 ± 11.5 years (24–77 years) at the time of the initial thoracic-spine MRIs (Figure 1). The remaining 120 volunteers, consisting of 66 men and 54 women with a mean age of 55.7 ± 15.9 years, could not be followed up for the second thoracic MRI investigation (Table 1). All subjects provided written consent for inclusion in the study after receiving a written and oral explanation of the study. Before obtaining MRIs for the present study, participants completed a questionnaire about their symptom, daily habits, including smoking (smoked daily for >10 years) and sports (regular participation in a sport at least once a week). At the time of the first thoracic MRI investigation, no volunteer complained of thoracic back pain or thoracic myelopathy; however, 42.7% of the volunteers had cervical or lumbar spine-related symptoms, such as neck pain (6.8%), stiff shoulders (25.2%), and low back pain (23.3%). We obtained approval from the institutional review board of each participating institution before starting this longitudinal follow-up study.

MRI Protocol

The initial MRI thoracic studies used a 1.5-Tesla (T) (Signa Excite HD 1.5 T, General Electronic, WI) superconducting

TABLE 1. Comparison Between Subjects Followed-up and Subjects Lost

	Follow-up	Lost	*P*
Age	44.2 ± 11.3	56.0 ± 15.5	<0.001*
Sex (male %)	55.3%	55.3%	0.550
Body height	1.65 ± 0.1	1.61 ± 0.1	0.606
Body weight	64.2 ± 12.9	62.0 ± 11.2	0.290
BMI	23.3 ± 3.3	23.1 ± 4.3	0.718
Smoking	27.2%	28.4%	0.539
Sports	21.4%	8.8%	0.012*
Progression of MRI findings in cervical spine	81.6%	87.7%	0.141

BMI indicates body mass index; MRI, magnetic resonance imaging.
**Statistically significant*

imager as previously described[8] and a fast spin-echo technique with the following sequences: T1-weighted sagittal images (repetition time [TR]/echo time [TE] 380/8.2; echo train length 2; 4-mm slice thickness; field of view [FOV] 24–30 cm; matrix size 256 × 192; number of excitations [NEX] 3), T2-weighted sagittal images (as for T1-weighted sagittal images except as follows: TR/TE 5000/100; echo train length 16; NEX 3), and T1- and T2-weighted axial images (as for T1-weighted sagittal images except as follows: TR/TE 5000/102; 5-mm slice thickness, FOV 16 cm). For the 10-year follow-up, we used a fast spin-echo technique with a 1.5-T superconducting imager (Signa Excite HD 1.5 T, General Electric, WI) to obtain T1-weighted sagittal images (TR/TE 380/8.2; echo train length 2; 4-mm slice thickness, spacing 1 mm; FOV 24 cm; matrix size 256 × 192; NEX 2), T2-weighted sagittal images (TR/TE 5000/100; echo train length 24; NEX 2; 4-mm slice thickness; spacing 1 mm; FOV 24 cm), and T2-weighted axial images (TR/TE 5000/102; 5-mm slice thickness; FOV 16 cm; matrix size 256 × 192, NEX 2).

MRI Evaluation

We evaluated degenerative changes on MRI by decreases in disc signal intensity (DSI), posterior disc protrusion (PDP), anterior compression of the dura and spinal cord (AC), and disc-space narrowing (DSN) in the thoracic and cervical spine. Cervical spine data were extracted from the same database used in our previous study, which evaluated the progression of cervical disc degeneration.[9] MRIs were graded in the four factors of degenerative change using Matsumoto *et al*'s MRI grading system[10] with a minor modification described by Okada *et al*[7,11] (Table 2). The initial and follow-up MRIs were graded independently by an experienced neuroradiologist in a blinded fashion. We defined progression of degeneration as a change of at least one grade at one or more intervertebral levels during the follow-up period, and defined the rate of progression as the percentage of subjects with a finding of progression.

We analyzed degenerative changes in thoracic intervertebral discs from the initial to the follow-up MRIs by χ^2 test and by logistic regression analysis for categorical data. We calculated kappa scores to test the interobserver reliability of the MRI grading. A P value <0.05 was considered significant. We used SPSS Statistics 22 software (IBM Corp, New York, NY) for all statistical analyses.

TABLE 2. MRI Grading System by Matsumoto *et al*[10]

Decrease in signal intensity of intervertebral disc	
Grade 0:	As bright or slightly less bright than cerebrospinal fluid
Grade 1:	Markedly darker than cerebrospinal fluid
Grade 2:	No signal
Posterior disc protrusion	
Grade 0:	No protrusion
Grade 1:	Disc material protruding beyond the posterior margin of the vertebral body without cord compression
Grade 2:	Disc material protruding beyond the vertebral body with cord compression
Anterior compression of the dura and spinal cord	
Grade 0:	No compression
Grade 1:	Compression on dural sac only
Grade 2:	Compression on less than one-third of the spinal cord
Grade 3:	Compression on more than one-third and less than two-thirds of the spinal cord
Grade 4:	Compression on more than two-thirds of the spinal cord
Disc space narrowing	
Grade 0:	100%–75% of the height of the upper healthy disc
Grade 1:	75%–50% of the height of the upper healthy disc
Grade 2:	<50% of the height of the upper healthy disc

MRI indicates magnetic resonance imaging.

RESULTS

Progressive Degenerative Changes in the Thoracic Spine

In this 10-year longitudinal MRI study, we found that degenerative changes progressed in at least one evaluation area in 63.1% of the subjects during the follow-up period. DSI, PDP, and AC progressed in 44.7%, 21.4%, and 18.4% of the subjects, respectively, whereas we did not see any progression in DSN.

When subjects were divided by age group (decade) at the time of the initial thoracic-spine MRIs, the progression rate of disc degeneration was highest in subjects in their 60s, (77.8%), followed by those in their 50s (75.0%), 30s (71.4%), 40s (56.7%), 20s (37.5%), and >70 (20.0%) (Figure 2). The rate of DSI progression increased with age. In contrast, the progression rate of PDP and AC was highest in subjects in their 30s.

By the percentage of discs affected at each level, the percentage affected by DSI ranged from 22.3% at T12–L1 to 48.5% at T6–7 in the initial MRI thoracic study (Figure 3A–C). At the initial study, the percentage of discs affected by PDP, AC, or DSN at each level was quite small (ranging from 0.0% to 4.9% for PDP, 5.8% for AC, and 1.0% for DSN). However, MRIs at the 10-year follow-up showed DSI progression at the upper thoracic spine (T1–2 to T4–5) in 20.4% to 25.2% of the subjects, at the middle thoracic spine in 11.7% to 17.4%, and at the lower thoracic spine in 12.6% to 15.5%. PDP progression was observed exclusively at the middle thoracic spine (T5–6 to T8–9) and was present in 1.0% to 6.8% of the subjects.

Comparisons With the Cervical Spine

In the cervical spine, MRI showed progressive degenerative changes in 96 subjects (93.2%) during follow-up (Table 3),

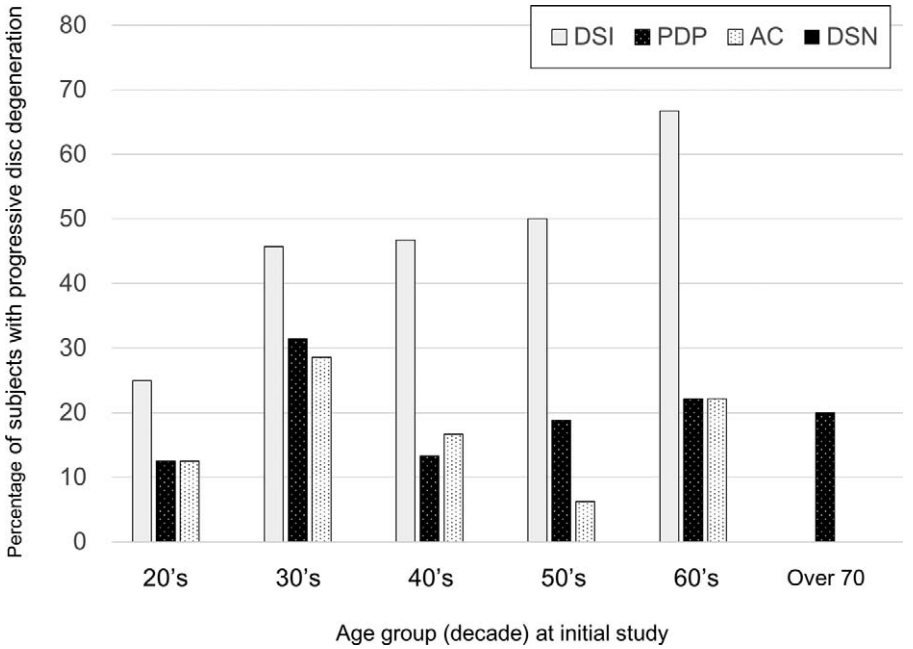

Figure 2. Percentage of subjects with progressive-disc degeneration at the 10-year follow-up, according to age. DSI indicates decrease in signal intensity of intervertebral disc; PDP, posterior disc protrusion; AC, anterior compression of dura and spinal cord; DSN, disc-space narrowing.

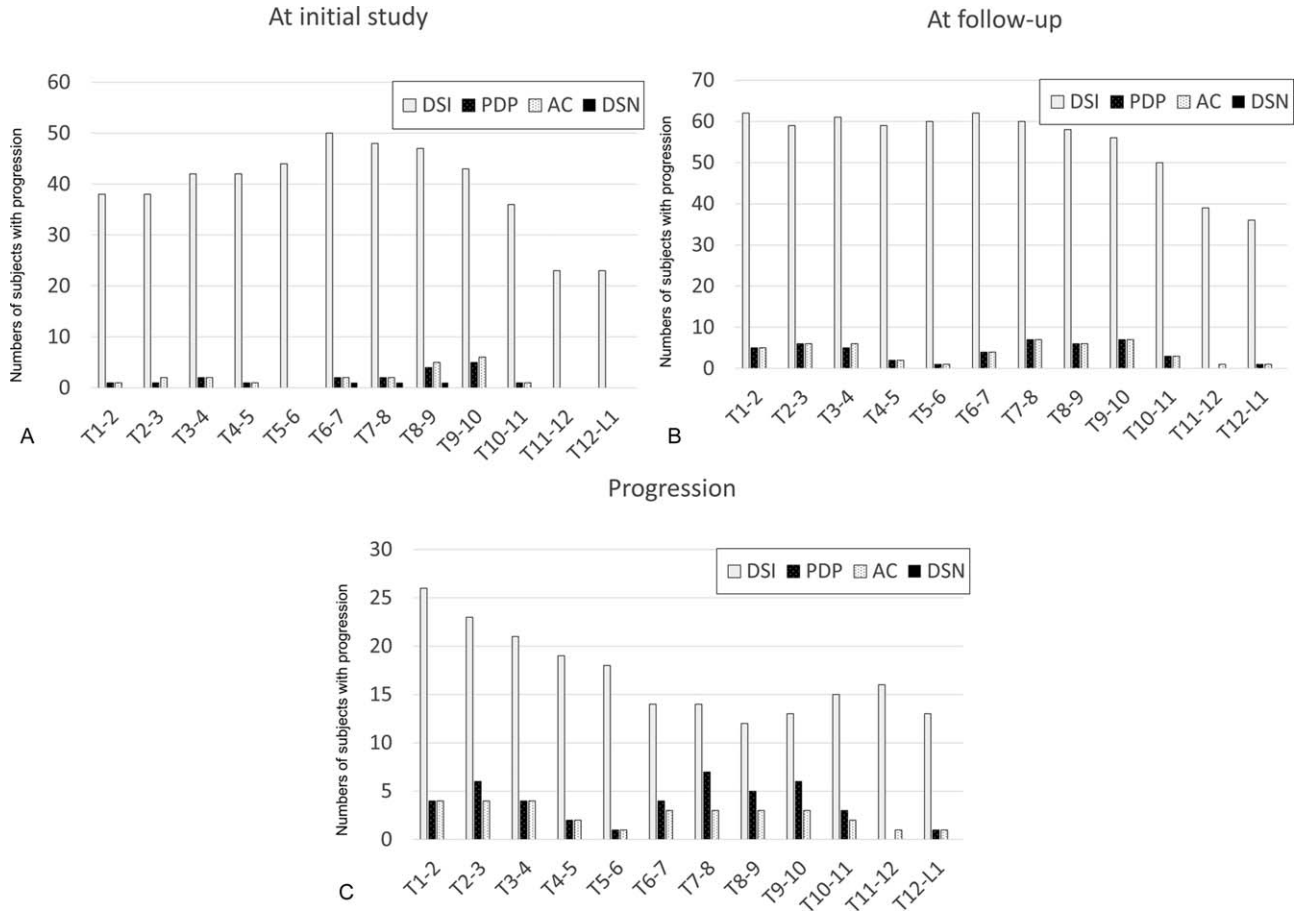

Figure 3. The number of discs with positive magnetic resonance imaging (MRI) findings at each intervertebral level at (**A**) the initial MRI investigation of the thoracic spine and at (**B**) the 10-year follow-up; and (**C**) the number of discs with progressive degeneration during the 10-year follow-up period.

TABLE 3. Percentage of Subjects With MRI Findings of Progressive Degeneration in the Cervical and Thoracic Spine

	Thoracic Spine	Cervical Spine	*P*
DSI	44.7	58.3	0.05
PDP	21.4	73.8	<0.001*
AC	18.4	66.0	<0.001*
DSN	0.0	13.6	<0.0001*
Any of the 4 findings	63.1	93.2	<0.001*

DSI indicates decreased signal intensity of the intervertebral discs; PDP, posterior disc protrusion; AC, anterior compression of the dural sac; DSN, disc-space narrowing; MRI, magnetic resonance imaging.

**Statistically significant*

including the progression of DSI in 58.3%, PDP in 73.8%, AC in 66.0%, and DSN in 13.6%. PDP, AC, and DSN progressed significantly less in the thoracic spine than those in the cervical spine.

Factors Associated with Degenerative Progression

Significant associations were found between DSI and degeneration of the cervical spine (odds ratio [OR] = 3.38; 95% confidence interval [CI] 1.46–7.82, $P = 0.004$), and between AC and smoking (OR = 3.93; 95% CI 1.09–14.15, $P = 0.036$). Neither PDP nor DSN was significantly associated with any of the evaluated factors (Table 4).

Association Between Clinical Symptom and Degenerative Progression on MRI

At the time of follow-up, 62.1% of the volunteers had cervical or lumbar spine-related symptoms, such as neck pain (17.5%), stiff shoulders (45.6%), and low back pain (35.0%). However, no volunteer had thoracic back pain or thoracic myelopathy. Regarding the association between clinical symptoms related to the cervical or lumbar spine and the observation of degenerative progression on MRI, no significant associations were observed (Table 5).

DISCUSSION

Progression of Thoracic Disc Degeneration

The present study revealed the natural course of aging in intervertebral discs of the thoracic spine. During a 10-year follow-up, degenerative changes progressed in 63.1% of the subjects. In a previous study of the cervical spine, Gore[12] reported a progression rate of 62.9% for disc degeneration in 159 asymptomatic volunteers during a 10-year follow-up. In our previous longitudinal study in the cervical spine,[7] MRI findings showed that degeneration progressed in 189 of 223 subjects (81.1%) during a 10-year follow-up period. In the lumbar spine, Boden *et al*[5] reported the frequency of positive MRI findings in 67 asymptomatic volunteers as follows: bulging disc (64.5%), moderate to severe disc degeneration (45.2%), disc herniation (32.2%), and spinal stenosis (32.2%). When Borenstein *et al*[13] followed up with the same cohort 7 years later through a questionnaire, 42.0% of the subjects complained of back pain.

In the present study, MRI findings showed that DSI had progressed in 44.7% of the subjects at follow-up, PDP in 21.4%, and AC in 18.4%. None of the subjects developed DSN during the follow-up period. At a 20-year follow-up study in the cervical spine,[9] the progression of DSN was observed in only 15.0%, whereas the progression of other degenerative findings was observed more frequently (DSI

TABLE 4. Relationships Between Progression of MRI Findings and Factors

Factor	Number of Volunteers	DSI	*P*	AC	*P*	PDP	*P*	Any 1 of 4 Evaluation items	*P*
Age									
<50	43	18 (41.9)	0.63	8 (13.3)	0.11	12 (27.9)	0.17	37 (61.7)	0.72
≧50	60	28 (46.7)		11 (25.6)		10 (16.7)		28 (65.1)	
Sex									
Male	58	23 (40.0)	0.25	9 (15.5)	0.38	16 (27.6)	0.08	35 (60.3)	0.51
Female	45	23 (51.1)		10 (22.2)		6 (13.3)		30 (66.7)	
Smoking									
Smoker	12	5 (41.7)	1	5 (41.7)	0.036*	4 (33.3)	0.28	9 (75.0)	0.53
Nonsmoker	91	41 (45.1)		14 (15.4)		18 (19.8)		56 (61.5)	
Sports									
Regularly	39	22 (56.4)	0.06	6 (15.4)	0.53	12 (30.8)	0.07	28 (71.8)	0.15
None	64	24 (37.5)		13 (20.3)		10 (15.6)		37 (57.8)	
BMI									
<25	76	36 (47.4)	0.35	7 (25.9)	0.24	8 (29.6)	0.22	18 (66.7)	0.66
≧25	27	10 (37.0)		12 (15.8)		14 (18.4)		47 (61.8)	
Progression in the cervical spine†									
+		34/60 (56.7)	0.004*	10/68 (14.7)	0.18	14/76 (18.4)	0.22	61/96 (63.5)	0.71
−		12/43 (27.9)		9/35 (25.7)		8/27 (29.6)		4/7 (57.1)	

DSI indicates decrease signal intensity of intervertebral discs; PDP, posterior disc protrusion; AC, anterior compression of the dura and spinal cord.

Values in parentheses are percentage values.

**$P < 0.05$ (logistic regression analysis).*

†MRI finding in the cervical spine corresponding to that in the thoracic spine in the rows.

TABLE 5. Association Between Clinical Symptoms and Degenerative Progression in Thoracic Spine MRI

	DSI			PDP			AC	
		P			*P*			*P*
Neck pain								
+	3 (42.9)	0.619	+	1 (14.3)	0.536	+	0 (0.0)	0.229
−	43 (44.8)		−	21 (21.9)		−	19 (19.8)	
Stiff shoulders								
+	12 (46.2)	0.519	+	8 (30.8)	0.141	+	3 (11.5)	0.229
−	34 (44.2)		−	14 (18.2)		−	16 (20.8)	
Numbness in the upper limbs								
+	3 (60.6)	0.339	+	1 (20.0)	0.711	+	1 (20.0)	0.647
−	43 (43.9)		−	21 (21.4)		−	18 (18.4)	
Low back pain								
+	13 (54.2)	0.202	+	7 (29.2)	0.214	+	7 (29.2)	0.109
−	33 (41.8)		−	15 (19.0)		−	12 (15.2)	

DSI indicates decrease signal intensity of intervertebral discs; PDP, posterior disc protrusion; AC, anterior compression of the dura and spinal cord. Values in parentheses are percentage values.

81.3%, AC 86.0%, and PDP 82.9%). Interestingly, all of the degenerative findings assessed by MRI in the present study were less frequent in the thoracic spine than in the cervical spine. In our initial MRI study of the thoracic spine,[8] DSN was found in only 4.3% of the subjects. One MRI study of the cervical spine[7] indicated that biochemical changes in the intervertebral disc, represented by DSI on MRI, and early structural changes in the disc, represented by AC and PDP, frequently occur in early degenerative phases, whereas the advanced structural changes represented by DSN occur at an older age. MRI can more easily detect chemical changes than structural ones. The subjects in the present study were relatively young (mean 45.0 years), which might have contributed to the low rate of DSN progression in the thoracic spine during the 10-year follow-up period. The thoracic spine's anatomical stability owing to the rib cage[14] and the relatively narrower disc space[15] also retards progressive disc degeneration in this part of the spine.

Disc Degeneration and Smoking

In the present study, we found that smoking and progressive cervical disc degeneration were related to thoracic disc degeneration. The contribution of smoking to disc degeneration remains controversial. In a study of 100 nonsmokers and 100 smokers, Gore *et al*[16] found no evidence that smoking was a risk factor for disc degeneration in the cervical spine. However, other research indicates that smoking accelerates disc degeneration.[17,18] Nasto *et al*[18] investigated whether smoking-induced DNA damage was causal for spine degeneration in a mouse model, and reported that exposure to high levels of inhaled tobacco smoke promoted disc degeneration. In our original cross-sectional study,[8] we concluded that smoking induced thoracic disc degeneration in healthy volunteers. The results of the present longitudinal study further support the finding that smoking induces disc degeneration in the thoracic spine.

Disc Degeneration in the Thoracic and Cervical Spine

In the present study, we found a strong association between progressive disc degeneration in the thoracic spine and disc degeneration in the cervical spine. Other studies have reported correlations in the degeneration of discs in different spinal segments. In 2011, Okada *et al*[19] evaluated 51 subjects diagnosed with disc herniation by MRI and reported that patients with lumbar disc herniation had a higher rate of cervical disc degeneration compared to healthy volunteers. In 2015, Parks *et al*[20] assessed the whole-spine MRIs of 460 patients with lumbar spinal canal stenosis and reported that 110 (23.9%) of them had concurrent cervical canal stenosis and 112 (24.3%) had concurrent thoracic canal stenosis without clinical symptoms. In 2018, Yamada *et al*[21] retrospectively analyzed 565 patients who underwent surgery for symptomatic lumbar spinal canal stenosis, and found that 202 patients (35.8%) had cervical stenosis. These results indicate that disc degeneration is a systemic phenomenon. The results of the present study indicate that even in healthy olunteers, the progression of intervertebral disc degeneration involves the whole spine, although the incidence of intervertebral disc degeneration was lower in the thoracic than in the cervical spine.

In the present study, experienced spine surgeons examined clinical symptoms of the volunteers at the initial and follow-up MRI investigation. Although 63.1% of the volunteers complained neck pain and/or low back pain, no volunteers complained of thoracic back pain or thoracic myelopathy at the follow-up. Thus, we could not evaluate the association between each MRI finding and clinical symptoms related to the thoracic spine. We also evaluated the association between clinical symptoms related to the cervical or lumbar spine and degenerative progression seen on the thoracic spine MRI; however, we found no significant associations. Roquelaure[22] conducted the 5-year prospective study investigating 1886 subjects without thoracic spinal pain at the baseline and reported that thoracic spinal

pain was observed in 5.2% for men and 10.0% for women at the follow-up. Thus, previous studies reported the lower incidence of thoracic spinal pain compare to higher rate of neck pain (16.7%[23] to 75.1%[24] mean 37.2%[25]) or low back pain (67.6%[26] to 84.1%[27]). The results of this study indicated that the thoracic disc degeneration can occur in normal population without symptom by age. Progression of thoracic disc degeneration does not always indicate future onset of clinical symptoms in health volunteers for 10 years. Further long-term investigation, >20 years, is needed to clarify the association between the natural disc aging and the onset of clinical symptom.

This study was limited by the moderate follow-up rate (46.2%), which might cause a selection bias between participants and nonparticipants. The subjects who we could not follow-up were significantly older than the followed-up subjects. This difference in age may have affected the results, especially the disc degeneration on MRI. Second, we could not evaluate the effect of intervention because none of the volunteers underwent physical therapy or surgery for the thoracic spine. However, to the best of our knowledge, this is the first longitudinal 10-year study to use MRI to evaluate the natural aging process of thoracic intervertebral discs. The results add to our understanding of natural aging in the thoracic spine, and can be used as control data for evaluating degenerative diseases such as adjacent segment disease after fusion surgery.

CONCLUSION

This 10-year follow-up MRI study of the thoracic spine revealed progressive disc degeneration in 63.1% of healthy asymptomatic subjects. Risk factors significantly associated with degenerative changes in thoracic intervertebral discs included smoking and progressive degeneration in the cervical spine.

➢ Key Points

- ❑ We assessed intervertebral disc degeneration in thoracic spine MRIs obtained 10 years apart (average 10.0 ± 0.6 years) from 103 of 223 healthy volunteers who participated in the initial MRI thoracic-spine study (follow-up rate 46.2%).
- ❑ MRIs were graded for four indications of degeneration; comparison of initial and follow-up MRIs showed that intervertebral disc degeneration had progressed at least one grade in 63.1% of the subjects.
- ❑ Degenerative changes during the 10-year period included decrease in signal intensity of intervertebral disc (44.7% of the subjects), PDP (21.4%), and AC (18.4%). Progression of DSN was not observed in any subject.
- ❑ Cervical-spine degeneration and smoking were significantly associated with degenerative changes in intervertebral discs in the thoracic spine.

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ORIGINAL ARTICLE

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A hypothesis of chronic back pain: ligament subfailure injuries lead to muscle control dysfunction

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Abstract Clinical reports and research studies have documented the behavior of chronic low back and neck pain patients. A few hypotheses have attempted to explain these varied clinical and research findings. A new hypothesis, based upon the concept that subfailure injuries of ligaments (spinal ligaments, disc annulus and facet capsules) may cause chronic back pain due to muscle control dysfunction, is presented. The hypothesis has the following sequential steps. Single trauma or cumulative microtrauma causes subfailure injuries of the ligaments and embedded mechanoreceptors. The injured mechanoreceptors generate corrupted transducer signals, which lead to corrupted muscle response pattern produced by the neuromuscular control unit. Muscle coordination and individual muscle force characteristics, i.e. onset, magnitude, and shut-off, are disrupted. This results in abnormal stresses and strains in the ligaments, mechanoreceptors and muscles, and excessive loading of the facet joints. Due to inherently poor healing of spinal ligaments, accelerated degeneration of disc and facet joints may occur. The abnormal conditions may persist, and, over time, may lead to chronic back pain via inflammation of neural tissues. The hypothesis explains many of the clinical observations and research findings about the back pain patients. The hypothesis may help in a better understanding of chronic low back and neck pain patients, and in improved clinical management.

Keywords Low back pain · Neck pain · Whiplash · Biomechanics · Hypothesis

Introduction

Low back pain is an important societal problem with significant costs. Up to 70–85% of the population in industrialized societies experience low back pain at least once in their lifetime, with point prevalence of about 30% [1, 24]. The total cost of low back pain has been estimated to exceed 50 billion dollars per year in the USA [17]. Although neck pain due to whiplash-associated disorder is less common and less costly, awareness of this disorder, diagnosis and treatment are equally baffling [63]. The term ''back pain'' as used here does not include back pain due to known infections, tumor, systemic disease, fractures or fracture dislocations [73]. Further, the term used here refers generally to the entire spine but in particular to the cervical and lumbar regions.

Back pain is complex. The exact cause of most back (low back and neck) pain remains unproven [72]. The multi-factorial nature of back pain is well recognized with respect to its causes, diagnosis, chronicity, disability and treatment [73]. Abnormal mechanics of the

spinal column has been hypothesized to lead to back pain via nociceptive sensors [72]. The path from abnormal mechanics to nociceptive sensation may go via inflammation [8, 11], biochemical and nutritional changes [6], immunological factors [44], and changes in the structure and material of the endplates [6] and discs [40, 41], and neural structures, such as nerve ingrowth into diseased intervertebral disc [15, 16]. The abnormal mechanics of the spine may be due to degenerative changes of the spinal column [18] and/or injury of the ligaments [43]. Most likely, the initiating event is some kind of trauma involving the spine. It may be a single trauma due to an accident or microtrauma caused by repetitive motion over a long time. It is also possible that spinal muscles will fire in an uncoordinated way in response to sudden fear of injury, such as when one misjudges the depth of a step. All these events may cause spinal ligament injury. Adverse psycho–social factors may also play an important role in transforming the back pain into disability [3].

The research literature on chronic back pain is vast. However, there are some important and common observations. Chronic low back pain patients have delayed muscle response when asked to perform a task [65] or when the spine is suddenly loaded [35], or in anticipation of raising an arm to horizontal position [20], and also delayed muscle shut-off after the external challenge has been withdrawn [52]. Further, they show poorer spinal posture control and balance, especially during complex tasks, when compared to subjects without back pain [10, 33, 53]. The findings in neck pain patients are similar, although the number of studies is fewer. Patients with whiplash-associated disorders have disrupted neck motion [2, 4, 14, 27, 34, 49, 51] and less efficient muscle control [14, 19, 22, 31, 34].

A few hypotheses have attempted to explain the clinical observations and research findings in back pain patients. As the nociceptive sensors are present in most components of the spinal column, the hypotheses have focused on disruption of the spinal column and its components, such as spinal column degeneration [25], injury and clinical instability [47, 73]; facet joint injury [13], and inferior facet-tip impingement on the lamina [77], and Schmorl's nodes [29]. Others have focused on spinal muscles. The pain adaptation [32] and pain–spasm–pain [54] hypotheses were evaluated in a recent review article [69]. The evidence was mixed, and authors suggested that other models, such as spinal instability [46, 47], may be explored. The role played by the injury to the mechanoreceptors embedded in the ligaments of the spinal column has not been explored by any hypothesis.

The spinal column, consisting of ligaments (spinal ligaments, discs annulus and facet capsules) and vertebrae, is one of the three subsystems of the spinal stabilizing system [46]. The other two are the spinal muscles and neuromuscular control unit, Fig. 1. The spinal column has two functions: *structural* and *transducer*. The structural function provides stiffness to the spine. The transducer function provides the information needed to precisely characterize the spinal posture, vertebral motions, spinal loads etc. to the neuromuscular control unit via innumerable mechanoreceptors present in the spinal column ligaments [26, 58], facet capsules [11, 36, 76] and the disc annulus [26]. These mechanical transducers provide information to the neuromuscular control unit which helps to generate muscular spinal stability via the spinal muscle system and neuromuscular control unit. [46] The criterion used by the neuromuscular unit is hypothesized to be the need for adequate and overall mechanical stability of the spine. If the structural function is compromised, due to injury or degeneration, then the muscular stability is increased to compensate the loss. What happens if the *transducer* function of the ligaments of the spinal column is compromised? This has not been explored. There is evidence from animal studies that the stimulation of the ligaments of the spine (disc and facets [21], and ligaments [59, 62]) results in spinal muscle firing. The mechanoreceptor-muscle firing relationships are modulated by several factors, such as ligament fatigue [61], static flexed posture [60], and cumulative microtrauma [75].

The observations from animal studies just mentioned, together with the possibility of transducer dysfunction in back pain patients, form the basis of a new back pain hypothesis. The purpose is to describe the hypothesis, use the hypothesis to explain the various important research findings, and suggest possible treatment options.

The hypothesis

The hypothesis consists of the following sequential steps:

1. Single trauma or cumulative microtrauma causes *subfailure injury* of the spinal ligaments and injury to the mechanoreceptors embedded in the ligaments.
2. When the injured spine performs a task or it is challenged by an external load, the transducer signals generated by the mechanoreceptors are corrupted.
3. Neuromuscular control unit has difficulty in interpreting the corrupted transducer signals because there is spatial and temporal mismatch between the normally expected and the corrupted signals received.
4. The muscle response pattern generated by the neuromuscular control unit is corrupted, affecting the spatial and temporal coordination and activation of each spinal muscle.
5. The corrupted muscle response pattern leads to corrupted feedback to the control unit via tendon organs of muscles and injured mechanoreceptors, further corrupting the muscle response pattern.

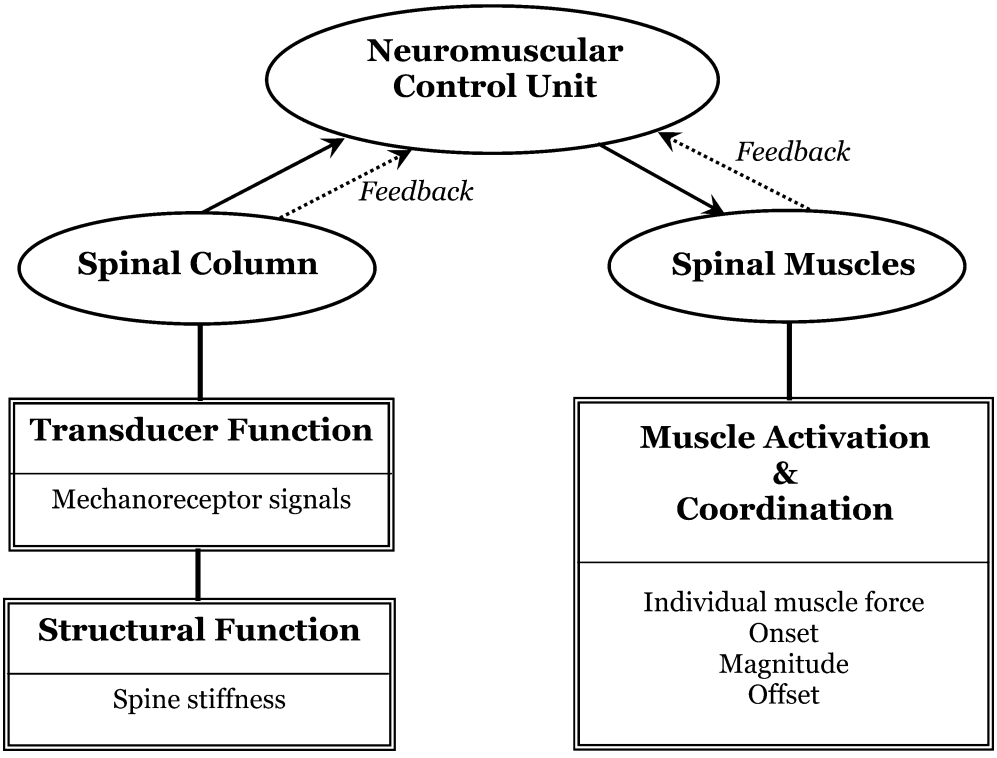

Fig. 1 Spinal stabilizing system. It consists of three subsystems: spinal column, spinal muscles, and neuromuscular control unit. The spinal column has two functions: structural—to provide intrinsic mechanical stability, and transducer—to generate signals describing spinal posture, motions, loads etc. via the mechanoreceptors. The neuromuscular control unit generates muscle response pattern to activate and coordinate the spinal muscles to provide muscle mechanical stability. There is feedback from the spinal muscles and mechanoreceptors to the control unit. (Adapted from Panjabi 1992)

6. The corrupted muscle response pattern produces high stresses and strains in spinal components leading to further subfailure injury of the spinal ligaments, mechanoreceptors and muscles, and overload of facet joints.
7. The abnormal stresses and strains produce inflammation of spinal tissues, which have abundant supply of nociceptive sensors and neural structures.
8. Consequently, over time, chronic back pain may develop. The *subfailure injury* of the spinal ligament is defined as an injury caused by stretching of the tissue beyond its physiological limit, but less than its failure point [48].

Under normal circumstances, to perform a task or to respond to an external challenge, the mechanoreceptors generate a complex and redundant set of transducer signals describing vertebral position, spinal motion, spinal load, and so forth, at each spinal level (Fig. 2). The signals are transmitted to the neuromuscular control unit for interpretation and action. The neuromuscular control unit evaluates the signals and produces a normal muscle response pattern, based upon several factors, including the need for spinal stability, postural control, balance, minimal stress/stain in various spinal components, and so forth. This is achieved via feedback from the muscle spindles and golgi tendon organs of the muscles as well as the mechanoreceptors of the ligaments. The muscle response pattern includes all the information needed to dynamically orchestrate the muscles: to choose the individual muscles needed, and to activate each muscle in a defined sequence with respect to its onset, activation level and shut-off. The entire dynamic procedure is relatively quick, non-injurious and leads to no adverse consequences.

The injured spine behaves differently (Fig. 3). The subfailure injuries of the ligaments disrupt and/or injure the embedded mechanoreceptors. When the spine performs a routine task or responds to an external challenge, the disrupted/injured mechanoreceptors produce *corrupted* transducer signals, describing vertebral position, motion, spinal loads etc. for each spinal level. There is loss of spatial and temporal integrity of the transducer signals received from multiple redundant mechanoreceptors distributed through the spinal column. The neuromuscular control unit, not affected by the injury itself, senses a mismatch between the normally expected and the received transducer signals, and, therefore, has difficulty in choosing the appropriate muscle response pattern. However, it must act. Consequently, the neuromuscular control unit produces a *corrupted* muscle response pattern, which is the closest match it can determine to the corrupted transducer signals. The corrupted muscle response pattern affects the choice of the spinal muscles to activate, and the individual muscle activation: force onset, intensity and shut-off. The orchestration of the various spinal muscles responsible for spinal stability, posture and motion is disrupted.

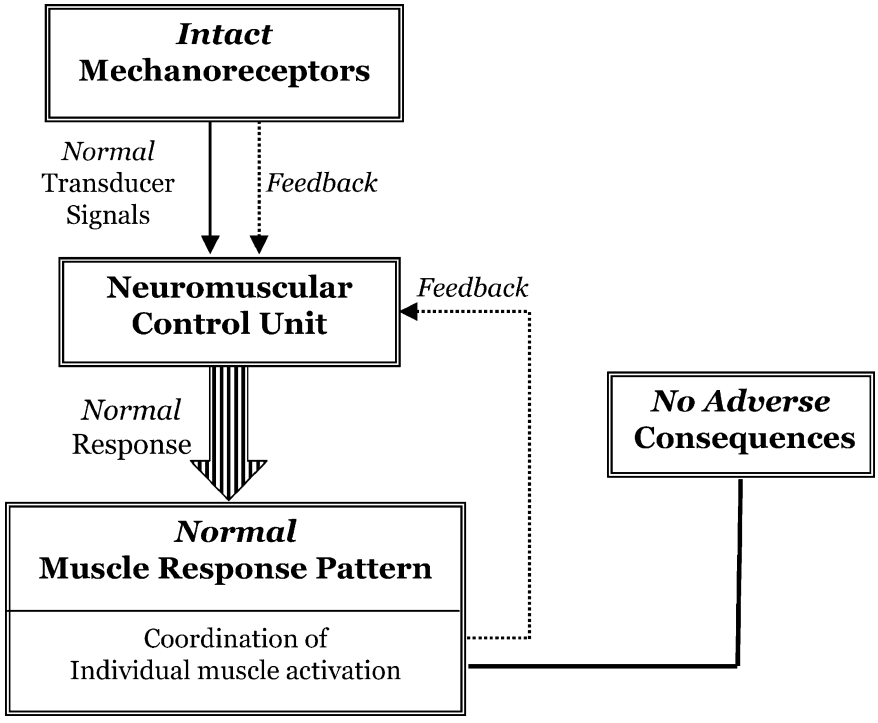

Fig. 2 Normal circumstances. The intact mechanoreceptors send transducer signals to the neuromuscular control unit, which evaluates the transducer signals and sends out muscle response pattern to coordinate the activation of individual spinal muscles. There is feedback from the muscle spindles and golgi tendon organs of the muscles and mechanoreceptors of the ligaments to the neuromuscular control unit. Under normal circumstances, there are no adverse consequences

Additionally, the feedback to the neuromuscular control unit and mechanoreceptors is also negatively affected, further corrupting the muscle response pattern. This has several adverse effects. Higher stresses, and strains and injuries may develop in the spinal ligaments, and mechanoreceptors. The facet joints may be overloaded, and the spinal muscles may fatigue or be injured. Over time, these injurious stresses and strains can initiate inflammation of neural tissues [12], and accelerate disc [40] and facet joint [9] degeneration. Thus, a vicious cycle is set up, leading to chronic dysfunction of the entire spinal system, resulting in back pain.

Discussion

The underlying concept of the spinal instability hypothesis was the need for adequate spinal stability provided by vertebrae and ligaments of the spinal column, and augmented by the spinal muscles under the neuromuscular control [46, 47]. In the present hypothesis, the focus is on the disruption of the mechanoreceptors due to ligament injury leading to corrupted transducer signals and muscle response pattern, and overall system dysfunction. What follows is an attempt, using the new hypothesis, to explain some of the observations concerning low back and neck pain patients, and to suggest treatment options.

Delayed muscle response is a common observation in low back pain patients. When low back pain patients were challenged by a sudden external load, the delayed muscle onset was observed [35], and delayed muscle shut-off was seen when the load was removed [52]. Similarly, the anticipatory response of the transverse abdominis was delayed [20]. These findings can be explained by the hypothesis. An individual with intact spinal system, when challenged by a sudden change in its load or posture, will produce a quick and normal muscle response pattern, specific to the challenge (Fig. 2). However, when the neuromuscular control unit receives corrupted transducer signals, it may take a longer time to choose a muscle response pattern that most closely matches the corrupted transducer signals, taking into account a multitude of factors such as spinal stability, postural balance, tissue overload and so forth (Fig. 3). Additional factors, such as muscle fatigue, complexity of the task, mental distraction, and so forth, may further decrease the efficiency of the neuromuscular control unit leading to the delayed muscle system response.

Balance and postural control are deficient in low back pain patients [10, 33, 53]. The balance and postural control includes a three-step process: generation of transducer signals by the mechanoreceptors; selection of appropriate muscle response pattern by the neuromuscular control unit based up mechanoreceptor signals; and feedback from the mechanoreceptors and muscle spindles and golgi tendon organs (Fig. 2). Therefore, subfailure injuries of the ligaments disrupt all the three steps involving the mechanoreceptors thereby resulting in poor balance and postural control.

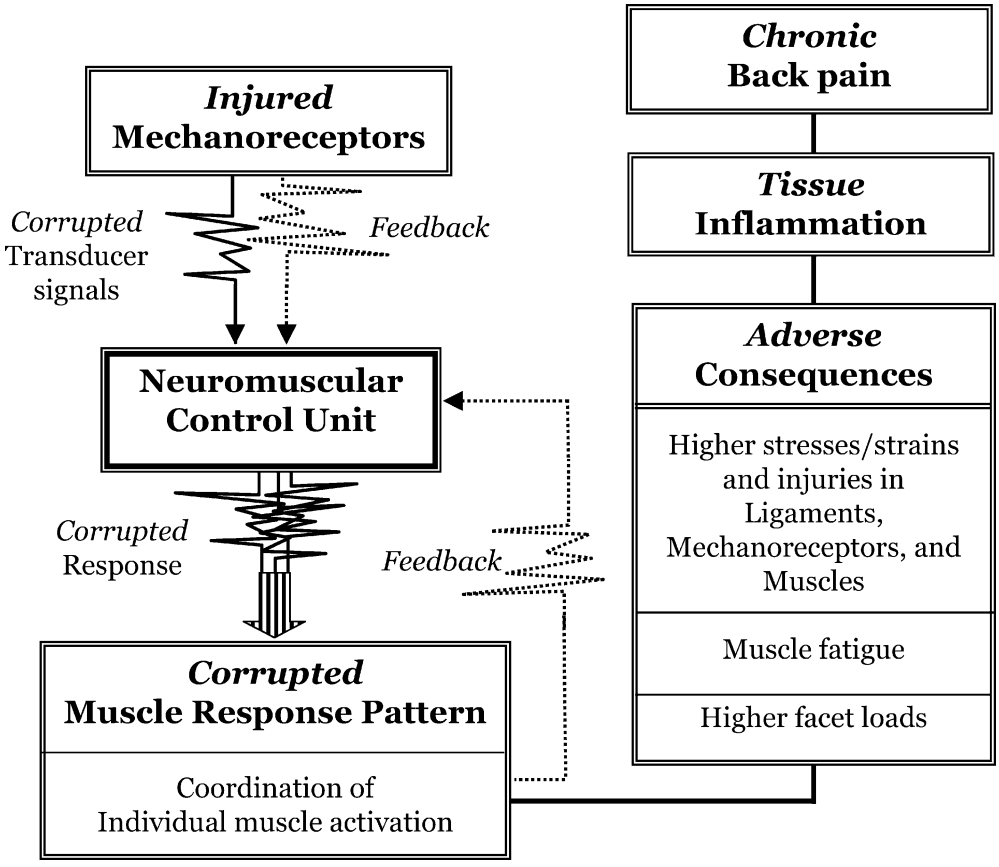

Fig. 3 Subfailure injuries of the ligaments. The injured mechanoreceptors send out *corrupted* transducer signals to the neuromuscular control unit, which finds spatial and temporal mismatch between the expected and received transducer signals, and, as a result, there is muscle system dysfunction and *corrupted* muscle response pattern is generated. Consequently, there are adverse consequenses: higher stresses, strains, and even injuries, in the ligaments, mechanoreceptors, and muscles. There may also be muscle fatigue, and excessive facet loads. These abnormal conditions produce neural and ligament inflammation, and over time, chronic back pain

Re-positioning error has been consistently found in both low back pain [7, 38, 42] and whiplash [19, 31] patients. The error occurs when the patient is asked, starting from an initial posture, to first bend or twist the spine to a certain posture, and then to return to the initial posture. Based upon the hypothesis presented, this is to be expected. The muscle response pattern generated to bring back the trunk or head to the initial posture makes use of the mechanoreceptor transducer signals, in the three-step process described above. With the ligament injury in back pain patients, the corrupted mechanoreceptor information and the corrupted muscle response pattern will both lead to the re-positioning error.

Among chronic whiplash patients, decreased neck motion has been observed in most studies [2, 4, 14, 34, 49, 51]. These were active motion studies in which the subject was encouraged to produce the motion. However, when the subject was relaxed and the motion was produced passively by the examiner, the motion was found to be increased in the whiplash patients compared to the control group [27]. How can one explain these contrasting findings? In the active motion studies, corrupted muscle response pattern (generated due to corrupted mechanoreceptor signals) applies higher muscle forces on the cervical spine. Such forces stiffen the spine and reduce the motion [50, 68, 74]. In the relaxed passive motion studies, care was taken to decrease the influence of muscle guarding, pain and lack of motivation by relaxing the neck and shoulder muscles with application of vapor coolant, and then letting the examiner move the patient's head into maximum flexion. Thus, when the abnormal muscle forces were minimized in the passive examination, the intrinsic injury of the spinal column was exhibited as the increased motion.

Muscle spasm is commonly observed in both low back pain [5, 30] and whiplash patients [39, 55, 67]. Muscle coordination may be thought of as an orchestrated activation of various spinal muscles to stabilize the spinal column and accomplish a certain task. The orchestration consists of activation of individual muscles with respect to the onset, magnitude of the force generated, and offset. With the injury of the ligaments, the mechanoreceptors generate corrupted transducer signals, and therefore, there is a mismatch between the expected and the received corrupted transducer signals. The neuromuscular control unit senses the mismatch and may fire simultaneously both the agonist and antagonist muscles at its command to temporarily stabilize the spine and minimize the intervertebral motions, corrupted transducer signals, and pain. If the situation does not improve with time,

then the muscle action may become chronic. Such simultaneous firing of agonistic and antagonist muscles has been observed in low back pain patients.

Greater variability has been observed in almost all parameters measured in low back [28, 33, 37, 42, 53] and whiplash [14, 34] patients. The new hypothesis can explain this increased variability. The subfailure injuries of ligaments are incomplete injuries, which may range between tearing of a few fibers to a nearly complete rupture of a ligament. Importantly, a complex joint, such as a functional spinal unit, includes many ligament structures. This collection of ligament structures may encompass a wide range of injuries, each structure with different injury severity, depending upon the magnitude and mode of the trauma. The density of the mechanoreceptors imbedded in the various ligament structures may also vary. The result of all these numerous variations can produce a wide spectrum of corrupted muscle response patterns for seemingly similar injury-causing events. Further, each low back pain patient is unique, for example with respect to the anatomy, mechanical properties of ligaments, and muscle response to the trauma, adding further to the muscle response pattern variability.

There are limitations to the hypothesis. Back pain is a complex multifactorial problem, and a single hypothesis cannot explain each and every clinical and research observation, and there may also be alternative explanations, such as instability [46, 47], and/or pain [32, 54]. It is recognized that the pain is a subjective experience. Besides affecting the muscle system via the corrupted mechanoreceptor signals, ligament injury may also result in muscle atrophy and weakness due to disuse, thus directly affecting the spinal system function. Additionally, muscle injury, fatigue, atrophy, and so forth may aggravate the spinal system dysfunction. As the muscles participate in the feedback loop via the mechanoreceptors in the form of muscle spindles and golgi tendon organs (Fig. 3), their disruption could further corrupt the muscle response pattern. However, an injured muscle may heal relatively quickly due to abundant blood supply, and, therefore, may not be the main cause of *chronic* back pain. In contrast, the ligament injuries heal poorly and, therefore, may lead to tissue degeneration over time [40, 41]. Thus, the ligament injuries are more likely to be the major cause of the chronic back pain. The corrupted transducer signals may be the result not only of the ligament injury, but also due to ligament fatigue and viscoelastic creep stretch [61], but such an effect is often reversible given sufficient rest, and, therefore, may not always lead to chronic back pain. The clinical and research studies presented constitute only a small, but an important and quite representative sample, of the vast literature available on the subject of back pain. It is recognized that there may be other studies whose explanation may or may not fit the new hypothesis. In general, hypotheses and models are extremely difficult, if not impossible, to fully validate [45]. They can only attempt to explain the available findings, and may be used to predict outcomes in specific situations.

Can the system adapt to the subfailure injury of the mechanoreceptors? A minor subfailure injury is probably repaired or compensated with no long-term consequences. A mild subfailure injury, on the other hand, may be successfully compensated in the short-term by temporarily modifying the chosen muscle response pattern. However, the modification may be difficult to maintain overtime, as it is likely to produce excessive tissue loads and muscle fatigue. Lapses in the maintenance of the modified muscle response pattern may occur from time to time. Could this be the mechanism for recurrent episodes of back pain that many patients experience? [57, 71] On the other hand, if the corrupted muscle response pattern becomes permanent, then it may result in abnormal posture, disturbed intervertebral motion pattern, altered gait, and, in general, a less efficient system to perform every day spinal functions.

One can speculate as to the possible treatment options based upon the hypothesis. The incoming corrupted transducer data may never become normal, even though the ligaments, incorporating the injured mechanoreceptors, may heal/scar over time. After breaking the cascade of injury, inflammation, and pain by suitable drug treatment, the patient may be encouraged to retrain the neuromuscular control unit to produce an altered muscle response pattern that is suited to both the corrupted transducer signals and activities of daily living. The criterion for the altered muscle response pattern may be the reduction of stresses and strains of the ligaments, loads on facet joints, and muscle forces, which may reduce the back pain. A set of tasks may be designed for this purpose. The tasks may be repeated and varied. Improvement in the efficiency of the neuromuscular control unit may develop over time, with concomitant relief of back pain. Several clinical studies have incorporated these and similar ideas. Re-training exercises involving muscle control have shown promising results in both chronic low back pain [22, 23, 70], and neck pain [56, 64, 66] patients, compared to traditional therapies. More research is needed in this area. I hope that the presentation of this hypothesis will stimulate discussion among clinicians and researchers in biomechanics to evaluate the usefulness of the hypothesis towards better understanding of back pain, development of more precise diagnostic methods, and design of more efficient treatments for back pain patients.

Conclusions

A new hypothesis of chronic back pain based upon muscle system dysfunction due to ligament injuries is

described. Subfailure injuries of the ligaments and embedded mechanoreceptors generate *corrupted* mechanoreceptor signals. Consequently, the neuromuscular control unit produces *corrupted* muscle response pattern, resulting in excessive loading and, possibly, injuries of the spinal structures, including additional injuries of the mechanoreceptors. The hypothesis accounts for many of the common and important experimental observations and clinical findings seen in low back pain and whiplash patients. In the low back pain patients, it explains findings of delayed muscle response, poor balance, inefficient postural control, greater error in re-positioning the trunk, muscle spasm, and greater variability in the tasks performed. In the whiplash patients, both the decreased motion in active testing and increased motion in passive-relaxed testing are explained. The hypothesis proposes that the dysfunction of the muscle system over time may lead to chronic back pain via additional mechanoreceptor injury, and neural tissue inflammation.

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Sensory – Motor control of ligaments and associated neuromuscular disorders

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Abstract

The ligaments were considered, over several centuries, as the major restraints of the joints, keeping the associated bones in position and preventing instability, e.g. their separation from each other and/or mal-alignment. This project, conducted over 25 years, presents the following hypothesis:

1. Ligaments are also major sensory organs, capable of monitoring relevant kinesthetic and proprioceptive data.
2. Excitatory and inhibitory reflex arcs from sensory organs within the ligaments recruit/de-recruit the musculature to participate in maintaining joint stability as needed by the movement type performed.
3. The synergy of the ligament and associated musculature allocates prominent role for muscles in maintaining joint stability.
4. The viscoelastic properties of ligaments and their classical responses to static and cyclic loads or movements such as creep, tension–relaxation, hysteresis and strain rate dependence decreases their effectiveness as joint restraint and stabilizers and as sensory organs and exposes the joint to injury.
5. Long-term exposure of ligaments to static or cyclic loads/movements in a certain dose-duration paradigms consisting of high loads, long loading duration, high number of load repetitions, high frequency or rate of loading and short rest periods develops acute inflammatory responses which require long rest periods to resolve. These inflammatory responses are associated with a temporary (acute) neuromuscular disorder and during such period high exposure to injury is present.
6. Continued exposure of an inflamed ligament to static or cyclic load may result in a chronic inflammation and the associated chronic neuromuscular disorder known as cumulative trauma disorder (CTD).
7. The knowledge gained from basic and applied research on the sensory – motor function of ligaments can be used as infrastructure for translational research; mostly for the development of ''smart orthotic'' systems for ligament deficient patients. Three such ''smart orthosis'', for the knee and lumbar spine are described.
8. The knowledge gained from the basic and applied research manifests in new physiotherapy modalities for ligament deficient patients.

Ligaments, therefore, are important structures with significant impact on motor control and a strong influence on the quality of movement, safety/stability of the joint and potential disorders that impact the safety and health of workers and athletes.

1. Historical background

For centuries the role of the ligaments was thought to be that of mechanical structures that maintain the bones associated with the joint in a relative position to each other, e.g. prevent the separation of the bones. Over the years additional information was obtained providing more details on the properties of the ligaments, their anatomy and mechanical functions. The collagen fibers of the ligaments were shown to be viscoelastic and the fibers were shown to be at various levels of laxity or tension such that

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elongation created a process of recruitment which increased with length allowing increase in tension (Woo and Buckwalter, 1988; Woo et al., 1980, 1981, 1987). Furthermore, the position, orientation and shape of a specific ligament was shown to also increase and decrease its tension at specific range of motion, providing resistance to joint separation in that range (Renstrom et al., 1986). It was also shown that interaction of several ligaments associated with the same joint provided joint stability for most of the range of motion in several axis, allowed equal pressure distribution of the two cartilage surfaces and kept the surfaces moving on a prescribed track. Such data confirmed the mechanical properties of ligaments as joint stabilizers.

As far back as the early 20th century, Payr (1900) suspected that ligaments may have a neurological function in addition to their mechanical properties. His hypothesis went without experimental proof for nearly 50 years until several anatomical studies demonstrated the existence of mechanoreceptors in ligaments (Gardner, 1944; Wrete, 1949; Freeman and Wyke, 1967a,b; Ekholm et al., 1960; Patridge, 1924).

Together with the earlier demonstration of articular nerves emerging from ligaments (Rudinger, 1857), the possible neurological role of the ligaments as a sensory element was emerging.

2. The ligamento-muscular reflex

At about the same time, in the mid-20th century, groups of Swedish researchers were attempting to demonstrate the possibility of a reflex arc from the knee ligaments to the thigh muscles. Palmer (1938, 1958) developed tension in the knee's medial collateral ligament of humans and was able to see some muscle activity in the semimembranosus, sartorius, and vastus muscles and noted decreasing activity as the transverse tension via a ligature was shifted distally along the ligament. Stener (1959, 1962) and Andersson and Stener (1959), failed to observe the reflex in the anesthetized feline, yet were able to record nerve activity in the articular nerves of the feline and unanaesthetized humans upon ligament loading, but no muscle activity. In patients with ligament rupture, pain sensation and some muscular activity was observed upon stretch of the damaged ligaments. It was assumed that ligament innervation was to deliver pain sensation upon damage.

The conflicting and confusing results from the two groups remained until 1987 when we were able to demonstrate a distinct reflex activity from the anterior cruciate ligament to the hamstrings in the in vivo feline and in unanaesthetized humans as shown in Fig. 1a–c (Solomonow et al., 1987). Several groups went on to independently confirm the existence of a reflex arc from various knee ligaments to the leg muscles in humans and animal models (Grabiner and Weiker, 1993; Beard et al., 1994; Raunest et al., 1996; Sjolander, 1989).

As the neurological functions of the knee ligaments and its reflexive activation of the thigh muscles were established, several new questions emerged; are all ligaments in the major joints innervated and capable of eliciting a reflex? And what is the biomechanical/physiological function of the reflex arc from the ligaments to the muscles?

Over the following years we have been able to demonstrate that mechanoreceptors exist in the ligaments of the major joints (Guanche et al., 1999; Solomonow et al., 1996; Petrie et al., 1997, 1998) and that a reflex arc could be elicited by either electrically stimulating the articular nerve emerging from the ligaments or applying tension directly to the ligaments. Mechanoreceptors and a reflex arc were demonstrated in the knee, elbow, shoulder, ankle, palmar wrist, and lumbar spine as shown in Figs. 2 and 3 (Solomonow et al., 1996, 1998, 2002; Phillips et al., 1997; Knatt et al., 1995; Guanche et al., 1995; Stubbs et al., 1998). It is, therefore, a fair conclusion that most ligaments are also a sensory organ and a source of reflex arc to relevant muscles.

Several interesting issues were also revealed. All ligaments are innervated with the same four types of afferents; Golgi, Pacinian Corpuscles, Ruffini endings, and bare endings. Furthermore, in some ligaments these afferents are distributed homogenously throughout the length of the ligament, whereas in other ligaments most afferents are distributed near the two insertions of the ligament to the bone with otherwise poor presences in their mid-substance. For example, afferents are evenly distributed throughout the annular and transverse medial ligaments but near the insertions of the radial posterior and anterior ligaments of the elbow (Petrie et al., 1998).

Such findings give rise to several suggestions regarding the role of the ligamento-muscular reflex. One possibility suggests that if afferents are distributed only at the bony insertion of the ligaments, where the higher tissue stiffness results in less strain, the excitation threshold of the afferents will be elevated and the reflex will become active only at high strains/tensions. This may be at levels which pose a risk for ligament damage and then the reflexively recruited muscular activity may serve to reduce the strain/stress in the ligament by load sharing. Conversely, if a ligament is evenly distributed with afferents, that may indicate an ongoing service as a sensory organ for detection of angle, position, load, joint velocity, etc., e.g. kinesthetic sensing organ. This may also indicate an ongoing synergistic reflexive activation of muscles during movement.

The absence of Pacinian afferents in the radial collateral ligament of the elbow may emphasize its role as a high threshold strain detector or a nociceptive role where near injurious loads may directly trigger a reflex response from the muscles (Petrie et al., 1998), assisting in preventing injury.

3. Biomechanical functions

The biomechanical function of the reflex initiated by the ligaments was proposed by us to be that of a joint

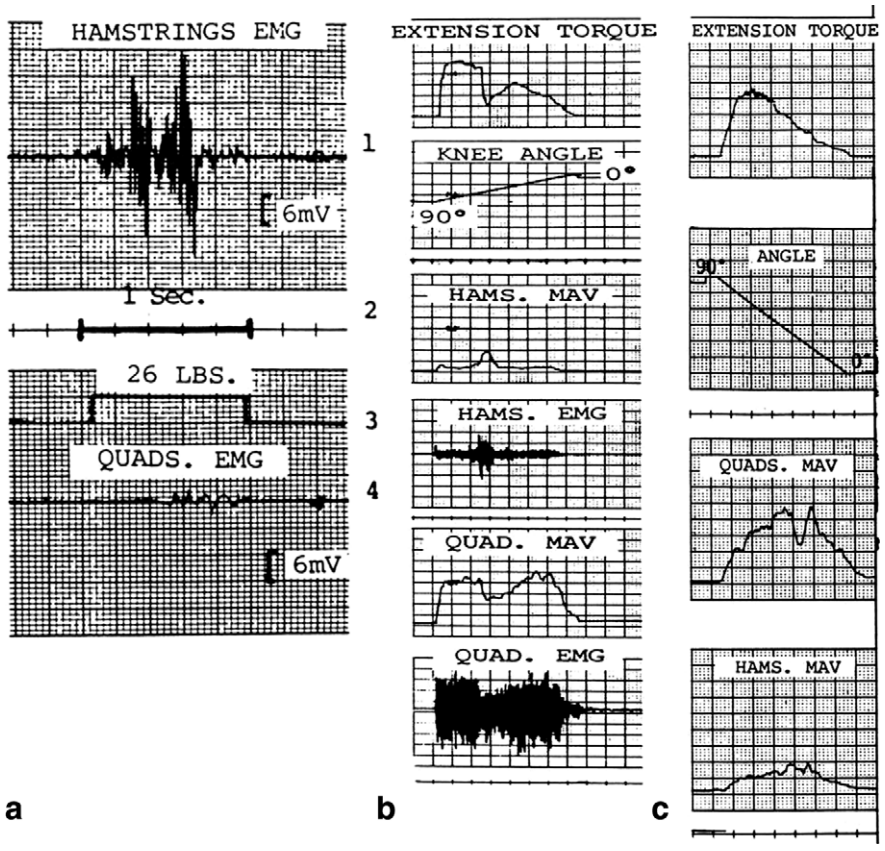

Fig. 1. (a) The substantial increase in EMG activity of the cat's hamstring (Trace 1) over 1 s duration (Trace 2) of direct load application (Trace 3) to the ACL. The quadriceps EMG (Trace 4) exhibits short initial low-level activity and then becomes inhibited for the duration of the ligament's loading. (b) Extension torque, knee angle, hamstring MAV (mean absolute value of the EMG) and EMG, and quadriceps MAV and EMG obtained from a patient with a midsubstance tear of the ACL. Note the large subluxation torque failure near 42°, which appears simultaneously with decrease in quadriceps EMG/MAV and increase in hamstring EMG/MAV, indicating the reflexive attempt of the muscles to correct the instability. (c) Extension torque, knee angle, quadriceps MAV, and hamstring MAV taken from an ACL deficient patient 2 weeks postarthroscopy. Note that the torque does not show any sign of failure, while the reflexive decrease in quadriceps MAV and increase in hamstring MAV do take place near 37° of flexion. The patient had abnormally tight hamstrings. Identical responses were obtained from subjects with hypertrophic knee muscles due to continuous participation in various exercise and sports activity.

stabilizer as well as the source of co-contraction which is so necessary for refined and controlled motion. Hirokawa et al. (1991, 1992) conducted a two stage study to assess the interaction of the thigh muscles, quadriceps and hamstrings, and the relative position of the distal femur and proximal tibia. Sequential X-rays of cadaver knee were taken while loading the quadriceps tendon at different loads and then applying loads to the hamstrings tendon simulating co-contraction, while the quadriceps were fully loaded as shown in Fig. 4. Small metal spheres embedded in the bones, as in the X-ray of Fig. 5a and b, served as markers that were analyzed geometrically. The study shows that anterior translation of the tibia was elicited in the range of motion of 60° flexion to full extension with quadriceps loading as shown in Fig. 6a. As the hamstrings were simultaneously loaded as shown in Fig. 6b, a substantial decrease in the anterior translation of the tibia occurred. It was clear, therefore, that the quadriceps can elicit instability and strain in the ACL due to anterior translation of the proximal tibia from 60° flexion to full extension, and that the hamstrings can substantially attenuate the anterior translation with just a few percent of co-activation.

We concluded that reflexive activation of the hamstrings as we observed in the feline and humans (Solomonow et al., 1987) could decrease the anterior translation of the tibia and decrease the tension in the ACL. This is specifically applicable for the range of motion from 60 degrees flexion to near full extension. In full extension both quadriceps and hamstrings could stiffen the joint and minimize instability, but without having direct impact on opposing anterior forces as was shown by Markolf et al. (1976, 1978) and Shoemaker and Markolf (1982).

4. Effects of velocity and training

Clear evidence was provided to explain the function of the ligamento-muscular reflex as a synergistic sensory-motor control scheme for maintaining joint stability, decreasing and/or preventing risk of damage to the

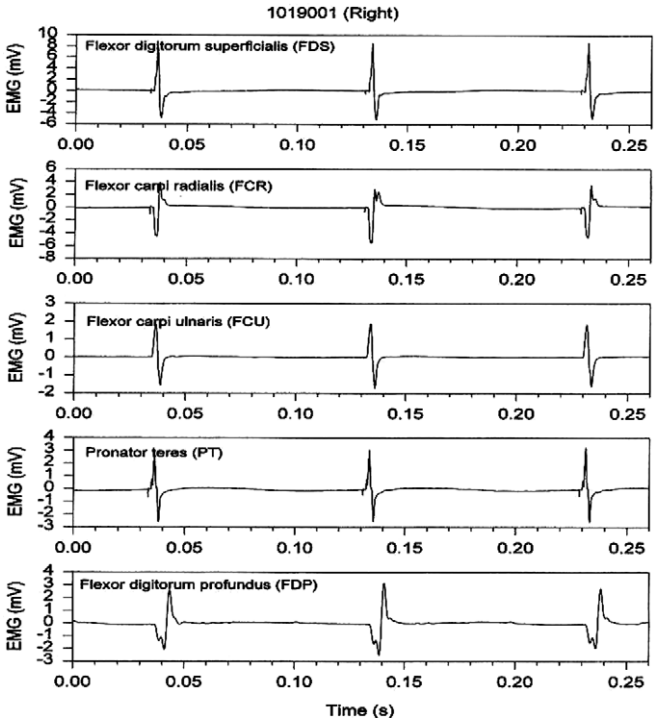

Fig. 2. Typical myoelectric discharge of the flexors digitorum superficialis and profundu, flexors carpi radialis and ulnaris, and the pronator teres in response to stimulation of the median articular nerve to the medial ligaments of the elbow.

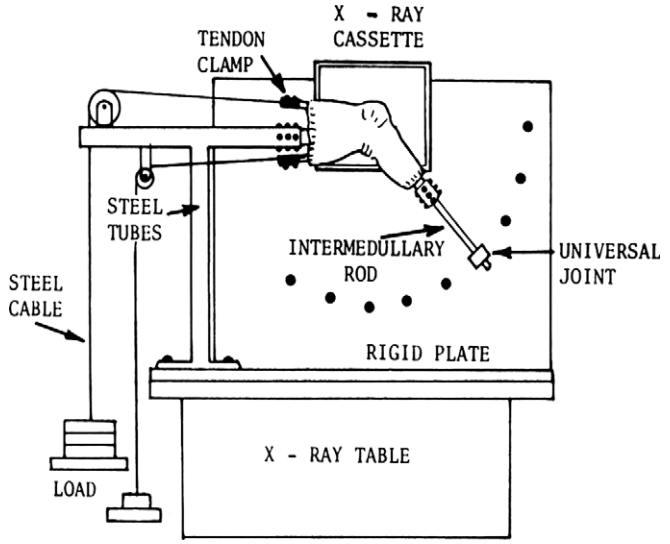

Fig. 4. Experimental apparatus constructed to fix the cadaver knee while permitting loading of the quadriceps and hamstring tendons and change in joint angle.

ligament via co-activation. In addition, one of the roles of ongoing co- activation during various types of joint movement was determined to be preserving joint stability in addition to allowing for joint acceleration, dynamic braking and smooth, controlled motion as shown in Fig. 7a

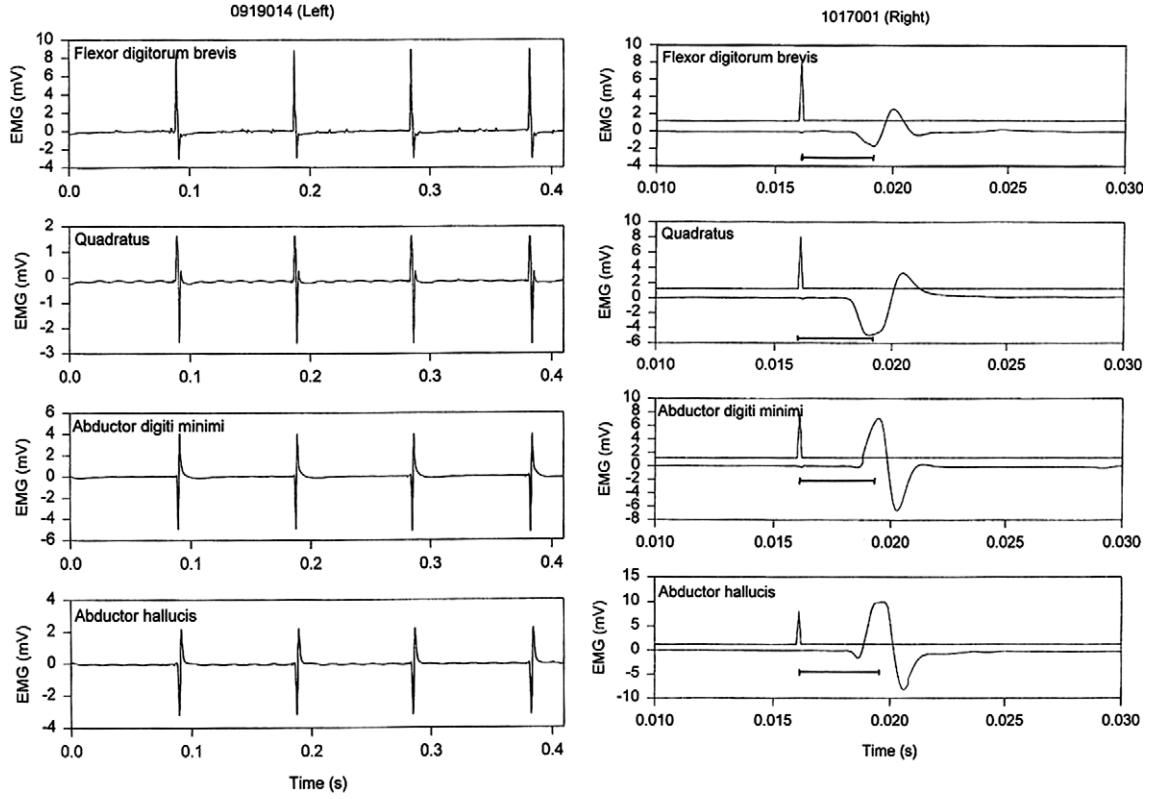

Fig. 3. (a) A typical EMG response of the four intrinsic foot muscles (FDB, Q, ADM, and AH) to a stimulus train of 10 pps. (b) A typical EMG response to one pulse showing the calculated time delay from the peak of the stimulus artifact to the peak of the resulting EMG.

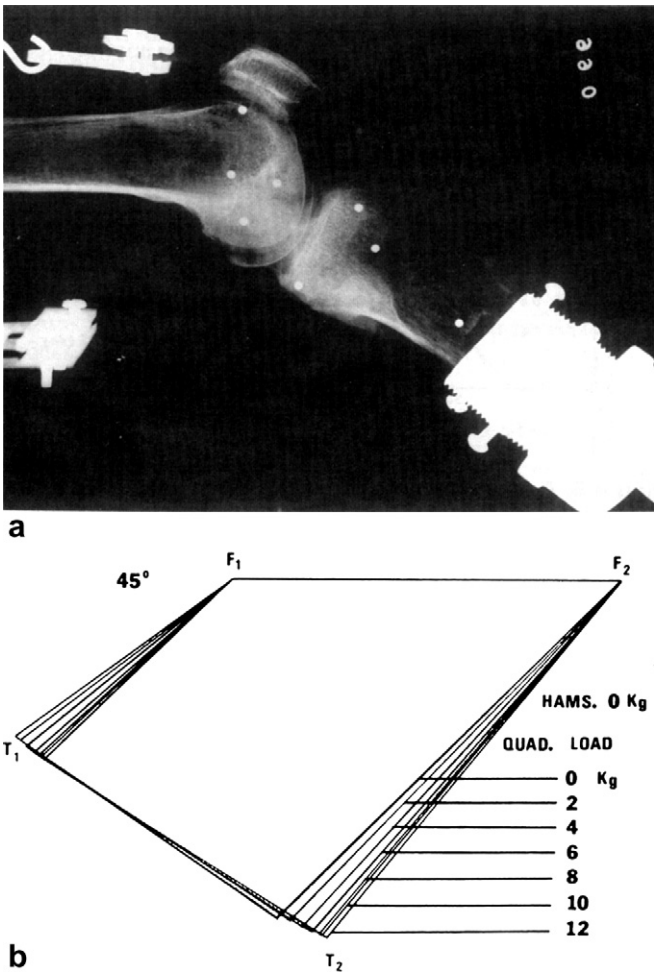

Fig. 5. (a) Typical radiograph of a cadaveric knee positioned at 45° of knee flexion. Note the four metal spheres in the femur and the four metal spheres in the tibia. (b) Seven sequential quadrangles generated from loading the cadaveric knee (set at 45° of flexion) from passive (no load) up to 12 kg load in the quadriceps tendon. Note the deformation of the quadrangle of the passive state in the anterior direction as the load is increased, pointing out the anterior displacement of the tibia. F_1, F_2, T_1, and T_2 correspond to points on the femur and tibia (see Fig. 3).

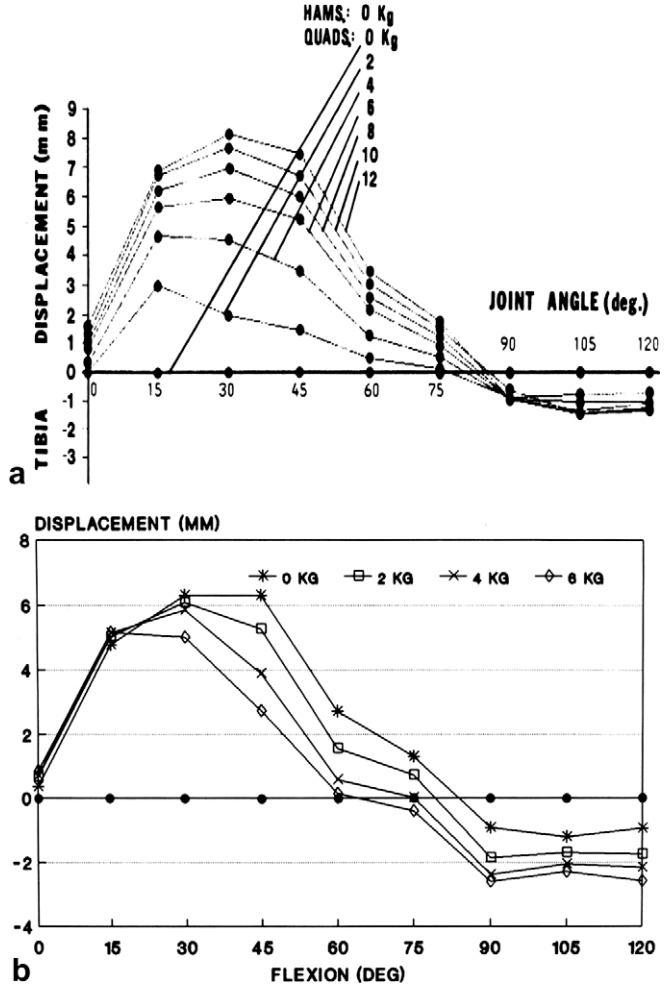

Fig. 6. (a) Anterior–posterior displacement of the tibia versus joint angle for various load levels in the quadriceps. The horizontal axis displays the data of the passive knee (no load). Positive displacement indicates anterior shift, while negative displacement indicates posterior shift. (b) Mean tibia displacement versus joint angle for constant 12 kg quadriceps load and simultaneous hamstrings loads of several magnitudes. Note decrease in anterior translation of the tibia as hamstrings load increases.

and b (Hagood et al., 1990; Solomonow et al., 1986, 1988, 1989; Baratta et al., 1988). While co-contraction allows for a measure of joint stability throughout normal motion, the triggering of the ligamento-muscular reflex can provide a fast dose of increase in joint stability when unexpected movement occurs, eliciting sudden increase in ligament tension. It is a protective reflex. We also demonstrated as seen in Fig. 8, that in athletes; jumping activity can decrease the hamstrings coactivation but that could be reversed by three weeks of hamstring retraining (Baratta et al., 1988).

Any protective reflex responding to a potentially damaging or risky stimulus must be a fast-acting one and generate forces in the appropriate muscles. Review of the studies we conducted on the ligamento-muscular reflexes in the elbow, knee, shoulder, ankle, and spine reveal a response time (or latency) ranging from 2.5 to 5 ms (see Fig. 3b for example). Considering the length of the nerves from the spine to the respective joints, a conduction velocity of 120 ms (for large afferents such as Golgi and Pacinian, Mountcastle, 1974) and a 0.5 ms for synaptic transmission, only a monosynaptic or bisynaptic reflex could be assumed. This may emphasize the importance of this reflex as a fast-acting, protective reflex, preventing damage to the ligament and potential risk to the joints.

So far it was shown that the ligaments of the major joints and the lumbar spine are equipped with sensory organs; that there are two patterns of the sensory organ distribution along the ligament with functional neurological implications; that a reflex arc exists from the sensory receptors to muscles associated with the respective joint and that the function of the muscular activation and co-activation is to unload the ligament from overload and prevent potential injury or damage.

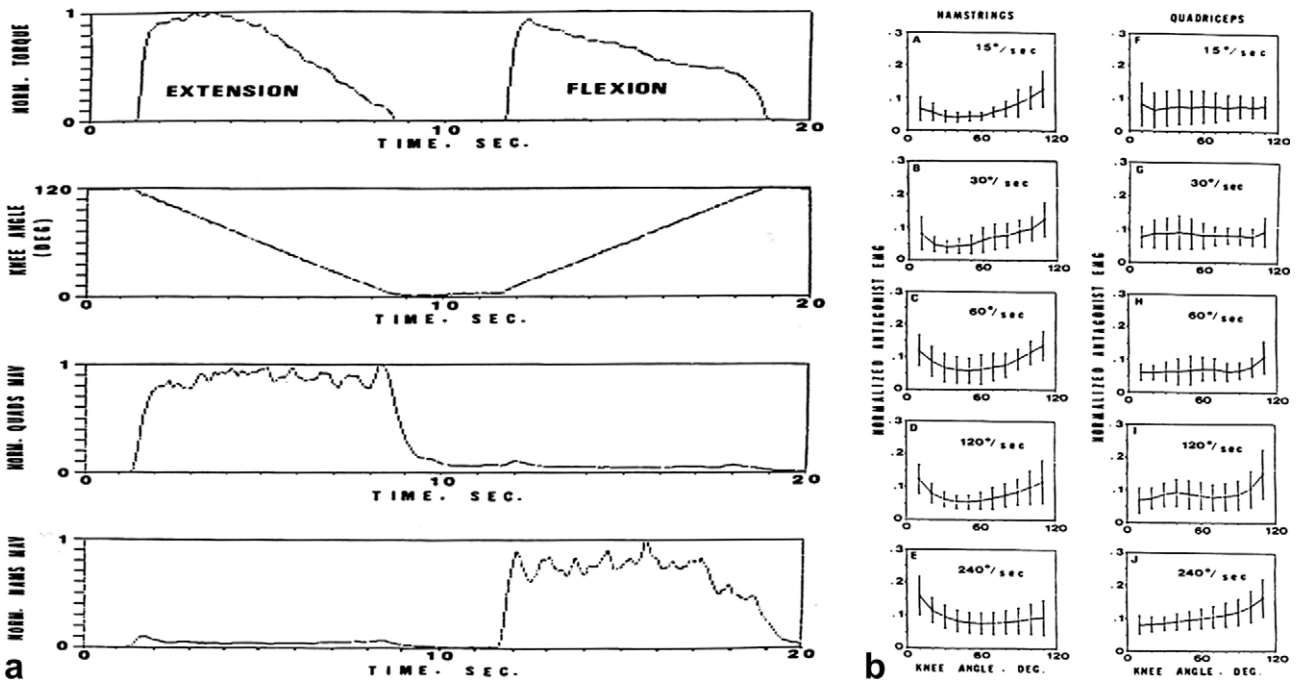

Fig. 7. (a) Typical recording of actual trial from one subject at isokinetic knee velocity of 15 degree/s. Traces show (from top to bottom) extension and flexion normalized torque, knee angle, normalized quadriceps MAV of its EMG during extension and flexion, and the hamstrings normalized MAV of its EMG during extension and flexion. Note that the quadriceps MAV during extension and the hamstrings MAV during flexion were nearly constant (despite the typical fluctuations at maximal force levels) throughout extension and flexion. (b) The antagonist coactivation patterns of the hamstrings (left column) and quadriceps (right column) are shown for increasing joint velocity as normalized antagonist EMG (MAV) versus knee angle. The plots are based on the data pooled from all subjects. The vertical bars indicate the standard deviation for each angle and the curve connects the mean value of the MAV value throughout the range of motion. Note the increase in hamstrings coactivation with increasing velocity just before full extension and decreasing coactivation at the initiation of the motion.

5. Neuromuscular neutral zones

Viscoelastic tissues, such as ligaments, have classical responses to elongation and tension which includes hysteresis and elongation rate dependence (Solomonow, 2004). Ligaments can display large elongations and relatively low associated tension when stretched slow. Fast rates of stretch, however, develop very high tensions that can result in severe damage (known as sprain) or rupture at relatively short elongations. Furthermore, when subjected to a stretch and release cycle, the length versus tension trajectory during the stretch is different than the trajectory during the release, e.g. hysteresis. These two mechanical factors are expected to have a substantial impact on the sensory-motor functions of the ligaments as expressed by the ligamento-muscular reflex.

The above issues were studied and reported in two reports (Eversull et al., 2001; Solomonow et al., 2001). We found that during a single sinusoidal stretch-release cycle of the supraspinous ligament, the reflex was initiated only after a certain length and tension were developed. The length–tension range prior to the triggering of the reflex was properly designated as a ''neutral zone'' indicating that small perturbation (1–2 mm) in the ligament length around its resting length are probably inconsequential for joint stability and do not require co-commitant muscular activation (see Fig. 9).

During the relaxation phase, the reflex disappeared at a different length and different associated tension, much larger than the length and tension thresholds observed during the stretch phase as seen in Fig. 9.

During the stretch phase, past the activation threshold of the ligamento-muscular reflex, the EMG gradually increased to the peak and then gradually decreased during the relaxation phase. It was clear that increasing length and tension in the ligament required an increase in muscular force in order to sustain joint stability. This emphasized the synergistic relationships of ligaments and muscles in maintaining that stability.

From Fig. 9, one can also see that as the frequency of the sinusoidal cycle increased from 0.1 Hz to 1.0 Hz, the length and tension thresholds of the reflex decreased (e.g. reflex was triggered earlier) during the stretch phase. During the relaxation phase, the length and tension thresholds increased (e.g. the reflex terminated earlier). Furthermore, as the stretch-release cycle frequency increased, the peak to peak EMG and its corresponding mean absolute value (MAV) increased as seen in Fig. 10, indicating that fast elongations of ligaments require much larger con-committant muscle force to maintain stability and minimize the potential risk of rupture. For fast ligament elongation, therefore, higher stiffness from the muscles protect the ligament from development of high tension and strain and potential rupture.

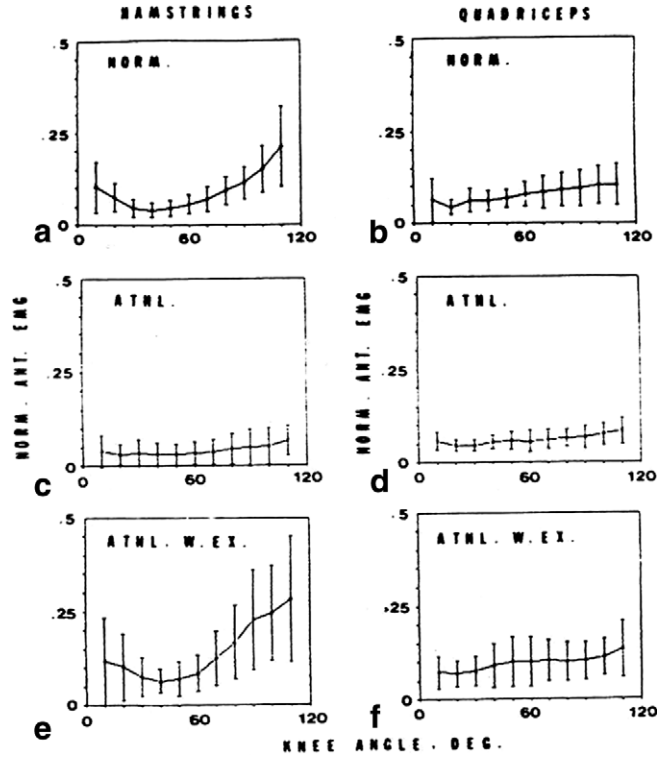

Fig. 8. The average normalized antagonist MAV versus knee angle for the hamstrings (a) and quadriceps (b) of normal subjects compared with the hamstrings and quadriceps MAV versus knee angle of verified athletes (c and d) and athletes who routinely exercise their hamstrings (e and f). The athletes had hypertrophied quadriceps, which resulted in inhibition of the hamstrings motor drive (EMG) when extension movement was performed (see c versus a and e). Quadricep coactivation patterns of normal subject group and athletes were nearly identical. The vertical bars at each data point represent the standard deviation from the mean of all subjects tested in that category.

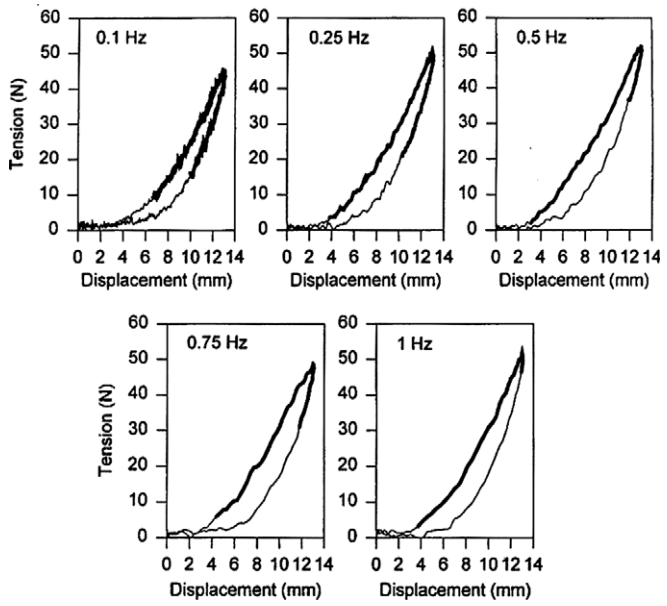

Fig. 9. Typical hysteresis curves where the tension versus displacement of a single cycle at each of the frequencies employed is shown; the period where the EMG was recorded from its initiation in the stretch phase to its termination in the release phase is designated in boldface on the curve.

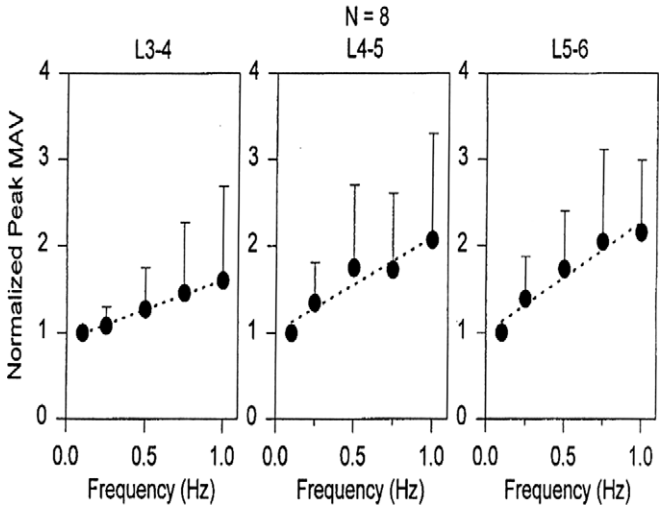

Fig. 10. The mean (±SD) of the peak MAV of the EMG is shown as a function of frequency, demonstrating that progressively stronger muscle contraction was associated with increasing cycle frequency.

Finally, when the ligament was exposed to continuous sinusoidal stretch-relaxation cycling, the reflex trigger thresholds increased and the termination threshold increased as well. The peak EMG amplitude decreased. In essence, prolonged exposure of ligaments to cycling stretch results in laxity and hysteresis accompanied with substantial decrease in the duration and magnitude of the reflexively activated muscular forces, exposing the ligament to increasing potential risk for injury. This was the early sign that prolonged cycling activity of ligaments is associated with risk of injury and/or a neuromuscular disorder, which will be fully addressed later.

6. Ligaments and the flexion-relaxation phenomena

Assessment of spinal function, as it relates to the lumbar region, in flexion-extension requires knowledge and ability to document the flexion-relaxation phenomena. This phenomena consists of active EMG recorded from the paraspinal muscles as anterior flexion begins. The EMG amplitude gradually decreases as flexion progresses and reaches a complete silence at or near 45– 50° flexion. The EMG silence persists through deep flexion and the initial range of extension. At mid-extension the EMG reappears and increases up to full extension (Ahern et al., 1988; Allen, 1948). The current understanding is that the upper body mass, when subjected to the effect of gravity, as it moves into flexion, requires counter resistance from the paraspinal muscles to prevent free collapse forward. As flexion progresses, the posterior ligaments (supraspinous, intraspinous, posterior longitudinal, and dorsolumbar fascia) elongate and develop tension. At some angle, in mid-flexion, the tension developed in the posterior ligaments exceeds the required counter force, allowing the muscles to relax. Further flexion is associated with contraction of abdominal muscles to overcome the increasing forces in

the posterior ligaments. Overall, the process is a load-sharing phenomena between posterior muscles, posterior ligaments, and abdominal muscles.

Since during flexion the posterior ligaments stretch, one would expect that the mechano-receptors within these tissues will be stimulated and trigger paraspinal muscles contraction to reduce the load in the ligaments. In fact, the opposite occurs; increased stretch in the ligaments during deeper flexion is associated with EMG silence. This immediately points out that perhaps the inhibitory component of the ligamento-muscular reflex is active in the flexion-relaxation process.

We conducted a series of experiments to assess the role and function of the ligamento-muscular reflex in the flexion-relaxation phenomena (Olson et al., 2004, in press, submitted for publication). In order to offset the effect of gravity, the same subject group was assesses while performing flexion-extension from erect posture and from the supine position (e.g. sit-ups). The results demonstrated that in the sit-up position, the flexion-relaxation in the paraspinal muscles disappeared and a similar pattern of activity (initial EMG activity and silence about the $\pm 90°$) was observed in the abdominal muscles. The conceptual conclusions point out the demand for dealing with the internal moments (generated by body mass and its orientation to the gravity vector) dictates the pattern of muscular activity in strength, timing and which muscles. From the reflexive standpoint, this is the first indication that the ligamento-muscular reflex is substantially modulated by the spinal and possible higher sensory and motor neurons of different systems (proprioceptive, vestibular, etc.) to yield excitatory or inhibitory responses. The mechanical requirements to execute the intended movement, therefore, are governing the ligamento-muscular reflex response pattern.

In the latest report (Olson et al., submitted for publication), passive flexion extension was executed with the aide of an active dynamometer. The dynamometer supported the body mass throughout the movement. Surprisingly, muscular activity was not observed in any of the anterior or posterior muscles. The results support the assertion made in the previous paragraph, e.g. there was no need to support internal or external moments (since the dynamometer took care of all movements), and the reflex did not trigger any muscular activity.

A tentative, and very fascinating, conclusion is that the ligamento-muscular reflex is much more complex than a hard-wired neurological process which triggers or suppresses muscles responses upon stretch of the ligaments. The reflex is governed by a complex neural network taking into account joint stability, internal mass and its implication in light of movement velocity and acceleration, orientation to gravity, etc.

Evidently, much is left to study on the interactions of the various components and internal or external factors associated with the ligamento-muscular reflex. It is not a simple reflex by any stretch of the imagination.

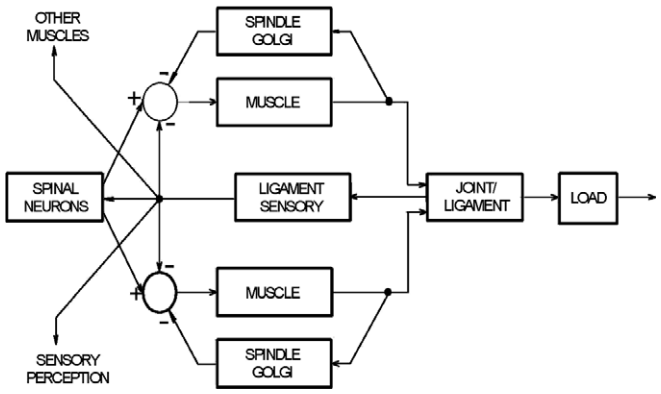

Fig. 11. A control diagram of the forward and feedback components of a joint including the muscles, ligaments, and spinal projections.

From the system viewpoint, one can draw the simplified diagram of Fig. 11 representing the interaction of ligaments and the motor control of a joint.

Reconsidering the mechanical properties of the ligaments; e.g. creep, tension–relaxation, hysteresis, etc. one can predict from the control diagram of Fig. 11 that several types of neuromuscular disorders can develop with time when performing occupational and sports activities. Similarly, an injury or rupture of a ligament could be assessed as a cause for a neuromuscular syndrome.

7. Clinical implications

Indeed, in the early 1980s, a large number of patients with anterior cruciate ligament (ACL) rupture underwent a surgical repair with a synthetic or autograft from part of the patellar tendon. In both cases, the initial results were encouraging, demonstrating a measure of restored stability in the knee. Overtime, however, it was observed that the implanted ligament became lax; that the quadriceps tended to atrophy in many patients; that muscular desynchronization due to the rupture could be restored with physical therapy, and that with time, the patients developed osteoarthritic knees. Overall, conflicting and misunderstood responses were accumulating, indicating that ACL injury is not an isolated deficit but most likely a complex syndrome.

With the help of Fig. 11, one can attempt to gain insight to the logical chain of events that were observed clinically.

1. Rupture of the ACL, even if repaired surgically, can leave a sensory perceptive (kinesthetic) deficit since the afferents in the ligaments are not functioning (ruptured or surgically removed). Indeed, Skinner and Barrack (1991) demonstrated that patients with ACL rupture demonstrated deficiency in kinesthetic perception; e.g. perception of the knee angle was deficient. Such a sensory deficit can be a harbinger of additional damage/injury to the knee when going up or down stairs, playing sports and performing occupational activities. Indeed,

many ACL deficient patients of that time were reporting with secondary knee injury incurred during demanding daily activity.

2. Quadriceps atrophy was commonly observed in ACL deficient patients. The natural response of orthopaedic surgeons and physical therapists was to subject the patient to a quadriceps strengthening program for several weeks to reverse the degeneration. Often, the patients with the now more powerful quadriceps were subjected to additional injury or increased episodes of instability.

   A part of the syndrome, quadriceps muscles at their normal strength can generate forces that increase anterior tibial translation and with the absence of an ACL also cause an anterior knee subluxation (Hirokawa et al., 1991, 1992). It seems that while the ligamento-muscular reflex in normal subjects excites the hamstrings in the range of motion from 60° flexion to full extension, it also inhibits the quadriceps muscles from exerting very large forces, preventing subluxation. The concept of muscular inhibition attracted little attention in the motor control field, but its implications are highly significant for joint stability. The quadriceps is apparently inhibited, in the normal subject, from generating its true maximal forces such that knee stability and overloaded ACL are prevented. In the ACL deficient patient the inhibition is substantially larger since the sensory ACL function is missing. In such conditions, even moderate quadriceps force in the range of 65° to full extension can subluxate the tibia. The weighted control of the ACL reflex seems to inhibit the quadriceps as necessary for the performance of the movement at hand. With its absence, however, deep inhibition occurs, probably via spinal networks. One can conclude that in addition to the excitatory reflex from ligaments to muscles, there is also an inhibitory ligamento-muscular reflex and that was shown in human subjects by Dyhre-Poulsen and Krogsgaard (2000), Solomonow and Krogsgaard (2001), Williams and Brance (2004), and Voigt et al. (1998). The overall objective of the inhibitory and excitatory ligamento-muscular reflex is to provide a stable and safe joint motion.

   The quadriceps strengthening program implemented in the period prior to 1987 was a contraindication as it increased the risk of sublaxation and the potential of new injury. In our report of 1987 (Solomonow et al., 1987), we concluded that hamstring strengthening is most beneficial in the early phase of ACL deficient patients rehabilitation, as it will increase the co-contraction level from the hamstrings, improve knee stability and allow increased force production from the quadriceps later on (Solomonow et al., 1989).

3. Muscular balance of the hamstrings and quadriceps, agonist and its antagonist, is therefore, one of the most important aspects in maintaining knee stability and preservation of the healthy, functional ACL. One important component in balancing an antagonist muscle pair of a joint is the sensory role of ligaments via their inputs to the spinal motor units in an excitatory and/or inhibitory mode.Indeed several groups managed to demonstrate that with an appropriate physical therapy program, advocating muscle re-education, ACL deficient patients could be successfully rehabilitated with conservative treatment (Giove et al., 1983; Steiner et al., 1986).

4. The implications of muscular imbalance or synchronization on the gait of patients with ACL damage was repeatedly reported in the literature (Hasan et al., 1991; Sinkjaer and Arendt-Nielsen, 1991), and increased quadriceps activity was observed in our research with normal subjects whose ACL was statically stretched and developed creep (Chu et al., 2003; Sbriccoli et al., 2005).

   In such circumstances, the ACL was intact, yet the laxity developed due to the creep prevented the mechanoreceptor within the ligament from properly firing at the appropriate threshold and inhibiting the quadriceps during maximal voluntary extension. It seems that rupture of the ACL, for example, can increase the inhibition imposed on a muscle, whereas stretched or lax ACL decreases the inhibition. The exact neural mechanism of the two phenomena may need further study, yet it is clear that the sensory-motor functions of the ligament plays a major role in both phenomena.

8. Neuromuscular disorders associated with ligaments

So far, neuro-muscular disorders associated with a complete rupture of a ligament: e.g. desynchronization of agonist – antagonist activity, changes in the natural inhibition of muscles, muscular atrophy, deficient kinesthetic perception and deficient gait were delineated.

In recent years we embarked on the assessment of neuromuscular disorders associated with an intact ligament, yet subjected to continuous activity such as found in many occupational and athletic environments. Indeed, in the occupational field, non-specific low back disorders/pain is one of the most common medical problems and is a costly problem from the standpoint of the loss of work, medical treatment, and cost to government and industry, etc. The diagnosis and treatment of such non-specific low back disorder or as it is also known as Cumulative Trauma Disorder (CTD) are poorly developed and/or understood (NAS, 2001).

The epidemiology, however, clearly establishes the relationship between static and repetitive (cyclic) work activities and CTD. Biomechanical or physiological validation of the epidemiology is lacking especially experimental validation.

A set of experiments imposing alternating periods of static and/or cyclic load on the lumbar supraspinous ligaments yielded a wealth of new information (Claude et al., 2003; Courville et al., 2005; Gedalia et al., 1999; Solomo-

now et al., 1999; Jackson et al., 2001; LaBry et al., 2004; Lu et al., 2004; Navar et al., in press; Sbriccoli et al., 2004a,b, 2005, in press; Solomonow et al., 2003a,b,c; Williams et al., 2000):

A. Substantial creep developed in the ligament within six periods of 10 min of load spaced by 10 min of rest. A continuous rest period of up to 7–8 h after the six work and rest sessions are not sufficient for the ligament to recover its original length and stress-strain condition. As seen in Fig. 12, the work periods display gradual decrease of reflexive EMG, spasms and cumulative creep. The long rest periods is characterized with initial hyperexcitability in muscle activity and very long recovery of the creep towards the return of the ligament to its original resting length and normal length–tension relationship. Several important issues should be addressed:
   - As the creep causes laxity in the ligament, the thresholds at which the ligamento-muscular reflex is triggered as well as kinesthetic perception change. The feedback signal (see Fig. 11), therefore, is corrupted and results in false perception and lower level activation of the muscles.
   - False kinesthetic or proprioceptive perception introduces errors in the precision of movements and may result in an accident or injury.
   - The decrease in muscular activity elicited by the ligamentous reflex also decreases the normal stiffness and stability of the lumbar spine, exposing it to increasing risk of injury.
   - The long recovery period (over 24 h) required to restore normal ligament operation renders the lumbar spine to prolonged function with decreased protective capacity and increased exposure to injury.

Therefore, an acute or transient neuromuscular disorder exists after a moderate work period during which an increased exposure to injury is present due to ligament laxity, reduced muscular activity and false sensory perception. The origin of this acute/transient disorder is in the creep/laxity of the ligament and its sensory-motor (neuromuscular) implications are due to the corrupt feedback signals from the sensory receptors within the ligaments.

B. It was also shown that several loading components have a critical impact on the development of an acute inflammation in the ligament.
   - Decreasing the rest period between each 10 min work session from 10 min to 5 min.
   - Increasing the number of repetitions from six to nine sessions.
   - Increasing the load from low or moderate to high load within the physiological range.
   - Increasing the work/load duration to sustained periods over 30 min.

All of the above factors elicit an acute inflammation in the ligament (Solomonow et al., 2003a). The neuromuscular component of the acute inflammation phase, observed 2–3 h after the load/rest session is a significant hyperexcitability of the musculature lasting for several hours. Since workers are required to return the work the next day, the

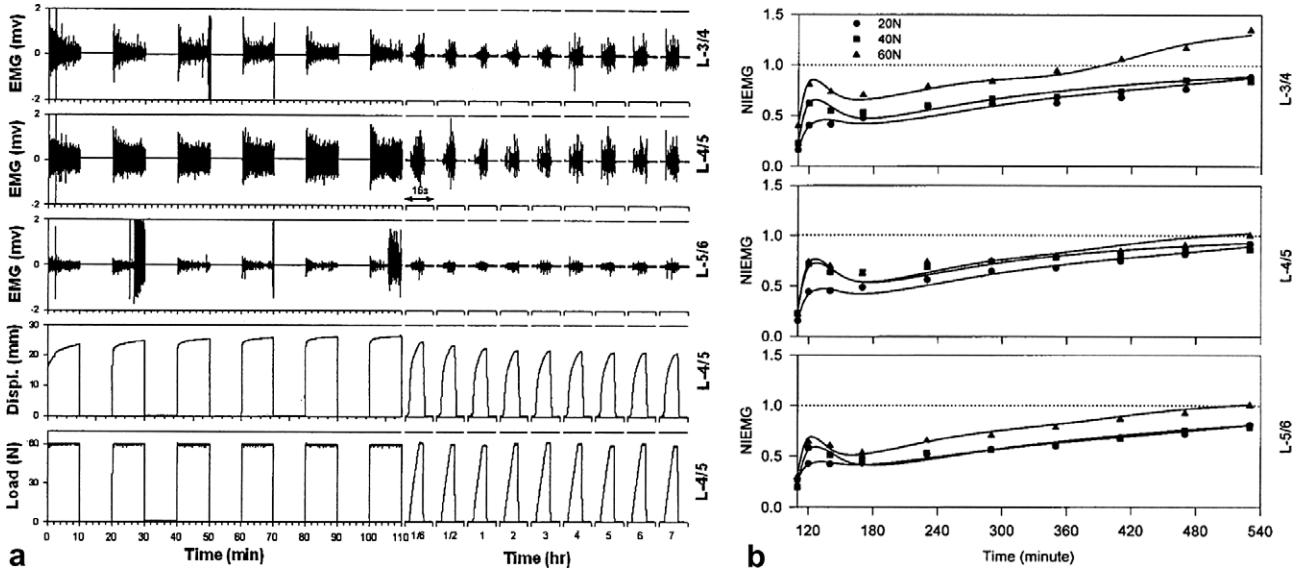

Fig. 12. (a) A typical recording of EMG from the L-3/4, L-4/5, and L-5/6 level (top three rows) as well as lumbar displacement and static load (bottom) recorded from one preparation subjected to a 60-N load. Note the large-amplitude spasms that are superimposed on the gradually decreasing EMG during different 10-minute static load periods. The time axis marked in units of hr. indicates the 7 h recovery period during which short samples of 12 s loading was applied to assess recovery of creep and EMG. (b) The mean NIEMG data and the developed models for the 7 h recovery period are shown superimposed for 20-, 40-, and 60-N loads. Note that the EMG for the 60-N load exceeds unity, indicating hyperexcitability development.

acute inflammation does not have sufficient rest period to heal the damage (micro-ruptures in the collagen fibers), the tissue is exposed to additional stretching and damage, and with continued exposure, develops chronic inflammation. In Fig. 13, samples of ligaments with inflammatory symptoms as evidenced by wide spread of neutrophils is compared to a control sample with few spontaneous neutrophils. The presence of neutrophils infusion in the ligament was always associated with a delayed hyperexcitability.

Chronic inflammation is not a medically treatable injury, is degenerative (results in conversion of ligament fibers to fibrous tissue) and is associated with pain, loss of muscular force (weakness), reduced range of motion of a joint and muscle spasms (Leadbetter, 1990). CTD is an overuse injury where the ligamentous tissues become chronically inflamed resulting in permanent disability (Leadbetter, 1990; Solomonow et al., 2003a).

Additional important observations were made. The work to rest ratio of 1:1 was observed to be a good rule to follow in order to prevent or attenuate the development of acute inflammation. This ratio, however, remained limited to durations of work and load up to 30 min (e.g. 10 min work: 10 min rest, 20 min work: 20 min rest, and 30 min work: 30 min rest). Tests at 60 min work and 60 min rest resulted in acute inflammation. Long work periods cannot be implemented without avoiding damage even if equal duration rest is allowed.

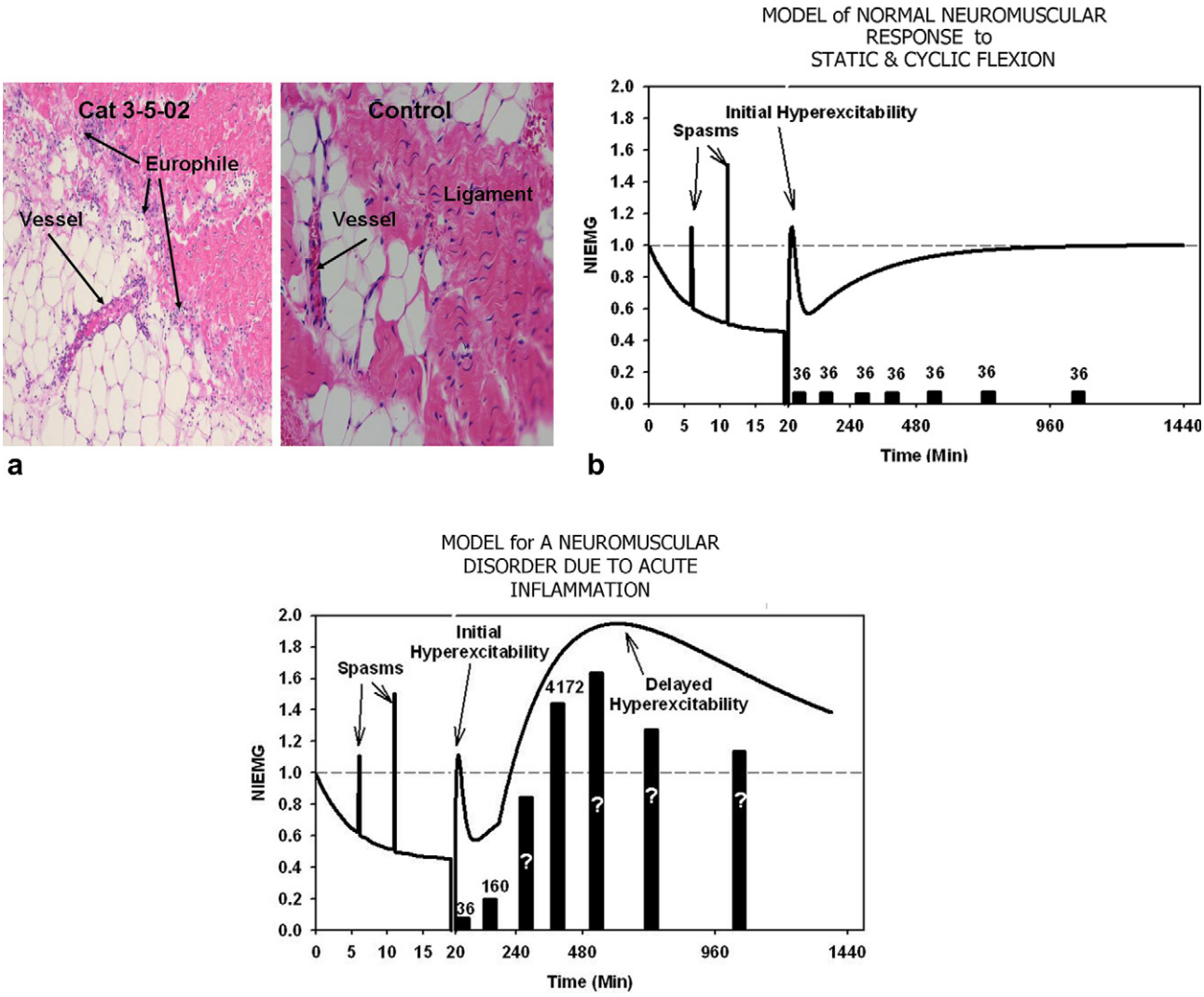

Fig. 13. (a) On the right is a slide showing the density of neutrophils in a ligament from the control group, not subjected to creep. Only spontaneous neutrophils appear. On the left is a slide showing the neutrophil density in a ligament subjected to overstimulation. The density is over 4000/mm^2 as opposed to 36/mm^2 in the control ligament. Note the higher magnification on the right slide. (b) A graphical presentation of the neuromuscular disorders model in a case where the risk factors load, load duration, load to rest ratio and repetitions were below the risk level. Note that during the recovery phase the NIEMG slowly recovers to its normal while the neutrophil density remains low and steady. (c) A graphical presentation of the neuromuscular disorder in a case where the risk factors exceeded the risk threshold triggering a delayed hyperexcitability associated with acute inflammation as expressed by the simultaneously rising neutrophil density in the ligaments. The question marks indicate time segments for which data is collected currently whereas the completed data is given by the number of neutrophils per mm^2.

An acute neuromuscular disorder associated with the creep of the ligament over time is therefore present and consists of reduced muscular activity as work goes on (and decreased spinal stability), development of spasms and the micro-fractures in the collagen fibers increase, significant increase in muscular activity 6–7 h after the work is completed and its association with acute inflammation. Such an acute neuromuscular disorder is the first step leading to chronic inflammation, and this phase should be avoided in any work or sports activity where a few days rest cannot be allowed. The long-term implications of inflammation and the associated neuromuscular disability are currently under intense investigations in our laboratory.

9. Model of neuromuscular disorder

Based on the large number of experiments on the spinal ligamento-muscular response to static and cyclic loading (or flexion-extension) we developed a model that can predict the neuromuscular response to a set of work and rest sequences. From the model, a determination could be made if a delayed hyperexcitability is present and in turn an acute inflammation. The model, therefore, can be useful in the assessment of risk factors (load magnitude, load duration, rest duration, load to rest duration ratio and loading repetitions) or their absence in a given work protocol. Safe work protocols could be designed also using the model.

The choice of the model was based on the physiological and biomechanical properties of the tissue in question, e.g. the ligament. It is well established as a viscoelastic element with responses accurately estimated by exponential equations. During lumbar flexion-extension or knee flexion-extension, the overall response is not that of a single ligament but that of several ligaments, the cartilage, capsule and in the spine also the discs and facet capsules. These different collagen tissues are all viscoelastic, yet the proportion of viscosity and elasticity is different in each one. The disc, for example, contains gel, a fluid, in its internal space, and therefore is more viscous than the supraspinous ligament or the longitudinal ligaments. A good model, therefore, should include bi or tri exponential components to describe the viscoelasticity of each of the various collagen tissues in order to provide accurate output (Solomonow et al., 2000).

The original model (Solomonow et al., 2000), therefore, included bi-exponential description of the displacement of the lumbar spine due to static or cyclic flexion. One component was utilized to describe the exponential elongation/deformation due to fibrous collagen tissues such as ligaments, facet capsule, dorsolumbar fascia, etc. whereas the second component was used to describe the exponential deformation of the lumbar discs which contain significantly more viscosity. The two components are exponential, yet the time constants and coefficients are largely different. The constructed model was successfully used to describe experimental data with high accuracy.

Furthermore, since the reflexive EMG was elicited by the deformation of the viscoelastic tissues, it was assumed to follow its deformation pattern; e.g. exponential decrease. That was executed, also with high accuracy. However, one issue that deteriorated the accuracy of the EMG model was the spontaneous, unpredictable spasms that occurred during the loading periods and also during the following recovery. Since the spasms varied widely in their amplitude and appeared at any time during loading without any predictable pattern, it is impossible to model this phenomenon. The spasms being superimposed on the predictable decrease of reflexive EMG due to viscoelastic deformation introduced an unavoidable inaccuracy in the model, yet allowed the general pattern of the EMG to emerge fairly clearly.

Therefore, the model developed provides good estimates of the deformation of the viscoelastic tissues during the development of creep and its recovery with rest. Similarly, the reflexive muscular activity was estimated well during the loading and rest periods. The spasms, however, should be distinctly noted but lacked representation in the model.

In our model, we simplified the equation in order to obtain a general conceptual behavior of the ligamento – neuromuscular responses. Yet, the accuracy can simply be optimized if one wishes, just by adding additional components representing the tissues at hand.

Model: The model considered is based on our previous work where continuous 20-minute static load was followed by a 7-hour recover period (Solomonow et al., 2000, 2003d; LaBry et al., 2004; Courville et al., 2005; Claude et al., 2003).

The Normalized Integrated EMG (NIEMG) during the cyclic loading period was described by Eq. (1) as follows:

$$\mathrm{NIEMG}(t) = A\mathrm{e}^{-t/T_1} + \mathrm{NIEMG}_{ss} \tag{1}$$

where NIEMG_{ss} is the steady state amplitude, A the amplitude of the exponential component, T_1 the time constant of the exponential component, and t is the time.

Correspondingly, the NIEMG during the long-term recovery was modeled by the following equation as:

$$\mathrm{NIEMG}(t) = tB\mathrm{e}^{-t/T_2} + E(1-\mathrm{e}^{-t/T_3}) + C(t-T_\mathrm{d})\mathrm{e}^{-(t-T_\mathrm{d})/T_4} + \mathrm{NIEMG}_{ss} \tag{2}$$

where B, C, and E are the amplitudes of the three terms; $tB\mathrm{e}^{-t/T_2}$ represents the initial hyperexcitability, which decays within one hour while reaching its peak in the first 10 min; $C(t-T_\mathrm{d})\mathrm{e}^{-(t-T_\mathrm{d})/T_4}$ represents the delayed hyperexcitability; this term is initiated during the rest period, mostly after the second hour of rest, with no effect in the first 2 h; $E(1-\mathrm{e}^{-t/T_3})$ represents the steady state recovery; this term is a slowly rising exponential throughout the rest period; T_d the time delay associated with the initiation of the delayed hyperexcitability; and NIEMG_{ss} is the steady state amplitude as defined in Eq. (1).

In order to convert Eqs. (1) and (2) to describe a series of work periods spaced by rest periods; two new components are defined:

T_W is the time period over which load was applied to the spine.

T_R is the period of rest between any two work periods (T_W).

n is the number of work periods.

Eq. (1) describing the NIEMG behavior during each of the work periods is rewritten as Eq. (3):

$$\mathrm{NIEMG}(t) = A_n \mathrm{e}^{\frac{-[t-n(T_W+T_R)]}{T_{n_1}}} \Bigg|_{n(T_W+T_R)}^{(n+1)T_W+T_R} + \mathrm{NIEMG}_{ss} \quad (3)$$

It was assumed that A and $\mathrm{NIEMG}_{ss}$are not constant throughout the work/rest periods and are changing from one work period to the next.

Furthermore, it was assumed that T_1 might not be the same for all the work periods.

Since this study uses only 10 min of rest, the first transient component of Eq. (2) will be dominant and the steady state component contribution as well as the delayed hyperexcitability term could be neglected for this particular case. During the rest periods, therefore, the modified Eq. (4) is as follow:

$$\mathrm{NIEMG}(t) = (t-[(n-1)T_W+nT_R]) \times B_n \mathrm{e}^{\frac{t-[(n+1)T_W+T_R]}{T_{n2}}} \Bigg|_{(n+1)(T_W+nT_R)}^{(n+1)(T_W+T_R)} + \mathrm{NIEMG}_{ss} \quad (4)$$

It was also assumed that the amplitudes of NIEMG_{ss} and B will vary from one rest period to the next and that T_2 may vary as well. The graphical representation of the model after being subject to non-inflammatory and inflammatory workloads is shown in Fig. 13b and c, respectively.

Similarly, the equation describing the development of displacement, a reflection of creep of the viscoelastic tissue, during a series of work periods spaced by rest periods is given by the following equation:

$$\mathrm{DISP}(t) = \left[D_{0n} + D_{Ln}\left(1-\mathrm{e}^{-\frac{[t-n(T_W+T_R)]}{T_{n5}}}\right)\right] \Bigg|_{n(T_W+T_R)}^{(n+1)T_W+nT_R} \quad (5)$$

where DISP(t) is the displacement as a function of time, D_{0n} the elastic component of amplitude, D_{Ln} the viscoelastic component of amplitude, and T_{n5} is the time constant governing the development of creep during flexion.

The recovery of the displacement during the rest periods is described by the following equation:

$$\mathrm{DISP}(t) = \left[D_{0n} + R_n + (D_{Ln}-R_n)\mathrm{e}^{-\frac{t-[(n+1)T_W+nT_R]}{T_{n6}}}\right] \times \Bigg|_{(n+1)T_W+nT_R}^{(n+1)(T_W+T_R)} \quad (6)$$

Such that R is the residual creep at the end of each rest period and T_{n6} is the time constant governing the recovery of creep in each rest period.

Again, D_0, D_L, and R were assumed to be a variable from one work/rest session to the next. T_{n5} and T_{n6} were also assumed to vary from one session to the next.

The long-term recovery after the work/rest session was modeled by Eq. (2).

Once the mean ± SD of the experimental data were calculated, attempts were made to generate the best fit models described above using the Marquardt–Levenberg non-linear regression algorithm; in some cases, the algorithm failed to converge satisfactorily; in these cases, initial and/or final values were arrived at by sequential recursive iteration, optimizing for regression coefficient.

10. Verification in human subjects

The research conducted on CTD development was carried out on the feline. Two distinct projects were conducted using human subjects in order to confirm that such neuromuscular disorders can be elicited in humans from the same or similar mechanical inputs (e.g. high loads, high number of repetitions, short rest, etc.). One project examined the responses of the lumbar paraspinal muscles to periods of static and cyclic flexion (Solomonow et al., 2003a; Olson et al., in press). The second project assessed the response of the ACL of human subjects to static and cyclic loads (Chu et al., 2003; Sbriccoli et al., 2005).

Spasms in the muscles and significant changes in muscular synchronization was observed after static and cyclic activity of the spine and the knee (see Figs. 14 and 15) confirming the development of an acute disorder. For safety purposes, the work or load was limited to mild exertion or short duration, yet it is evident that adverse functional changes are elicited.

The results in both projects reveal that similar response to those obtained in the feline are observed from normal, healthy subjects subjected to mild static or cyclic (repetitive) activity. Furthermore, similar behavior could be obtained from the ligaments of the lumbar spine and the ACL of the knee.

Recently, additional confirmation that static and cyclic lumbar flexion in humans elicits a neuromuscular disorder similar to those depicted in the feline model were reported by Granata et al. (2005), Rogers and Granata (2006), Dickey et al. (2003), Kang et al. (2002), McGill and Brown (1992), and Shultz et al. (2004).

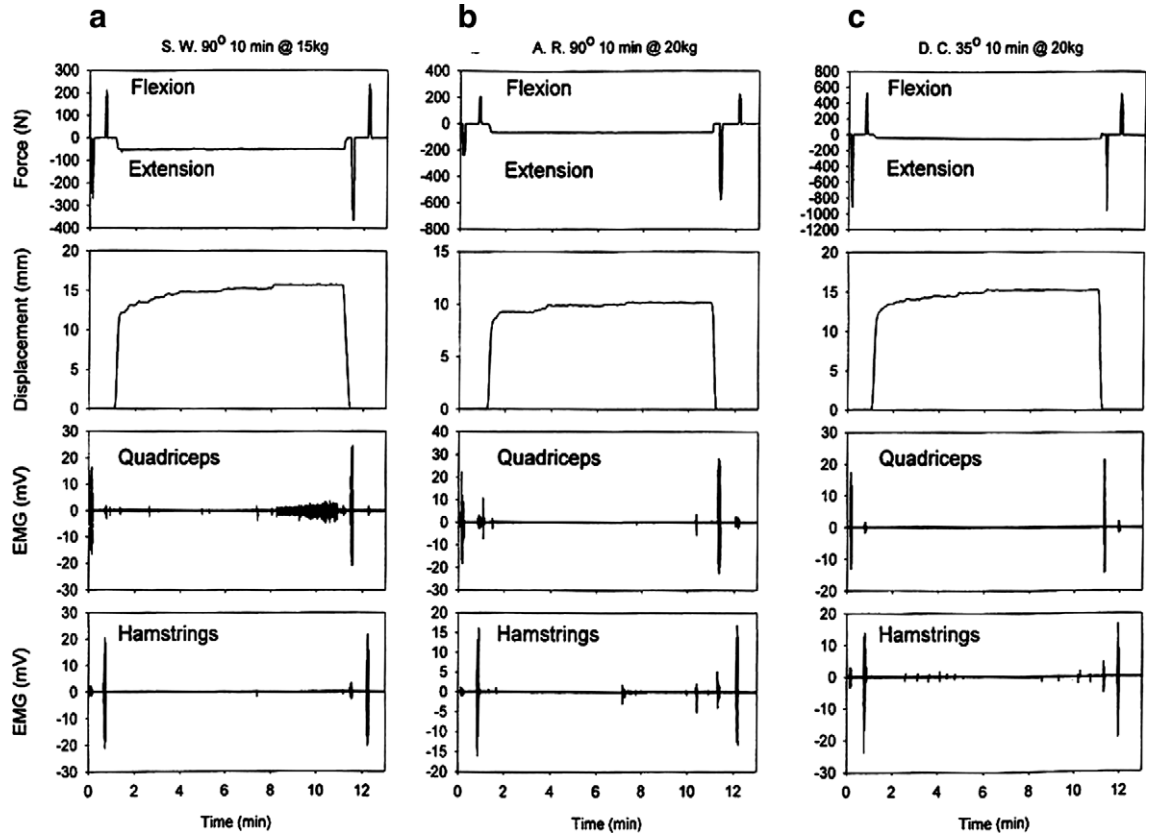

Fig. 14. (a–c) Three typical recordings from three different subjects at 90° and 35° knee angle showing the extension and flexion MVC forces before and after the 10 min loading session (top trace), the anterior displacement of the tibia during the 10 min loading period (second trace from top), quadriceps EMG (third trace) and hamstring EMG (bottom trace). Note the strong continuous burst of spasms in the quadriceps EMG trace of (a) from the 8th minute to the 11th minute. Similarly, in (b), two bursts of spasms are seen, one at about the 7th minute and the second just after the 10th minute, with a corresponding spasm in the quadriceps. IN (c) short bursts of spasms are seen in the hamstrings EMG throughout the 10 min loading period. Note the large increase in quadriceps force at MVC (negative peak) after the 10-minute period of loading the ACL.

11. Translational research – clinical applications

As most research, the ultimate benefit of many years of wondering in the different highways and alleyways of basic and applied medical investigations is some modicum of practical improvement of medical care offered to the patient population, and the associated improvement of the patients lifestyle. Preventive measures are also significant and beneficial.

The lesson we learned so far tells us that in order to maintain knee stability, weighted posteriorly directed force has to be applied to the tibia in the appropriate range of motion. Such a force comes from the ACL in the intact human in the range of motion of 60° flexion to near full extension. Furthermore, such force is not coming exclusively from the ACL, but also from the hamstrings via the ACL-hamstrings reflex. In the ACL deficient patient, the ACL tension is absent and so is the contribution of the hamstrings. In order to allow as close a function to normal as possible, any external device, e.g. orthosis, needs to supply such forces.

In 1983, we surveyed the available knee braces to ACL deficient patients as well as the literature evaluating them. It was clear that most braces consisted of thigh/calf uprights and a knee joint with some connecting members or straps. A posteriorly directed force in the appropriate range of motion was not provided by the braces and the literature evaluating the braces confirmed that they had little impact, if any, on knee stability as required.

We developed a new knee brace (US Patent No. 4,781,180) which incorporated mechanical programmable bilateral levers connected to an anterior retaining strap placed over the proximal tibia as shown in Fig. 16a. The mechanical programming was provided by the knee joint such that at near 60° flexion the levers were activated and developed a constant or gradually increasing posteriorly directed force to the proximal tibia throughout full extension. This ''Smart Brace'', therefore, provided the knee with a similar function of the absent ACL.

In its commercial phase, the ''Smart Brace'' was available from the Bledsoe Brace System (Grand Prarie, Texas) and was consequently evaluated by Acierno et al. (1995). It was found, as shown in Fig. 16b, that ACL deficient patients could generate isokinetic maximal voluntary extension effort throughout the full range of motion with significantly increased quadriceps activation and without

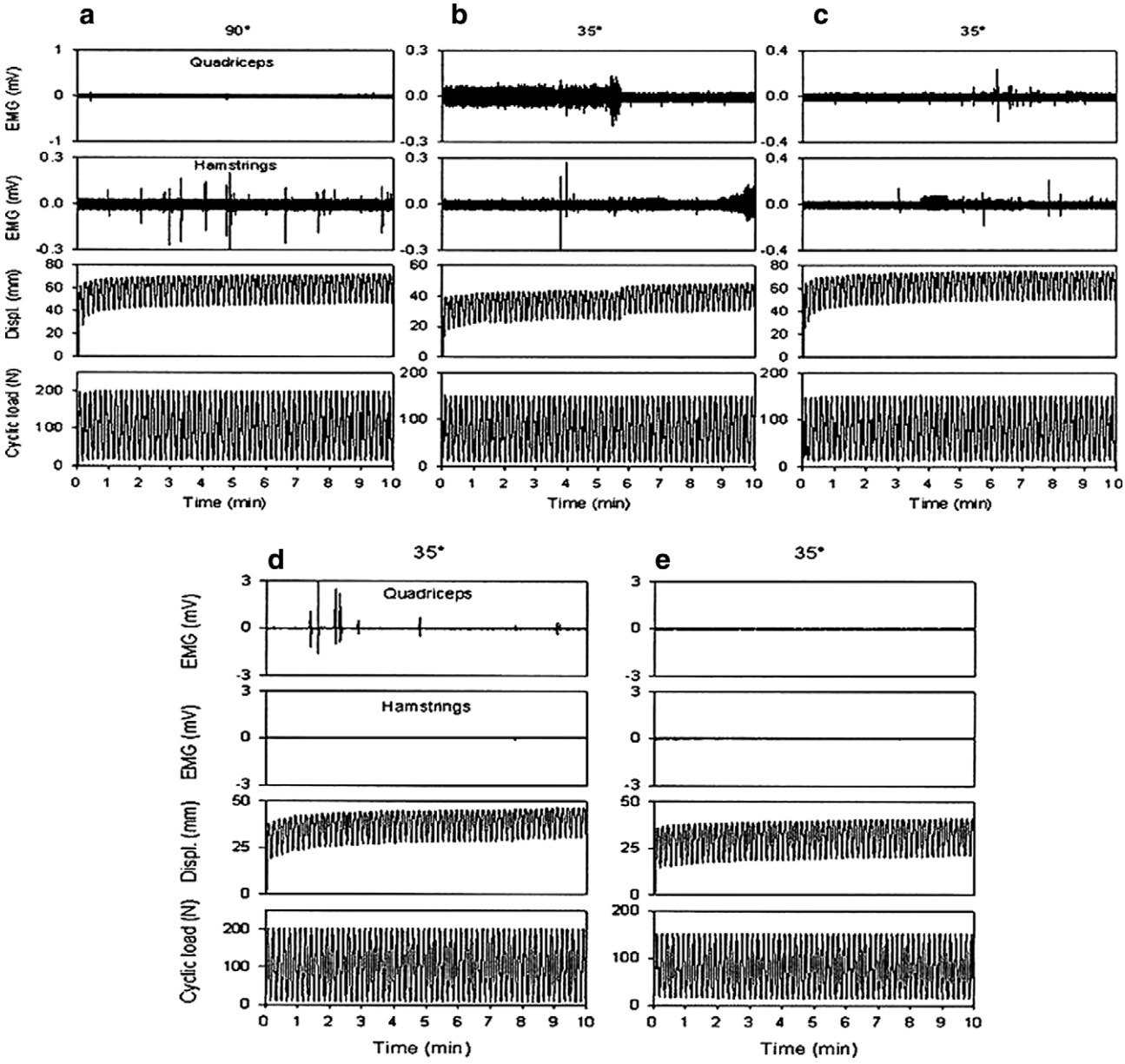

Fig. 15. (a–e) Five typical recordings from five different subjects exposed to cyclic loading of the ACL for 10 min at 90° and 35°. IN the top 2 traces, the EMG recordings from quadriceps and hamstrings during the 10-minute cycle are shown. The two bottom traces represent the anterior tibial displacement and the cyclic load, respectively. Note the presence of EMG spasms in both the quadriceps and hamstrings (a–d). An example with no reflex EMG activity is also reported (e). Displ, displacement.

episodes of knee subluxation. A noticeable decrease in hamstrings co-activation was also noted, as it was not required. The "Smart Brace" found wide acceptance in clinics around the world and performed well, especially in the post-injury period and in daily life of patients with chronic episodes of knee subluxation secondary to ACL rupture.

One of the limitations of knee braces made of metal, plastic or composite materials is that their weight is applied to an inverted cone, the thigh. During activity, gravity tends to cause gradual migration of the brace to the lower leg and reduction in its effectiveness. One approach to prevent this problem is the tightening of the attachment straps to the limb. This, however, applied excessive pressure to the skin and occluded circulation resulting in discomfort and pain within a short duration of use.

A second generation of the "Smart Brace", an electronic version, was consequently developed and applied (US Patent No. 5,628,722). The new version consisted of a light weight elastic sleeve worn over the knee. A miniature electronic sensor monitored knee angle and triggered a muscle stimulator to deliver weighted activation of the hamstrings via surface electrodes incorporated in the elastic sleeve. The posteriorly directed force to the proximal tibia was delivered this time by the hamstrings which were activated in the desired range of motion. The results to date

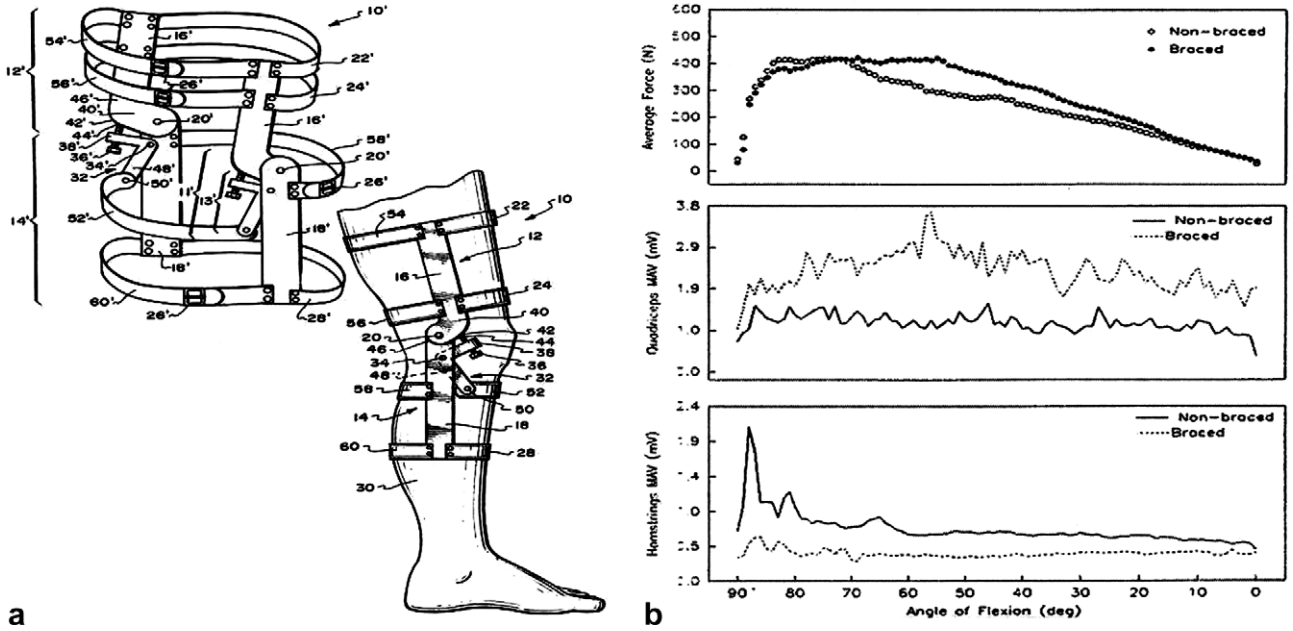

Fig. 16. (a) A schematic of a "Smart Brace" which generates a function similar to that of the ACL in the proper range of motion. (b) Average results from four trials for a symptomatic subject showing average force (top trace), quadriceps MAV, and hamstrings MAV (third trace) also as a function of joint angle. Note the increase in quadriceps MAV and the decreases in hamstring MAV when the brace is worn, demonstrating a return to normal muscle function due to the use of the brace.

demonstrate that the triggered coactivation of the hamstrings could be adjusted as necessary for the condition and convenience of the patient while preventing knee subluxation. An additional finding demonstrated that within a few days of use, a muscle re-learning occurs, with the spontaneous hamstrings coactivation is elevated to prevent subluxation even if the "Smart Brace" is deactivated (Fig. 17).

Similar conditions exist in workers engaged in repetitive (cyclic) or static activities of the lumbar spine. The ligaments and other viscoelastic structures of the lumbar spine become stretched or lax after a period of activity and the afferents within the tissues generate a significantly decreased or corrupted stimulus for activation of the ligamento-muscular reflex. The muscular activity which maintains lumbar stability decreases or becomes absent leaving the spine exposed to injury. A lumbar "Smart Brace" was

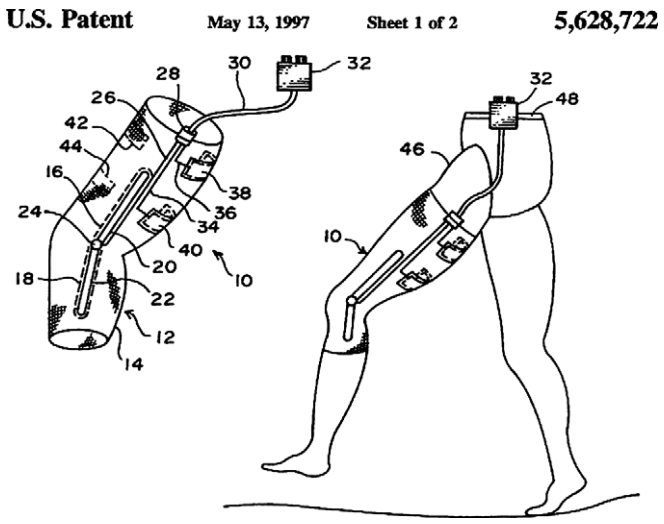

Fig. 17. A schematic diagram of the electronic version of the "Smart ACL Brace" where a sensor about the knee joint triggers surface stimulation of the hamstrings to prevent excessive anterior translation of the tibia and subluxation.

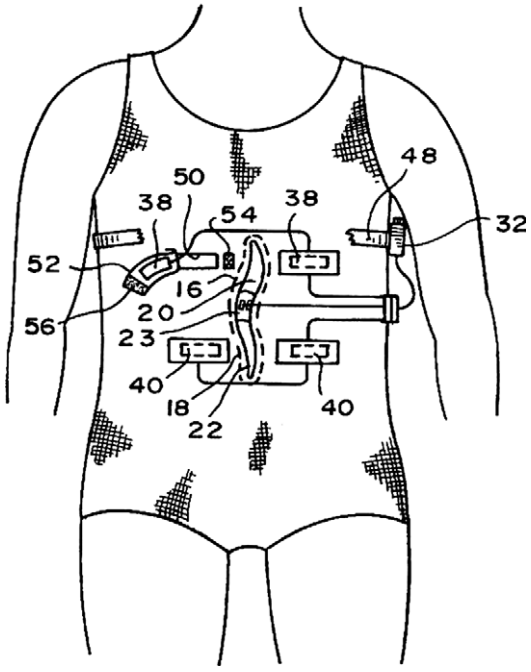

Fig. 18. A schematic of a lumbar electronic "Smart Brace" restoring muscular forces lost due to creep/laxity of the ligaments.

developed (US Patent No. 5,643,329) (see Fig. 18) and is in the stage of evaluation. The brace consists of an elastic garment commonly worn for dance or sport with miniature sensors over the lumbar spine. A muscle stimulator is activated by the sensors and the stimulus delivered via surface electrodes over the bilateral paraspinal muscles. The muscles contract in a weighted mode in the appropriate range of motion as we identified in the studies exploring the flexion-relaxation phenomena (Solomonow et al., 2003a; Olson et al., 2004, in press).

12. Conclusions

Ligaments are not passive tissue. From the sensory standpoint and from their sensory-motor function, ligaments are highly dynamic and non-stationary, yet predictable important organs. The inherent structure of ligaments and their response to static and cyclic loads, as found in work and sports activities, allow us to predict non-stationary behavior as expressed by creep, hysteresis, tension–relaxation, etc. These responses in turn, diminish activity of sensory perception and reflexive coordination of muscular activity such as excitation and inhibition and consequently reflect adversely on joint stability and movement.

The same stimuli or inputs can adversely affect the ligament when applied for long duration, large loads or repetitively without sufficient rest to result in an acute inflammation and its associated acute neuromuscular disorder. The acute disorder is the first stage, if not allowed to resolve with sufficient rest, of a chronic disorder which is devastating and non-reversible, inflicting misery and losses to society.

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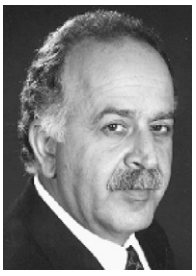

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IDEAS AND TECHNICAL INNOVATIONS

How old is your cervical spine? Cervical spine biological age: a new evaluation scale

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Abstract
Purpose This article aims at presenting a scale that, through the analysis of MRI images, clearly charts the various degenerative stages of the cervical spine and establishes its biological age. We have created this scale by summing together various scores linked to a selection of parameters according to which MRI images are analyzed.
Method We examined 423 cervical spine MRI scans, belonging to patients who had been admitted to the Medical Imaging Service of the Military Hospital of Rome between January 2010 and July 2011. We selected 6 parameters for the analysis of the MRI scans of the cervical spine: (1) the degeneration of the intervertebral discs, (2) the degeneration of the yellow ligaments, (3) the degeneration of the vertebral bodies, (4) the possible presence of spondylolistheses, (5) the presence or absence of foraminal stenosis, and (6) the diameter of the spinal canal. We assigned to each parameter a score system based on a graduated scale. The cervical spine physiological age can be determined by summing up the scores obtained for each parameter.
Results We submitted the data obtained from the study to a statistical enquiry. The results of the enquiry confirmed the suitability of the parameters selected for the evaluation of the aging process of the cervical spine.
Conclusions The effectiveness of the various treatments for cervical spine degenerative disorders is influenced by the overall anatomical conditions of the cervical spine. Up until now there has been no objective criterion for the evaluation of these anatomical conditions. We believe that this scale will be a useful tool to homogenize retrospective studies and to correctly set up prospective studies on the degenerative conditions of the cervical spine and relative treatments.

Keywords Biological aging · Cervical spine · Spinal disease · MRI · Intervertebral disc · Myelopathy

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Introduction

Many scientific papers [1–4] have shown that degenerative cervical spine disorders are closely linked to aging. Lifestyle, hereditary factors, posture, sports, and work-related activities can, however, influence the course of degenerative disorders [5–7]; moreover, in a number of cases, the cervical spine biological age does not match the person's chronological age. In short, aging of the spine appears to be a complex and inhomogeneous process.

In our daily clinical practice, it is not unusual to find individuals whose cervical spine scans show a much

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different result than what would normally be expected taking into account the subjects' chronological age (Fig. 1). In the literature, so far, there are no tools to measure the degree of degeneration of the cervical spine. A scale such as the one presented in this article might prove essential to standardize studies on degenerative pathologies and relative treatments. So far such standardization has not been possible. There is a distinct lack of homogeneity in treatment guidelines, so much so that selection of appropriate treatment is often wholly lead by the preference of the physician; moreover, population samples in clinical studies have been formed mainly according to chronological age [8–11]. As previously mentioned, our study shows that chronological age alone is not a comprehensive and satisfactory parameter when it comes to researching degenerative disorders of the cervical spine.

The decision on whether a patient should be treated surgically or otherwise, and, in the case of surgery, on which type of intervention should be carried out, is taken on the basis of many parameters, such as medical history, the general and neurological conditions of the patient, the presence of osteoporosis and/or osteopenia, as well as the presence or absence of clear signs of myeloradicular compression caused by degenerative pathology of the spine. Given such premise, it is, however, necessary to recognize that the general condition of the cervical spine is an element that influences the effectiveness of treatments and since such condition can greatly vary from person to person even within the same age group, it is not accurate nor helpful to carry out studies that compare tout court groups of patients homogeneous only because sharing the same age range.

This article aims at presenting a scale for the analysis of MRI images that, by clearly charting the various degenerative stages of the cervical spine, can establish with precision the overall state of degeneration of any given cervical spine, or as we prefer to call it, the spine's biological age. The evaluation system created complies with the following requirements: objectivity, comparability, and replicability.

The cervical spine biological age is determined by summing together various scores linked to a selection of parameters according to which MRI images are analyzed.

Materials and methods

For this article, we have examined the MRI scans of the cervical spine belonging to all the patients who were admitted to the Medical Imaging Service of the Military Hospital of Rome between January 2010 and July 2011, for a total of 508 scans. The exclusion criteria applied to this sample were:

- Patients aged under 20,
- MRI scans performed due to recent trauma to the spine,
- MRI scans performed due to neoplastic growths,
- MRI scans performed after surgery to the cervical tract, and
- MRI scans performed due to inflammatory/infectious diseases of the cervical tract.

Following these criteria, our sample was narrowed down to 423 scans.

The MRI scans were performed using a 2010 Release 2.1.5.5 Philips Achieva with gradients between 33 mT/m and 1 slew rate of 150 T/ms; T1 SE sagittal sequences with 400 ms repetition time (TR), 7.4 ms echo time (TE), 90° flip angle with a thickness of 3 mm and 3′. 43″ scanning time as well as T2 FFE sagittal sequences with 3500 ms TR, 120 ms TE, 90° flip angle with a 3 mm thickness and 3′. 44″ scanning time; axial sequences on T2 FFE 3D, 50 ms TR, 12 ms TE, 7° flip angle, 0.5 mm thickness, 3′ scanning time.

For our study, all images were re-elaborated with Osirix software.

The scans were reviewed by two independent teams. Each team included a neuroradiologist with over 15 years of experience, a senior neurosurgeon with over 15 years of

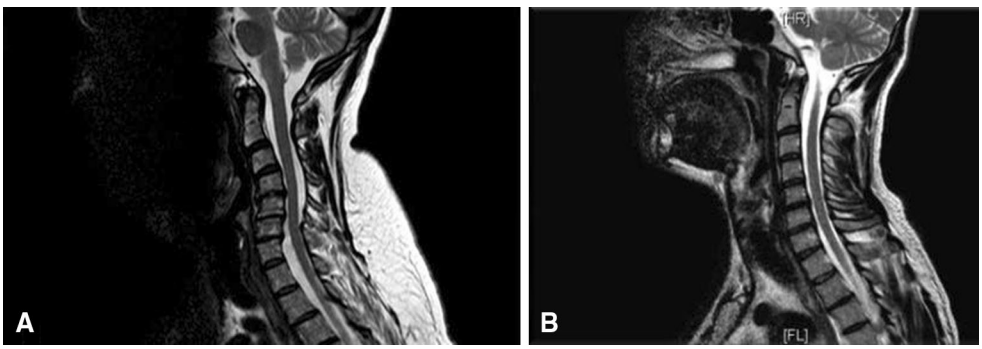

Fig. 1 **a** MRI of a 46 years old man and **b** MRI of an 80 years old man: it seems the opposite

experience in the field of cervical spine and a junior neurosurgeon with less than 15 years of experience.

On the grounds of literature and of our experience, we selected six parameters by which to analyze the sample MRI scans. We assigned to each parameter a score system based on a graduated scale. The cervical spine biological age could then be determined by summing up the scores obtained for each parameter.

The following six parameters were:

1. The degeneration of intervertebral discs,
2. The degeneration of yellow ligaments,
3. The degeneration of vertebral bodies,
4. The possible presence of spondylolistheses,
5. The presence or absence of foraminal stenosis, and
6. The diameter of the spinal canal.

All these factors were evaluated through the use of graduated ordinal scales with incremental scores, whereby each score denoted the state of one of the selected elements as it appeared on the MRI image. Each of these factors was analyzed per single subaxial cervical spine level (C2-D1) as extensively shown by Table 1.

Table 1 The scale

Biological age scale	
(A) Disc (C2–D1 = 6)	Scores between 6 and 30
Normal disc (isointense to CSF on T2-weighted MR images)	1
Dehydrated disc (hypointense to CSF on T2-weighted MR images)	2
Black disc	3
Disc material extrusion and/or anterior and/or posterior osteophytosis	4
Presence of osteophytic bridges	5
(B) Ligaments (C2–D1 = 6)	Scores between 6 and 18
Normal	1
Hypertrophic/with calcification	2
Leaving posterior impression on the canal	3
(C) Vertebral bodies (C2–C7 = 6)	Scores between 6 and 18
Normointense	1
Signal alterations (T1 and/or T2)	2
Presence of Modic changes	3
(D) Segmental alignment (C2–D1 = 6)	Scores between 6 and 12
Normal	1
Misaligned	2
(E) Connecting foramina (C2–D1 = 12)	Scores between 0 and 12
Normal	0
Presenting stenosis	1
(F) Diameter of the canal of the worst level	Scores between 1 and 8
Normal	1
Less than 25 %	2
Between 25 and 50 %	3
Between 50 and 75 %	4
Over 75 %	5
Hyperintense spinal chord at one level	6
Hyperintense spinal chord over several levels	7
Spinal chord atrophy	8
Total	Scores between 25 and 98

Results

Statistical analysis

Initially, the results obtained by the two examining teams underwent the Pearson's test to assess inter-operator dependency: the correlation coefficient equal to 0.891** showed that this scale is not dependent on the operator's subjective view.

We then submitted the data obtained from the study to a statistical enquiry with SPSS v. 18 software.

We first carried out a descriptive statistics analysis; the results of which are displayed in Table 2.

The following variables were added to the six parameters selected:

- Scale total (sum of the individual scores per parameter),
- Chronological age of the subject of the MRI scan,
- The difference between these last two variables.

As it is easily deduced from the table, the average value and standard deviation (SD) of the two variables scale total and chronological age is very similar, indicating a significant super imposability of the two diagrams. The difference of the averages between these two variables is below one point ($N = 423$, $m = -0.929$), while the SD of the difference is once again similar to the SD of the two variables, thus indicating similarity between the dispersion indexes. The Compare Means Test confirmed this observation.

We then carried out on the sample two types of inferential statistics study: Pearson's product-moment correlation coefficient (Table 3) and Factor analysis (Table 4).

The Pearson's product-moment correlation coefficient between the variables, 'chronological age' and 'scale total', was found to be statistically high ($r = 0.726$, $p < 0.01$); as was also the case for all the other scale parameters used as variables, since they too presented a significant positive

Table 2 Descriptive statistics analysis results

	N	Minimum	Maximum	Mean	SD
Interv. disc	423	6.00	29.00	16.5768	4.19525
L. Flavum	423	6.00	18.00	10.0473	3.06759
Soma	423	6.00	17.00	9.1844	2.78010
Listhesis	423	6.00	13.00	6.5768	0.99674
Foramina	423	0.00	10.00	2.6927	2.32850
Canal diameter	423	1.00	8.00	2.2411	1.11793
Total scores	423	26.00	86.00	47.3191	11.39031
Age	423	16.00	90.00	48.2482	12.94748
Variance(age/tot)	423	−29.00	27.00	−0.9291	9.12653
Valid N (list wise)	423				

correlation with the chronological age of the sample subjects ($p < 0.01$).

We then submitted the sample to a Factor analysis (Table 4): a single statistical factor (Fig. 2) was able to determine, in our sample, 56.26 % of variance in the scores obtained using the scale. We hypothesized this factor to be aging.

Discussion

To create our scale we used parameters suggested by the relevant literature on the subject. We examined age in correlation with the following anatomical structures of the cervical spine:

1. Vertebral bodies. In 1988, Modic et al. [12] published the renowned work on MRI scans showing the degeneration of vertebral bodies' bone marrow and of the adjacent endplates. From then on numerous studies were carried out on the subject. We have simplified the analysis of the degeneration of vertebral bodies using a scale with only three base measuring units or degrees:

Score of 1. Absence of non-homogeneity of signal on T1 and T2-weighed images of the vertebral body.
Score of 2. Presence of non-homogeneity.
Score of 3. Presence of any kind of degeneration classified according to the Modic scale.

2. Intervertebral discs. The progressive disc degeneration caused by aging can easily be verified by MRI scan examination. In 2001, Pfirrmann proposed a measuring system for lumbar disc degeneration [13]. For the cervical spine we adopted a similar system with five base measuring units or degrees:

Score of 1. Disc that is hyper or isointense to the cerebrospinal fluid (CSF) on T2-weighted MR images.
Score of 2. Hypointense disc.
Score of 3. Black disc.
Score of 4. Protruded or extruded disc from any side.
Score of 5. Absence of disc space/presence of osteophytic bridges between vertebrae.

3. Intervertebral ligaments. The degeneration of the ligaments is due to changes in the collagen fibers and in calcium content. Numerous articles [14–17] highlight how, with aging, the cervical spine ligaments present a marked tendency toward calcification, in particular toward OPLL (ossification of the posterior longitudinal ligament). We have selected the degeneration of the posterior ligamentous complex (yellow ligament/interspinous ligament), while discounting the remaining ligamentous compartment as it was already included in other parameters (disc, intervertebral foramina, presence of spondylolisthesis, and canal). For this parameter, we established three base measuring units or degrees of progressive degeneration: healthy (score of 1), calcified (score of 2), and projecting into the canal (score of 3).
4. Intervertebral foramina. We can evaluate the degenerative process of the zygapophysial joints and the facet joints by examining the deterioration of connecting foramina [18]. To achieve this, we used the axial sequences for the vertebral bodies studied and the T2-weighed sagittal sequences. On the levels that were not clear, we used 2D reconstruction with Osirix software, thus obtaining the images of the foramina on an orthogonal plane compared to the axis of the foramen in consideration [19]. For each foramen, we established the following base measuring units or degrees: score of 0 if healthy, score of 1 if it presented any form of deterioration [20].
5. Spinal Canal. The degenerative processes of the spine caused by aging provoke a progressive narrowing of the spinal canal with myelopathic signal manifestations in MRI scans [21, 22]. For this reason, we included a parameter to evaluate the AP diameter at the worst level. We adopted the following scale system:

Score of 1. Normal diameter.

Table 3 Pearson's correlation between criteria

	Int. disk	L. Flavum	Soma	Listhesis	Foramina	Canal diameter	Total scores	Age	Variance (age/tot)
Int. disk									
Pearson's correlation	1	0.616**	0.539**	0.444**	0.677**	0.486**	0.891**	0.644**	0.199**
Sig. (2-tailed)		0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
N	423	423	423	423	423	423	423	423	423
L. Flavum									
Pearson's correlation	0.616**	1	0.518**	0.347**	0.558**	0.419**	0.808**	0.605**	0.150**
Sig. (2-tailed)	0.000		0.000	0.000	0.000	0.000	0.000	0.000	0.002
N	423	423	423	423	423	423	423	423	423
Soma									
Pearson's correlation	0.539**	0.518**	1	0.348**	0.512**	0.258**	0.742**	0.549**	0.147**
Sig. (2-tailed)	0.000	0.000		0.000	0.000	0.000	0.000	0.000	0.002
N	423	423	423	423	423	423	423	423	423
Listhesis									
Pearson's correlation	0.444**	0.347**	0.348**	1	0.441**	0.355**	0.554**	0.412**	0.108(*)
Sig. (2-tailed)	0.000	0.000	0.000		0.000	0.000	0.000	0.000	0.027
N	423	423	423	423	423	423	423	423	423
Foramina									
Pearson's correlation	0.677**	0.558**	0.512**	0.441**	1	0.500**	0.817**	0.574**	0.205**
Sig. (2-tailed)	0.000	0.000	0.000	0.000		0.000	0.000	0.000	0.000
N	423	423	423	423	423	423	423	423	423
Canal Diameter									
Pearson's correlation	0.486**	0.419**	0.258**	0.355**	0.500**	1	0.586**	0.390**	0.178**
Sig. (2-tailed)	0.000	0.000	0.000	0.000	0.000		0.000	0.000	0.000
N	423	423	423	423	423	423	423	423	423
Total score									
Pearson's correlation	0.891**	0.808**	0.742**	0.554**	0.817**	0.586**	1	0.726**	0.218**
Sig. (2-tailed)	0.000	0.000	0.000	0.000	0.000	0.000		0.000	0.000
N	423	423	423	423	423	423	423	423	423
Age									
Pearson's correlation	0.644**	0.605**	0.549**	0.412**	0.574**	0.390**	0.726**	1	−0.513**
Sig. (2-tailed)	0.000	0.000	0.000	0.000	0.000	0.000	0.000		0.000
N	423	423	423	423	423	423	423	423	423
Variance (Age/Tot)									
Pearson's correlation	0.199**	0.150**	0.147**	0.108*	0.205**	0.178**	0.218**	−0.513**	1
Sig. (2-tailed)	0.000	0.002	0.002	0.027	0.000	0.000	0.000	0.000	
N	423	423	423	423	423	423	423	423	423

Asterisks indicate significant correlations

Score of 2. Reduction up to 25 % compared to a normal adjacent space.
Score of 3. Reduction between 25 and 50 %.
Score of 4. Reduction between 50 and 75 %.
Score of 5. Reduction above 75 %.

Table 4 Factor analysis

Component	Initial eigenvalues			Extraction sums of squared loadings		
	Total	% of variance	Cumulative %	Total	% of variance	Cumulative %
1	3.376	56.262	56.262	3.376	56.262	56.262
2	0.767	12.778	69.041			
3	0.679	11.310	80.350			
4	0.442	7.371	87.721			
5	0.424	7.061	94.782			
6	0.313	5.218	100.000			

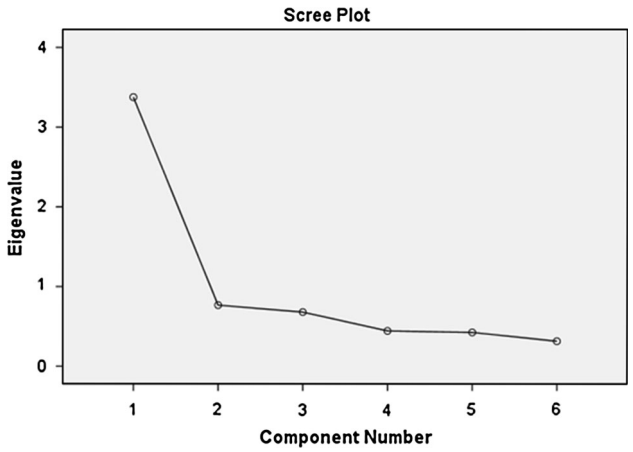

Fig. 2 A single statistical factor was able to determine, in our sample, 56.26 % of variance in the scores obtained using the scale

Score of 6. Presence of myelopathic signal on T2 at single level.
Score of 7. Presence of myelopathic signal over more levels.
Score of 8. Presence of spinal cord atrophy.

The last three degrees do not refer to the diameter of the spinal canal, but to pathologies of the spinal cord that occur in very serious anatomical conditions; in these instances, the walls of the spinal canal no longer represent the element that contains and protects the spinal cord, but they actually become the cause for pathologies of the nervous tissue.

6. Alignment or misalignment between two vertebrae. Degenerative spondylolistheses, which has long been known in the lumbar region, has been studied at cervical level only since 1986 [23]. Its presence increases with aging and it has been found to be high in people over 50 [24]. This is why we chose to include this parameter in our scale by simply acknowledging its absence (score of 0) or presence (score of 1) for each vertebral unit under consideration.

We have not included osteoporosis among the parameters under observation, even though it is an element that needs to always be kept in mind for the selection of treatment for the spine, because osteoporosis represents a very clear pathology of the bone, which is not derived from the degenerative process [25–27].

The results of the statistical analysis show that to evaluate the cervical spine aging process, the choice of the aforementioned parameters has been correct. Since the degeneration caused by aging is not in itself a pathology but an unavoidable physiological occurrence for everyone without exception, whether symptoms are present or not [28], we did not consider it necessary to gather data from a "healthy" sample. Any spine expert is aware that the radiological appearance of the spine does not always correlate with the clinical picture; thus, a patient with spine degeneration may not show any symptoms and, therefore, not require treatment.

The effectiveness of the various medical, physiatrical, and surgical treatments for cervical spine degenerative disorders is influenced by the overall anatomical conditions of the cervical spine. Up until now there has been no objective criterion for the evaluation of these conditions. Moreover, as already stated, the aging processes of the spine are not always homogeneous per age band. These factors contribute to the extreme difficulty in achieving any sort of objective comparison among therapeutic strategies. We believe that this scale will be useful to homogenize retrospective studies and to correctly set up prospective studies on the degenerative disorders of the cervical spine and the relative treatments; it is effective and simple tool for the objective classification and staging of degenerative processes and for the measurement of the cervical spine's biological age; our team has been using it for over a year and found it extremely helpful to determine the appropriate therapy for each patient. In fact, recently, we have begun a prospective study on the choice, in relation to patients' age, of either the artificial disc or the cage as prosthesis during anterior surgery of myeloradiculopathy caused by disk herniation or by cervical spondylosis. This study involves two groups of patients. The choice of prosthesis for the first group will rely solely on the subjects' chronological age, which is currently common practice; while for the other group, the choice will be based on the spine's biological

age, calculated according to our scale. Early data shows that all the patients who were given a disc prosthesis having scored 50 or below on our scale, irrespective of their actual age, even after two years have had no signs of prosthesis' fusion and the consequent lessening of mobility; whereas the only two patients who were given an artificial disk because younger than 50 years old, but whose score was above 50, both showed an early prosthesis fusion process.

In conclusion, our work means to contribute, through a statistical model, to the standardization and simplification of the complex phenomenon that is cervical spine aging, and thus it offers a tool for the greater homogenization of studies concerning the treatments of pathologies linked to spinal degeneration. The sample we chose to build the scale from is statistically sufficient [29, 30]; however, the topic we chose is so varied, vast, and complex that it certainly deserves a larger sample as well as a different approach to the research. In conclusion, we consider ours a pilot study that may lead to a larger multicenter study.

Conflict of interest None.

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