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**Effects of repetitive work on proprioception and
of stretching on sensory mechanisms.**

**Implications for work-related neuromuscular
disorders.**

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ORIGINAL PAPERS

This thesis is based on the following papers, which in the text are referred to by their Roman numerals:

- I. Position sense acuity is diminished following repetitive low-intensity work to fatigue in a simulated occupational setting. Björklund M, Crenshaw AG, Djupsjöbacka M, Johansson H. *Eur J Appl Physiol*, 2000, 81:361-367.
Appendix to the paper: Letter to the editor. *Eur J Appl Physiol*. 2003, 88:485-486.
- II. Effects of working time and retention of subjective fatigue on proprioception in a low-intensity repetitive work task. Djupsjöbacka M, Björklund M, Crenshaw AG, Johansson H. (*Manuscript*)
- III. Acute muscle stretching does not alter position sense acuity. Björklund M, Djupsjöbacka M, Crenshaw AG, Johansson H. (*Submitted*)
- IV. Stretchability of the rectus femoris muscle: investigation of validity and intratester reliability of two methods including x-ray analysis of pelvic tilt. Hamberg J, Björklund M, Nordgren B, Sahlstedt B. *Arch Phys Med Rehabil*, 1993, 74:263-270.
- V. Sensory adaptation after a 2-week stretching regimen of the rectus femoris muscle. Björklund M, Hamberg J, Crenshaw AG. *Arch Phys Med Rehabil*, 2001, 82:1245-1250.
- VI. Muscle stretch-induced modulation of noxiously activated dorsal horn neurons of feline spinal cord. Björklund M, Radovanovic S, Ljubisavljevic M, Windhorst U, Johansson H. *Neurosci Res*, 2004, 48:175-184.

ABBREVIATIONS

AC	Agonist contract
AE	Absolute error
CCM	Common clinical method
CNS	Central nervous system
CR	Contract relax
CRAC	Contract relax & agonist contract
CV	Coefficient of variation
CWRND	Chronic work-related neuromuscular disorders
EMG	Electromyographic activity
HFF	High-frequency fatigue
KJM	Knee joint method
LFF	Low-frequency fatigue
MVC	Maximum voluntary contraction
MVE	Maximum voluntary electrical activity
MSA	Muscle spindle afferent
NDM	Newly developed method
PNF	Proprioceptive neuromuscular facilitation
RFM	Rectus femoris muscle
ROM	Range of motion
RSF	Retention of the subjective fatigue
SDHN	Superficial dorsal horn neuron
SS	Static stretching
VE	Variable error

GENERAL INTRODUCTION

Understanding how work-related musculoskeletal disorders develop and become chronic is crucial for the chances to progress in the prevention and treatment of these disorders. Common symptoms in patients suffering from these disorders include pain and discomfort in muscles and a feeling of stiffness and fatigue of the painful muscles. Static or repetitive work aggravates the pain. The pain is likely to originate in the activation of sensory receptors that are specialized in responding to tissue-threatening chemical, mechanical and/or thermal stimuli (nociceptors). The signals arising in nociceptors are conveyed to the central nervous system (CNS) by small-diameter group III and IV afferent nerve fibers. Within the CNS, these signals will evoke the sensation of pain and at the same time initiate and maintain a complex assembly of parallel and serial processes that ultimately influence many body systems. The body systems modulated by nociceptive signals include the emotional/affective system, the neuro-endocrine system, the autonomic nervous system, and the motor control system. The activation of these processes may in turn augment the peripheral processes underlying the activation of nociceptors, thus leading to potentially detrimental feedback actions. Furthermore, prolonged nociceptive activation may permanently change the ways in which nociceptive signals are processed and thus induce and sustain chronic pain. Research on processes that induces and sustain work-related pain suggests complex multiple interactive pathophysiological mechanisms, which may work at different times in the disease process. How this complex network of interactions comes about is as yet not well understood, thus requiring intensive research.

The present thesis is concerned with pathophysiological mechanisms behind chronic work-related muscle pain and focuses on effects of low-intensity repetitive work on proprioception (the sense of limb position and movement), and on sensory effects of muscle stretching, a proposed way to prevent and alleviate work-related muscle pain. The introduction is therefore composed to give a background and relevant information on work-related disorders associated with repetitive work exposure, proprioception and muscle stretching.

Work-related musculoskeletal disorders

This section presents a background to work-related musculoskeletal disorders followed by a presentation of possible integrative mechanisms underlying these disorders, especially those related to repetitive work exposure. For a comprehensive review of neuromuscular mechanisms behind work-related chronic muscle pain, the interested reader is referred to Johansson et al. (2003).

Nomenclature, epidemiology and risk factors

The existence of an association between working life conditions and muscle pain disorders has been described in the literature for centuries and the nomenclature for these disorders is diverse. The labels of such disorders have often been related to the

activity triggering the pain or the profession of those suffering from the pain. For instance, already in the 18th century, Ramazzini described the *Diseases of Scribes and Notaries*, in the 19th century Sir Charles Bell described the *Writers' Cramp* in male clerks, and Samuel Solley denoted patients as having *the Scriveners' Palsy*. Other examples in line with this are *Tailors' Cramp* and *Telegraphist' Cramp* both described at the turn of the 19th to 20th century. (For references to the above see Blair et al. 2003). Etiology-related names of the disorders appeared frequently in the 1970's and 1980's, such as *Repetitive Strain Injury*, which was particularly popular in Australia (Ferguson 1984), and its American correlate *Cumulative Trauma Disorders* (Blair 1995). A third category of designations of the disorders rather uses the anatomic region of occurrence. Examples of these are *cervico-brachial disorders*, *neck-shoulder myalgia*, *low back pain*, *myofascial pain syndromes*, *tension headache* and *temporomandibular pain and dysfunction syndromes*. Unfortunately, few of these labels, as well as the well-known terms *work-related musculoskeletal disorders* and *chronic musculoskeletal pain syndromes*, acknowledge the fact that muscle pain related to working life primarily involves, in addition to muscles and tendons, also the nervous system rather than the skeletal system (Johansson et al. 2003). Therefore, an updated scientifically appropriate term for these conditions would rather be chronic work-related neuromuscular disorders (CWRND). Hence, this is the term used throughout this thesis when referring to general non-specific muscle pain syndromes associated with working life.

Today, CWRNDs are an extensive health burden to the industrialized world. Not only does it constitute an enormous cost to society but naturally also human suffering of great proportions. Statistical comparisons between countries of the prevalence of CWRNDs are difficult due to different incentives for reporting CWRNDs, social insurance systems, record-keepings and case definitions. Nevertheless, the U.S. Bureau of Labor Statistics reported that work-related musculoskeletal disorders accounted for over 67% of all occupational illnesses for the year 2000 (Bureau of Labor Statistics 2001), and this figure is of a similar magnitude in Sweden. In Sweden, the body region most afflicted by occupational diseases is the neck-shoulder region accounting for 33% of all occupational diseases while the corresponding number for the second largest region, the low back, is 22%, according to the Swedish Work Environment Authority and Statistics Sweden (Arbetsmiljöverket och SCB 2001). The cost for the Swedish society due to muscle pain disorders resulting from increased sick leave, early retirement and production losses, has been estimated to be about 1.7% of the Gross National Product (Norlund and Waddell 2000).

The disorders are especially prevalent among those working in the manufacturing industry, health care, trade and commerce, and communication.

The identification of work-place risk factors has been the object of a large number of epidemiological studies as recently reviewed by several of European and American occupational health organizations (Bernard 1997; Buckle and Devereux 1999; National Research Council 1998, 2001). However, to derive causal inferences about the associations of biophysical and psychosocial work-place factors and the development

of CWRNDs, the integration of information from laboratory research, observational epidemiology and workplace interventions are needed. Some reviews on the topic have therefore extended the scope outside the epidemiological sphere in order to arrive at a more valid evaluation of possible risk factors (e.g., National Research Council 1998, 2001). These reviews reflect an increasing awareness of the existence of certain patterns of associations between biophysical and psychosocial exposures and increased risks for the development of CWRNDs. Biophysical risk factors promoting CWRNDs include repetitive and stereotyped movements (even at low mean force levels), demands on high precision of low-intensity muscle contractions, non-neutral postures, biomechanical restraints (reducing the degree of freedom of movements) and time constraints and high work rates (Johansson et al. 2003). During prolonged repetitive work, the lack of periods of complete relaxation over the working day may also be an additional risk factor (Veiersted et al. 1993). Between the years 1990 and 2000, the exposure of the working population in the European Union to the risk factor “repetitive motions” remained unchanged, whereas it increased for the exposure to “painful/tiring postures” and to “handling of heavy loads”, according to the surveys carried out by the European Foundation for the Improvement of Living and Working Conditions (Paoli and Merllié 2001). Thus, despite development of production technology, the exposure to physical risk factors in working life is not decreasing in the industrialized part of the world.

In general, females are at higher risk for work-related neck and upper limb disorders (e.g., Ekberg et al. 1995) but the reason for this gender difference is not clear. However, there are also reports of high prevalence of work-related neck and shoulder pain for males in work exposure including low-level static and monotonous work, such as forest machine operators (Rehn et al. 2002). In line with this, Punnett and Herbert (2000) concluded that a large part of the difference appears to be attributable to differences in work place ergonomic exposures between males and females.

Psychosocial risk factors are closely linked to biophysical risk factors. For example, high levels of demand combined with low job control may involve stereotyped motions and a limited ability to vary the work pace, in such a way that links “stress” with a biophysical exposure of repetitiveness/monotony. Thus, psychosocial factors complement and aggravate the biophysical risk factors. However, evidence for an association of psychosocial factors in the work environment and CWRNDs is still evolving. For example, lacking autonomy and decision latitude seem to be important factors for the development of CWRNDs (Bongers et al. 1993). Psychosocial factors, like fear avoidance and notably distress, may also be of importance in the transition from acute to chronic pain (Klenerman et al. 1995; Pincus et al. 2002; Burton et al. 2004).

Pathophysiological mechanisms related to repetitive work exposure

Exactly how repetitive work exposure could lead to CWRND is still a matter of intense research. In the following sections, this issue will be discussed in terms of muscle contraction and movement patterns and their possible consequences for events in the neuromuscular system contributing to the development of CWRND. It has to be pointed out that the links presented should be considered as working hypotheses rather than established paths.

Muscle contraction and movement patterns

The type of repetitive work that is frequently associated with disorders in the neck, shoulder and upper extremities usually involves prolonged sustained or repetitive muscle activation with low external force demands, often combined with high demands on precision, for example, computerized data entry or assembly operations (Ariëns et al. 2000; van Dieën et al. 2003). The required contraction patterns of distal muscles differ from those of proximal muscles, with short repetitive contractions for the former and more prolonged static stabilizing co-contractions for the latter muscles (Armstrong et al. 1993; Sjøgaard and Sjøgaard 1998). Static work postures, especially with muscles in shortened positions, may also result in asymmetric shortening of muscles and in compression and tension on nerves (Mackinnon et al. 1994).

Stereotyped low-intensity repetitive work has some important characteristics, which may be of importance for the possible causal relation to CWRNDs. A constrained movement pattern during the work task not only leads to a restricted load distribution between muscles but could also have deleterious effects on specific subsets of muscle fibers. Since muscle fibers belonging to low-threshold motor units are the first to be recruited and the last to be de-recruited, according to the ordered recruitment principle (Henneman et al. 1965), they are most susceptible to long-lasting fatiguing overload, for which reason these fibers have been denoted “Cinderella” fibers (Hägg 1991; Forsman et al. 2001). A correlate to the existence of Cinderella fibers is the absence of so-called electromyography (EMG) gaps, defined as a period of at least 1 sec of EMG activity below 0.5% maximal voluntary contraction (MVC). Veiersted and co-workers (1993) showed, in a longitudinal study over 60 weeks, that female packers with fewer EMG-gaps were predisposed to development of myalgia. On the other hand, observation of no differences in the presence of EMG-gaps during work between healthy and myalgic groups has also been reported (Vasseljen and Westgaard 1995). However, it is not likely that the Cinderella hypothesis, implying a recruitment pattern that systematically overloads single muscle fibers, applies to normal patterns of motor unit recruitment. A protective mechanism against the Cinderella syndrome may be the rotation of different motor units where units take turn in being activated during prolonged contraction periods (Westgaard and DeLuca 1999). This protective mechanism may, however, fail especially during prolonged work exposure with

biomechanically constrained work tasks involving stereotypic movement patterns. The reason for this failure is probably complex and not yet well understood. One possible reason may be that the freedom for the CNS in choosing motor units may be reduced in repetitive work tasks with biomechanical restraints. Also, low-intensity work is likely to cause only a moderate metabolic effect, which may be too weak to trigger any protective mechanism for motor unit rotation.

Thus, in some work tasks, the Cinderella mechanism may come to bear on muscle performance. If so, muscle fibers connected with low-threshold motor units will be overloaded and eventually fatigued. The type of fatigue brought about by prolonged low-intensity work is called “low-frequency fatigue” (LFF). In contrast to “high-frequency fatigue” (HFF), LFF shows a very slow recovery and its effects persist in the absence of larger metabolic or electrical disturbances in the muscle (Jones 1996). Due to the slow recovery, this kind of fatigue may accumulate over hours and days and increase the risk for intramuscular accumulation of substances that are involved in the development of pain. The importance of the retention of fatigue in the processes underlying CWRND is, however, poorly understood. In the present thesis, Paper II addresses this issue with regard to proprioception.

Muscle blood flow regulation

There are two competing mechanisms regulating blood flow during muscle contractions. Activation of the sympathetic nervous system leads to vasoconstriction of arterioles, and muscle activity induces the release of metabolites that in turn bring on local vasodilatation. The balance of these mechanisms is dependent on the type and level of contraction. During rhythmic contractions at levels exceeding 10-15% MVC, an induced sympathetic vasoconstriction will be overridden by metabolic vasodilatation by that assuring an appropriate level of muscle oxygenation (Hansen et al. 1996). By contrast, sympathetic activation during lower contraction levels might impede the blood flow to the working muscles (Hansen et al. 1996). This would increase the risk of the accumulation of metabolites and inflammatory substances and augment the activation of group III and IV muscle afferents, thus potentially giving rise to a vicious circle.

Indeed, there are observations of reduced blood flow (Larsson et al. 1990; Larsson et al. 1999) and morphological changes in chronically myalgic muscles. The morphological changes include hypertrophy of type I muscle fibers (e.g., Larsson et al. 1988; Kadi et al. 1998) and signs of a decreased capillary supply to the myalgic muscles (Lindman et al. 1991; Kadi et al. 1998). Furthermore, reduced numbers of capillaries per fiber area were shown to be associated with high pain intensities (Kadi et al. 1998).

Activation of chemosensitive group III and IV muscle afferents

Somatic pain involves the activation of sensory receptors, supplied by group III and IV muscle afferents, specialized in responding to tissue-threatening stimuli (nociceptors). These receptors are activated by chemicals such as metabolites and inflammatory substances, which thereby may become elements in the genesis of work-related muscle pain. In contrast to high-intensity muscle contractions, which are usually less frequent in work place settings, it is not quite clear whether low-intensity work may lead to the intramuscular accumulation of metabolites or inflammatory substances (see also *Muscle blood flow regulation* above). LFF has been proposed to be associated with increased intracellular concentrations of Ca^{2+} in the afflicted muscle fibers (Gissel 2000). The breakdown in Ca^{2+} homeostasis may induce a chain of reactions leading to damage and leakage of the muscle fiber membrane, thus allowing pain-producing substances to leak out.

This mechanism is supported by the study of Barbe et al. (2003), in which rats were trained to reach for food pellets with a rate of 4 reaches per minute for 2 hours per day, 3 days per week. After 6 to 8 weeks, there were signs of cellular and tissue responses associated with inflammation. The study of Barbe et al. (2003) did not only reveal an inflammatory tissue response to the repetitive work, but in parallel also a gradual derangement of motor control with time. To compensate for the deranged motor control, increased co-activation of muscles may occur (Sainburg et al. 1995; Ghez and Sainburg 1995). This increase in co-activation will most likely lead to a reduction of relaxation periods for the involved muscles, that, in turn, will augment the development of fatigue and the release of substances activating group III and IV muscle afferents.

The activation of chemosensitive group III and IV muscle afferents does not only elicit pain, but also affect the γ -motoneuron-muscle spindle system.

The muscle spindle

Muscle spindles are of great importance for proprioception and motor control (for more details, see *Proprioception* below). The activation of chemosensitive group III and IV muscle afferents has strong reflex effects on the γ -motoneurons, which in turn affect the activity and sensitivity of muscle spindles and therefore has influence on proprioception and motor control. Before dealing with this, a description of the anatomy and function of the muscle spindle will be presented.

Muscle spindles are small muscle-length-sensitive mechanoreceptors connected in parallel to the extrafusal muscle fibers (for review see Matthews 1972; Hulliger 1984). The number of muscle spindles is generally higher in proximal than in distal muscles, which corresponds well with reports of higher proprioceptive acuity for proximal than distal joints (Scott and Loeb 1994). The muscle spindle has a capsule bulging out at the equatorial region and thus resembles the spindles used for spinning wool, hence the name muscle spindles (Lat. *fusus*=spindle). The intrafusal fibers con-

sist of a non-contractile central region and contractile regions at the poles of the fibers. These regions receive a motor innervation of two sorts. First, static and dynamic γ -motoneurons can be selectively controlled, independently from the extrafusal muscle fibers, by the CNS (Prochazka 1996). Secondly, β -motoneurons project to both extra- and intrafusal fibers. Finally, many muscle spindles also receive an innervation from postganglionic sympathetic fibers (for references see Passatore and Roatta 2003). The sensory innervation of spindles is also complex. The central non-contractile regions of the intrafusal fibers are surrounded by spirals of receptor ending merging into one group Ia muscle spindle afferent (MSA) and usually one or more endings merging into group II MSAs. Group Ia MSAs possess a higher dynamic sensitivity to muscle-length changes than do group II MSAs. Group II MSAs fire more regularly during stretch and release of stretch compared to group Ia. The response characteristics of group Ia and II MSAs are influenced by the neural drive from the γ -motoneurons. For example, stimulation of static γ -motoneurons increases the background discharge but decreases the dynamic sensitivity of group Ia MSAs. The delicate sensory ability of MSAs to signal muscle lengths and length changes makes the muscle spindle most important for the perception of position and movements of our limbs, also known as proprioception, as well as for the regulation of motor control. It should be noted that the ability of afferents to discriminate muscle stretches of different amplitudes is greater for simultaneously recorded ensembles of MSAs than for single MSAs (e.g., Bergenheim et al. 1995; Tock et al. 2003). This discriminative ability of ensembles of MSAs, and consequently the proprioceptive acuity, is under strong influence of the prevailing γ -motoneuron drive.

Effects of group III and IV muscle afferents on the muscle spindle activity

An increased input from chemo-sensitive group III and IV muscle afferents may exert potent effects on several neuronal systems, of which the γ -motoneuron- muscle spindle system is just one. Below two simplified positive feedback loops with their hypothetical consequences are outlined.

The metabolites and/or inflammatory substances induce activation of chemosensitive group III and IV muscle afferents, which then exert excitatory effects predominantly on static γ -motoneurons, projecting to muscle spindles of the same as well as neighboring muscles (Djupsjöbacka et al. 1995; Pedersen et al. 1997; Hellström et al. 2000). The γ -motoneuron-induced change in activity and sensitivity of MSAs could have the following effects, leading potentially to vicious circles:

- i) Deterioration in the information transmitted by ensembles of MSAs \longrightarrow reduced acuity of proprioceptive information \longrightarrow less efficient intramuscular coordination and deteriorated intermuscular coordination. This impaired motor control could further increase the concentration of inflammatory substances, since the CNS may try to compensate for the impairment by increasing the co-activation of muscles (see *Activation of chemosensitive group III and IV muscle afferents* above).
- ii) Group II MSAs polysynaptically excite the static and dynamic γ -motoneurons

projecting to muscle spindles of the same and other (even contralateral) muscles, thus reinforcing the effects on the muscle spindles.

The mechanisms whereby these positive feedback loops may develop into vicious circles are not clearly understood. A key role in this process may have the reflex loop involving the group II MSAs (outlined above under ii). The γ -motoneuron-muscle spindle system is influenced by many further inputs from peripheral and central sources (e.g., skin receptor afferents, joint afferents, sympathetic and descending systems). For example, stimulation of mechanosensitive joint afferents exerts potent reflex effects on γ -motoneurons (Johansson et al. 1998; Sjölander et al. 2002), implying that loads on joints during awkward work postures could add substantially to the reflex loop (ii). The secondary MSAs connect, via the γ -motoneurons, to muscle spindles of both homo- and heteronymous muscles on both sides of the body. This “peripheral neuronal network” interconnecting muscle spindles may play an important part in the spread of CWRNDs to neighboring muscles. It is also conceivable that the total input to γ -motoneurons, emanating from multiple sources, may have to reach a threshold before the above positive feedback loops develop into vicious circles. This transition may be promoted by plastic processes, such as peripheral (nociceptor) and central sensitization. Furthermore, vicious circles might also be established by the actions of group III and IV afferents on brainstem structures whose activity in turn facilitate the transmission of nociceptive signals in the spinal dorsal horn (for references see Windhorst 2003).

Proprioception

The term proprioception, once introduced by Sherrington (“*The integrative action of the nervous system*”, 1906), has received various definitions. Proprioception in this thesis is defined as the perception of positions and movements of the body segments in relation to each other, without the aid of vision, touch or the organs of equilibrium.

Proprioception involves two submodalities, a static component of position sense and a dynamic component of movement sense (McCloskey 1973; Sittig et al. 1985). This partition receives clear support from experiments of muscle vibration-induced illusions, showing that subjects can perceive the position and velocity of a passive limb separately (McCloskey 1973) and that position and movement information can be used distinctly for separate controls of limb position and limb velocity, respectively (Sittig et al. 1985). Also, extremely slow passive movements are perceived as changes in limb position without the perception of movement, which corroborates the notion of separate neural pathways of movement and position sense (Horch et al. 1975; Clark et al. 1985, for review, see Gandevia and Burke 1992).

In the present thesis, Papers I-III are concerned with proprioception.

Sources of information for proprioception

The sense of proprioception, as defined in this thesis, utilizes information derived from peripheral sensory receptors and centrally generated motor commands.

Peripheral receptors

Peripheral mechanoreceptors subserving the sense of proprioception are called proprioceptors. The information conveyed by the proprioceptors is not only used by CNS for motor control, but are also involved in other processes at unconscious levels in the CNS. Proprioceptors include mechanosensitive muscle, joint and skin receptors, but their relative contribution and importance for proprioception has been extensively debated over the past 150 years or so, and the “common view” has varied. For example, during the era of Sherrington in the beginning of the 20th century, muscle mechanoreceptors were considered as the main source of information. This contention shifted, so that during the 1960’s it was even questioned if a “muscle sense” existed at all (Gelfan and Carter 1967). Soon thereafter, however, the importance of muscle spindles in proprioception was restored, owing to the demonstration that illusions of movements were induced by tendon vibration (for references see Gandevia and Burke 1992). Today, the general view is that proprioception depends on signals from all three classes of receptors. Nevertheless, their relative importance may differ at different joints. Therefore, the following sections give brief descriptions of the proprioceptive functions of each individual class of receptors.

Muscle receptors

Muscle mechanoreceptors thought to contribute to proprioception are the muscle spindles and the Golgi tendon organs. (For information on MSA characteristics, see *The muscle spindle* above). Today, the importance of muscle receptors, particularly muscle spindles, for proprioception is undisputed. There is abundant experimental evidence indicating that the information conveyed by MSAs contribute to the perception of position and movements in humans. Illusions of joint movements can be induced by 60-80 Hz vibration of the tendons and muscles, thereby exciting mainly primary MSAs (e.g., Goodwin et al. 1972; Sittig et al. 1985; Calvin-Figuieri et al. 1999), and by pulling exposed tendons of stationary limbs (Matthews and Simmonds 1974; McCloskey et al. 1983, but see also Moberg 1983). Also, particularly the position sense was disturbed when a vibrated muscle was loaded (McCloskey 1973). The importance of muscle receptors is further substantiated by the finding that proprioception was only partially reduced when the joint and the surrounding skin were anesthetized (e.g., Clark et al. 1979). However, differences have been found for different body parts with little or no effect of knee and ankle joint anesthesia, but a markedly reduced proprioceptive acuity by anesthesia of the fingers (for references see Gandevia and Burke 1992).

The Golgi tendon organ is primarily a force sensor. It is innervated by group Ib afferents and responds less to passive than to active tension. In fact, it can respond to the contraction of only 1-2 muscle fibers with a threshold falling below 0.1 g (Houk and Henneman 1967). The specific role of Golgi tendon organs in proprioception is

largely unknown, but it has been shown that mixed ensembles of primary and secondary MSAs as well as Golgi tendon organ afferents discriminated muscle stretches of different amplitudes significantly better than ensembles of only one or two types of these afferents (Bergenheim et al. 1996). Finally, it cannot be excluded that stretch-sensitive group III muscle afferent could have a proprioceptive function.

Joint receptors

Mechanosensitive joint receptors are situated in the capsules and ligaments of the joints. Their afferents are believed to mainly fire at extreme joint positions (for reviews see Gandevia and Burke 1992; Grigg 1994). However, Ferrell (1980) showed that 18% of mechanoreceptors in cat knee joint responded across the mid-range of joint motion, and joint afferents active in the whole range of motion (ROM) have been observed in the cat hip joint (Carli et al. 1979). These observations and the finding of Macefield and co-workers (1990) that sensations of joint pressure and movements could be induced by micro-stimulation of joint afferent fibers, suggest a role for joint afferents in other movement ranges than just the extremes. Still, the contribution of joint receptors in proprioception may be larger at the end-ROM.

Skin receptors

The proprioceptive properties of mechanosensitive skin afferents have been studied particularly for the hand and face (for references see Edin 2001). It has been shown that slowly adapting mechanoreceptor afferents show high dynamic and static sensitivities to skin stretch (Edin 1992). Also, illusions of finger movements can be induced by stretch of the dorsal skin of the hand (Edin and Johansson 1995; Collins and Prochazka 1996) and by electrical stimulation of skin afferents (Collins and Prochazka 1996). The contribution of skin receptors to proprioception for other parts of the body is largely unknown, but microneurography recordings from skin afferents of the thigh support a role for slowly adapting skin afferents in knee joint proprioception (Edin 2001).

Central motor commands

Proprioceptive information is used for the control of movements. Grossly, this control could be divided into so-called closed-loop and open-loop control. In the closed-loop control, e.g., during slow movements, the movement-produced sensory feedback is used for the regulation of movement, i.e., detection and correction of errors in performance via feedback and reflex mechanisms. In open-loop control, usually occurring during fast (ballistic) movements, sensory feedback would come too late because of time delays. In this case, the motor system operates with feed forward commands that cannot be corrected by feedback during the execution of fast movements. Thus, in order for the motor commands to be precise, they should be well calibrated to the properties of the peripheral body parts to be moved (see below). The

sensory centers will still get information about whether the movement is executed according to plan. According to an idea tracing back to the “reafference principle” of von Holst and Mittelstaedt (1950) this can be achieved as follows:

In order to inform the sensory processing centers of the expected sensory consequences from the movement, the motor centers send them a “copy” of the motor command referred to as *corollary discharge* or *efference copy*. The efference copy is thus a complement to the proprioceptive information arising from peripheral mechanoreceptors.

For motor learning, proprioceptive afferent information is compared with the efferent signals of the motor command. In this way, sensory feedback, of which the information from MSAs is prominent, will continuously contribute to the calibration and updating of internal dynamic limb models used for modulating motor commands.

Factors affecting proprioception

There are several factors that could affect proprioception, such as age, clinical disorders, injuries, muscle fatigue and muscle pain. Due to the scope of the thesis, extra attention will be paid to muscle fatigue and its impact on proprioception.

The impact of muscle fatigue on proprioception

Muscle fatigue could be seen as any reduction in the maximal capacity to generate force or power output (Völlestad 1997). Thus, muscle fatigue is associated with an impairment of motor performance that includes a perception of increased effort to sustain the task and the eventual failure to do so due to the reduced force capacity. The motor task or type of exercise (especially the intensity of the work) leading to fatigue influences its manifestation. In most studies of fatigue, the effects of exercises, tetanic stimulations and ischemic conditions are explored (Völlestad 1997). Fatigue referred to as HFF involves high rates of motoneuron activation and the consequent loss of force is rapidly reversed (Jones 1996). However, this type of fatigue is less frequently occurring in occupational situations. Under these conditions, fairly low motoneuron firing rates of around 10-20 Hz prevail and may entail what is referred to as LFF (for references see Völlestad 1997). In LFF, recovery is substantially slower than in HFF (see also *Muscle contraction and movement patterns* above). As pointed out earlier in the introduction (see *Activation of chemosensitive group III and IV muscle afferents*), the fact that LFF can accumulate over time may be an important mechanism leading to muscular pain (Westerblad et al. 2000; Gissel 2000).

Science as well as common experience suggests that fatigue in general impairs motor performance and motor control in terms of coordination, balance, precision etc. But exactly how this impairment comes about is less clear. It is possible that one factor is reduced proprioceptive acuity.

Effects of fatigue on proprioception

In an acute animal model, electrically induced muscle fatigue caused a clear reduction in the ability of ensembles of MSAs to separate muscle stretches of different amplitudes, thus deteriorating the quality of proprioceptive information (Pedersen et al. 1998). It was also shown that this effect was induced by the actions of group III and IV afferents on γ -motoneurons. Thus, it is likely that the metabolites and inflammatory substances released by the fatiguing muscle contractions constitute the fuel for this reflex effect on the γ -motoneuron-muscle spindle system, a notion corroborated by several other studies (Johansson et al. 1993; Djupsjöbacka et al. 1994, 1995; Pedersen et al. 1997; Hellström et al. 2000). In humans, the effect of fatigue on proprioception has been investigated at various joints. For the shoulder joint, the proprioceptive acuity following fatigue has been shown to be reduced (Voight et al. 1996; Carpenter et al. 1998; Pedersen et al. 1999), ambiguous (Lee et al. 2003) or unchanged (Sternier et al. 1998). Sternier and co-workers (1998) showed that the force capacity of the subjects was rapidly reversed after the fatiguing protocol used, suggesting that the fatigue state was not deep and long-lasting, which might explain the missing effect on proprioception. For other joints, fatigue effects on position sense were somewhat divergent, but in line with the studies on shoulder proprioception, most studies showed reduced position sense acuity after fatigue (e.g., Saxton et al. 1995; Lattanzio et al. 1997; Brockett et al. 1997; Forestier et al. 2002), and only a few studies failed to show any effect (Sharpe and Miles 1993; Marks and Quinney 1993). In two of the studies demonstrating a reduction in position sense acuity after fatigue, the effect was long-lasting (Saxton et al. 1995; Brockett et al. 1997). In these studies, fatigue was evoked by eccentric exercise, resulting in alteration of position sense for days. It has to be emphasized that the fatigue regime used by Saxton and co-workers (1995) and Brockett and co-workers (1997) induced delayed onset muscle pain and may not be representative for fatigue in working life.

In conclusion, findings of disturbed proprioception following muscle fatigue are frequent in the literature, but put together they are not entirely conclusive. For example, studies show great variability in the duration of the fatigue-induced effects, ranging from very short times (Taimela et al. 1999) to periods lasting days (Saxton et al. 1995; Brockett et al. 1997). These discrepancies most probably resulted from the different muscle contraction regimes used, with eccentric exercises used in the latter two studies. Longer lasting reduction in proprioceptive acuity may also be the result of fatigue evoked by low-intensity work, considering the different recovery times of LFF versus HFF (see above). Remarkably, there has been no study investigating this issue. Thus, one of the aims of this thesis was to address the effects on proprioception from fatigue resulting from low-intensity work tasks frequently found in working life (Papers I and II).

Muscle Stretching

Introduction

History of muscle stretching

It has been claimed that flexibility training was used in ancient Greek gymnastics for medical (prophylactic and therapeutic), military and athletic purposes (Alter 1996). For thousands of years, the Near Eastern and Far Eastern tradition has used stretching postures (so called *asanas*) in yoga, and stretching training as a vital component in developing skills in various martial arts (e.g., karate). When it comes to modern times, Weber and Kraus already in 1949 compared the effects of two stretching techniques on joint ROM (Weber and Kraus 1949). But it was within the rehabilitation of neurology deficits during the 1950's and 1960's that stretching techniques were developed as part of proprioceptive neuromuscular facilitation (PNF) treatment (Kabat and Knott 1953; Voss 1967). The stretching techniques either aimed to diminish muscle tone and improve the ROM or to enhance muscle tone in order to improve muscle function; all depended on the diagnosis of the patient. Shortly after the introduction of PNF, static stretching as employed for flexibility purposes in sports (de Vries 1962) and prolonged stretching for the treatment of contractures (Kottke et al. 1966) was introduced.

Different kinds of muscle stretching

In flexibility training, muscle-stretching techniques can be divided into dynamic flexibility training, such as ballistic stretching, and static flexibility training, such as static stretching (SS) and PNF techniques. This latter group is usually subdivided into contract relax (CR), agonist contract (AC), and the combination of the two in contract relax and agonist contract (CRAC) stretching techniques (Hutton 1993; Enoka 1994). Ballistic stretching is a dynamic and usually fast bouncing movement into the end-ROM of the joints of concern. Static stretching involves a slow-speed passive movement to the end-ROM, where the stretch torque is maintained. In CR, the muscles to be stretched are first isometrically contracted and then stretched according to SS. In AC, the agonist is contracted to produce the stretching force on the opposite target muscle(s) (antagonist). CRAC is performed as a CR stretch but with the assistance in the stretch by agonist contraction. Also, in clinical settings, more continuous and long-term stretching of soft tissues is performed with the help of orthoses and other devices (Schultz-Johnson 2002).

The PNF-stretch techniques were designed with the purpose to engage known basic reflex connections to promote the relaxation of the stretched muscles and thereby increase the ROM. However, some of the underlying assumptions have been shown to be incorrect (see *Neurophysiological effects of stretching* below).

The papers in this thesis (Papers III-VI) as well as those referenced in the following

background regard passive muscle stretching, i.e., the muscles undergoing stretch are in a passive non-contractile state.

Physiological effects of stretching

The terminology of muscle length-related terms is quite ambiguous in the stretching literature. For example, the terms “flexibility” and “muscle stiffness” may be used interchangeably, creating confusion as to what has been measured or discussed. Therefore, this section will begin with defining terms of frequent occurrence.

Flexibility

Flexibility is defined as the ROM about a joint (Kell et al. 2001), but could also involve more than one joint. Flexibility measures can be defined as active or passive ROM measures (Gajdosik and Bohannon 1987). The literature also divides flexibility into static and dynamic flexibility, referring to available ROM (typically tested isometrically) and the ease of movement within the obtainable ROM, respectively (Gleim and McHugh 1997). The use of the term “dynamic flexibility” in this context is unfortunate since there are more appropriate and well-defined expressions for the resistance during movement (see below). Another meaning of the term dynamic flexibility is “the ability to use a range of joint movement in the performance of a physical activity” (for references see Alter 1996).

Passive properties

When stretching a muscle, several different structures will be put under strain. In a gross anatomical view, the elongation will occur in the muscle and the intramuscular connective tissue rather than the tendon, which is substantially stiffer than the muscle (De Deyne 2001; see however Herbert et al. 2002). It should also be noted that different muscles exhibit a variety of passive properties depending on architectural factors such as pennation angle, ratio of muscle to tendon length, cross-sectional area etc. (Gareis et al. 1992), and fiber type composition, with slow twitch muscles being stiffer than fast twitch muscles (for references see Gajdosik 2001).

The passive properties accounting for the resistance of a muscle-tendon unit when passively stretched can be divided into series elastic components and parallel elastic components (Gajdosik 2001). Series elastic components can be further divided into contractile and non-contractile proteins. The contractile proteins mainly produce an initial resistance to passive stretch through so-called resting filamentary tension or short-range elastic component. This resistance is due to the existence, even in the passive muscle, of a small number of stable actin-myosin cross bridges which form and dissolve spontaneously (Hill 1968). This phenomenon of slowly cycling cross bridges is considered responsible for “muscle thixotropy”, a term used to describe the initial nonlinear behavior of muscle, which depends on the preceding history of contractions and length changes (Kostyukov and Cherkassky 1992; Proske et al. 1993)

(see *Neurophysiological effects of stretching* below). These phenomena also occur in intrafusal muscle fibers and may lead to history dependent “after-effects” in spindle discharges (Kosyukov and Cherkassky 1992; Proske et al. 1993). In addition to the tendon, the non-contractile series elastic components are composed of the sarcomere cytoskeleton proteins. In this group, the resistance to passive stretch has mainly been attributed to the giant protein of titin, but desmin may contribute as well. Titin is thought to contribute to the elongation resistance, particularly when the sarcomere is stretched beyond the actin-myosin overlap (for references see Gajdosik 2001).

The contribution to passive stretch resistance from the parallel elastic component is believed to originate in the extra-cellular connective tissues of the muscles. Particularly the perimysium, which appears crimped at resting length, has been shown to become uncrimped at longer muscle lengths and is believed to prevent over-stretching of the muscle fibers (Purslow 1989).

In conclusion, both intramuscular connective tissues and cytoskeleton sarcomere proteins account for the passive resistance during stretch. If and how these structures adapt to long-term stretch training is poorly understood.

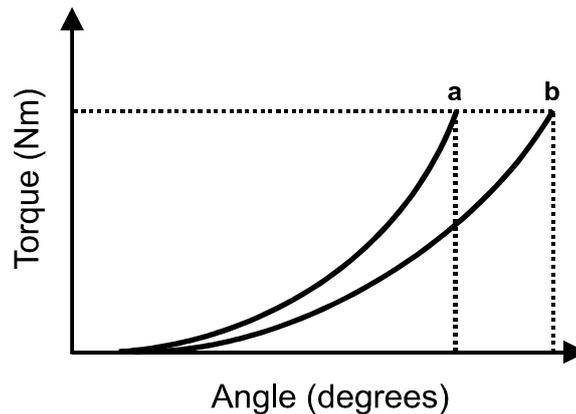
The resistance of skeletal muscles to stretch depends on both load and velocity, according to their *viscoelastic properties*. In clinical practice, *muscle tone* is measured as the resistance to passive movement, which may be tested either slowly in order to test for the load dependence to stretch (“elastic stiffness”), or by fast movements testing for “viscoelastic stiffness”, which is important in the assessment of spasticity (Simons and Mense 1998).

Muscular viscoelastic properties are also reflected in *stress relaxation*. When the muscle is stretched and held at a constant length, the tension or passive resistive force will gradually decline. Stress relaxation has been shown *in vivo* during hamstring stretch (Magnusson et al. 1995) and during calf muscle stretch (Duong et al. 2001; Kubo et al. 2002a). Another viscoelastic property is *creep*. When stretching a muscle with a fixed torque, the deformation will continue until it approaches a new length (Taylor et al. 1990). Creep may account for the immediate increase in ROM with therapeutic stretching (Gajdosik 2001). Viscoelastic tissue also shows *hysteresis*, which is the difference in the load-deformation relationship between loading and unloading (Taylor et al. 1990). In a stress-strain curve with loading and unloading, hysteresis is evident as a steeper curve at loading (stretching) than at unloading (return to the shortened length), i.e., a hysteresis loop. The area between the curves represents the energy loss while the area under the unloaded curve is the energy recovered in the elastic recoil (for reference see Kubo et al. 2002a).

Muscle Stiffness

Physically, the stiffness of a material is the relationship between stress and strain, and is expressed as the slope of the stress-strain curve. Correspondingly, muscle stiffness could be expressed in a load-elongation curve and defined as the slope of the linear

Figure 1. Graphic representation of passive muscle stiffness of a tight (*a*) and a flexible (*b*) person. The stiffness corresponds to the slope of the torque-angle curves. For a given torque the joint angle is greater in *b* compared to *a*.



portion of the curve, i.e., the ratio of the change in force to the change in length ($\Delta F/\Delta L$) (Gleim and McHugh 1997; Gajdosik 2001). Muscle stiffness can be passive or active, dependent on the absence or presence of significant EMG activity. Passive muscle stiffness in human studies is indirectly measured via changes in joint angles and therefore the operational definition of passive muscle stiffness is the slope of the torque-joint angle curve (Magnusson 1998). This is also the definition for passive muscle stiffness in this thesis. It should be noted that this definition more correctly denotes passive joint stiffness. A change in passive muscle stiffness could also be tested as a decreased passive resistance (torque) at the same joint angle, or if a greater joint angle can be achieved with the same resistance (torque) (Magnusson 1998), congruent with the evaluation of changed knee flexion ROM in Paper V of this thesis. Figure 1 shows an example of two passive torque – joint angle curves representing two subjects with different passive muscle stiffness.

In active stiffness, the muscle is activated at a particular level during the stiffness test. The activation may either be voluntary or reflex mediated (Akazawa et al. 1983). The degree of the reflex-mediated stiffness depends on the level of excitability of the α -motoneuron pool and the activity in the primary MSAs. It has been shown that the reflex-mediated stiffness contributes significantly to postural tasks and to the variability in overall muscle stiffness during dynamic movements (Akazawa et al. 1983; Toft et al. 1991). The reflex-mediated stiffness may decline after stretching due to the thixotropic properties of the muscle (Proske et al. 1993, see also *Neurophysiological effects of stretching* below). However, when it comes to slow passive stretching, the reflex-mediated stiffness is not likely to contribute to a great extent (Davidoff 1992), as repeatedly shown by negligible EMG activity during the stretch (McHugh et al. 1998; Magnusson 1998).

Effects of stretching on ROM and passive muscle stiffness

Stretching may increase the extensibility of soft tissues by two mechanisms. *Viscous deformation* is a mechanical phenomenon that most probably reverses over minutes

or hours, while *structural adaptations of muscles* are less readily reversible (Harvey et al. 2002). A structural adaptation is likely to entail changes in the passive muscle stiffness, but the length-tension curve (torque-joint angle curve in humans) may also get shifted to the right, with the slope of the curve being retained (Gajdosik 2001). However, a right-shift of the curve would still present as either an increased joint angle at the same torque or as a decreased torque at the same joint angle (Magnusson 1998, see also Figure 1). A further option to explain increased ROM following stretching is an *altered perception of stretch*, so that the subject can tolerate a higher torque after stretching (Magnusson 1998). This effect might occur without concomitant changes in passive muscle properties. Combinations of different mechanisms are also possible, of course.

There seems to be little doubt that stretching does increase joint ROM. Increased ROM has repeatedly been reported for SS and for PNF-stretching both after acute bouts of stretching (e.g., Etnyre and Abraham 1986a; Godges et al. 1989; Magnusson et al. 1996b; Halbertsma et al. 1996, Wiemann and Hahn 1997) and after long-term stretching training (e.g., Hardy 1985; Gajdosik 1991; Halbertsma and Göeken 1994; Magnusson et al. 1996a; Chan et al. 2001; see also reviews Magnusson 1998; Gajdosik 2001; Harvey et al. 2002). Thus, there is substantial support for the notion that muscle stretching exercises increase flexibility, but whether this effect results from changes in the material properties with reduced passive muscle stiffness is uncertain. Based on the finding of only a small transient effect of acute stretching on the viscoelastic behavior (see below), the idea that stretching might permanently change the material muscle properties has been questioned (Magnusson 1998). However, conclusions about long-term effects of stretching cannot really be drawn from acute effects since no correlation between the two has been reported (Toft et al. 1989).

The ROM may increase without a change in passive muscle stiffness, as shown by the fact that higher torques may be tolerated at the end-ROM (Magnusson 1998). Accordingly, acquired increases in ROM have been attributed to an increased stretch-tolerance as a short-term (Magnusson et al. 1996b; Halbertsma et al. 1996; Wiemann and Hahn 1997) as well as a long-term effect of hamstring stretching (Halbertsma and Göeken 1994; Magnusson et al. 1996a). However, Medeiros and colleagues (1977) showed a significantly increased ROM after an 8-day stretching regimen of the hamstring muscles (20 X 3 seconds/day), measured at the same resistive torque before and after the treatment. For the calf muscles, Muir et al. (1999) reported no effect on passive resistive torque at a certain angle after 4 X 30 seconds of static calf muscle stretch. In contrast, Rosenbaum and Hennig (1995) found an increased ankle-joint ROM combined with decreased passive muscle stiffness after 6 X 30 seconds SS of the calf muscles. Furthermore, Toft and co-workers (1989) showed a significantly reduced passive tension of the ankle 90 minutes after a bout of CR stretching of the calf muscles (total stretch time 40 seconds). They also observed that, after a 3-week stretching regimen, passive tension during ankle dorsiflexion was reduced by on average 12%. These findings corroborate those of Kubo et al. (2002b) who found a 13.4%

reduction in passive calf muscle stiffness after a 3-week SS regimen. Thus, there are disagreements between studies trying to discern between changes in viscous properties and changes in perception of stretch tolerance as the causes behind the stretch-induced increased ROM (see also reviews Magnusson 1998; Gajdosik 2001). Part of this discrepancy may reside in differences in the stretching-techniques and the study designs used, where intensity and time aspects seems to be critical. In a study of the effects of hamstring stretching on flexibility and passive resistance, a 4-week stretch-training protocol was compared to an 8-week protocol and control paradigms (Chan et al. 2001). The results revealed an increase in flexibility for both stretch-groups, but in contrast to the 8-week stretch-training group, the 4-week group showed a significantly increased resistance at the point of “maximum stretch without pain”. This indicates an association between the gain in flexibility and the increased stretch tolerance for the 4-week group, and changed material properties for the 8-week group. It is not far-fetched to assume that, in the study of Chan and co-workers (2001), the 4-weeks of stretching were insufficient for an adaptation of material muscle properties but sufficient for sensory adaptation, suggesting that increases in tolerance may precede plastic changes in the material properties after stretching. It is also likely that the threshold for adaptive material changes after stretching varies between individuals as well as between muscle groups, in part explaining more readily attainable material effects of the triceps surae muscles compared to the hamstrings. Much less is known about stretch effects on ROM and passive muscle stiffness of other clinically important muscle groups susceptible to tightness, such as the rectus femoris muscle (RFM) (cf. Gajdosik 1985). This issue was focused in this thesis (See Papers IV and V).

Structural adaptations

Muscle hypertrophy

In a study on chicken wing muscles, Frankeny and colleagues (1983) showed that 30 minutes of physiological passive stretch per day for 6 weeks increased muscle weight by 70%, muscle cross-sectional area by 60% and induced a fiber-type transformation from anaerobic to aerobic muscle fibers with a 72% increase of red fibers. The authors concluded that the trophic processes seen probably had a threshold duration less than 30 min/day for the stretch. The reversal of stretch-induced hypertrophy seems to follow a similar time course as the induction (Day et al. 1984). Muscle hypertrophy induced by passive muscle stretching has repeatedly been demonstrated in animal studies, and the body of knowledge of mechanisms behind the protein synthesis is constantly growing (see e.g., Yang et al. 1997; Sakamoto et al. 2003).

Addition of sarcomeres

Animal studies with immobilization of muscles in lengthened position show evidence of structural adaptations to increased muscle lengths, manifested by a shift to the right

of the passive length-tension curves without a change in slope, brought about by the addition of sarcomeres (see the following reviews for references: Gossman et al. 1982; Herbert 1988; De Deyne 2001; Gajdosik 2001). Conversely, immobilization of muscles in a shortened position leads to an even greater adaptation manifested by loss of sarcomeres, catabolism with a loss in weight, increases of connective tissue and a shorter and stiffer muscle (Herbert 1988). Contraction of shortened muscles increases the rate of these adaptations (Gajdosik 2001). Intermittent stretch has been shown to counteract negative adaptive changes of immobilized muscles in shortened positions. Passive stretches for 15 min every second day were sufficient to prevent the connective tissue remodeling (Williams 1988), and 30 min/day prevented the loss of sarcomeres (Williams 1990).

In humans, sustained muscle stretching can be achieved with the help of casts and orthoses. Even though this may be beneficial in the treatment of contractures, with 1-2 X 30 minutes orthosis-stretch per day for 1-3 months re-establishing elbow ROM (Bonutti et al. 1994; for review see Schultz-Johnson 2002), there is no evidence of sarcomere adaptations in humans (see however, Tardieu et al. 1979).

Retention of chronic increases in flexibility

The maintenance of stretching-acquired flexibility after the cessation of flexibility training is poorly understood. The maintenance of hamstring flexibility after 6 weeks of stretching was determined in two studies (Van Roy et al. 1987; Willy et al. 2001). The gain of flexibility was lost 2-4 weeks after the cessation of stretching. To retain the acquired hip-flexion flexibility, a 25 min stretching regime at least twice a week has been proposed (Van Roy et al. 1987). Wallin and colleagues (1985) showed that one stretching session per week was sufficient to maintain the improved flexibility in a preceding 30-day flexibility-training period (3 sessions/week). McCarthy and co-workers (1997) showed that a one-week CRAC stretching regimen for the neck muscles significantly increased the active cervical rotation ROM, but at re-test one week later, the baseline ROM was re-established. The scarcity of studies evaluating the retention of flexibility after long-term stretching training makes it impossible to draw any firm conclusions on this issue.

Neurophysiological effects of stretching

In humans, the α -motoneuron excitability, as assessed by the Hoffman-reflex (H-reflex), has been shown to be reduced during but not after soleus muscle stretch (Robinson et al. 1982; Etnyre and Abraham 1986b; Guissard et al. 1988). Robinson et al. (1982) could exclude skin and joint afferents as responsible for the decreased H-reflex. Guissard and co-workers (1988) showed that the inhibition was positively correlated to the magnitude of stretching, and that PNF-stretching resulted in a greater reduction of the H-reflex and greater increases in flexibility than an SS procedure. Recently, Guissard and colleagues (2001) showed that not only the H-reflex but also

an exteroceptive reflex, induced by electrical stimulation of mainly cutaneous afferents, and motor-evoked potentials were reduced during calf-muscle stretching of large amplitude. This indicated the operation of both pre- and postsynaptic mechanisms behind the reduced α -motoneuron excitability. The authors concluded that the postsynaptic inhibition dominated at larger stretching amplitudes, and suggested that the group Ib afferents from Golgi tendon organs supplied the major input for this inhibition.

Following large-amplitude muscle stretch, MSA activity has been shown to be reduced in both animal and human studies (for review see Proske et al. 1993). This effect has been attributed to the “muscle thixotropy” concept. If the stretch is sufficiently large, it will break pre-existing actin-myosin cross bridges, which then re-attach when holding the muscle at the longer length for a couple of seconds. At the release of stretch and passive return to the starting length, the muscle fibers fall slack (Jahnke et al. 1989). The presence or absence of slack in intrafusal fibers influences stretch responsiveness of muscle spindles and, consequently, the reflex EMG (Jahnke et al. 1989). The length of the thixotropic after-effects of a reduced MSA activity depends on what is done to the muscle after slack is formed. If left undisturbed, effects may last for up to half an hour (Morgan et al. 1984). When feeling more flexible after briefly stretching out arms and legs in the morning, muscle thixotropy effects may be the underlying mechanism (Proske et al. 1993).

It has repeatedly been shown that history dependent after-effects in intrafusal fibers (muscle thixotropy) affect proprioception (e.g. Wise et al. 1996). However, the effect of a bout of muscle stretching on proprioceptive acuity has not been directly investigated until the present thesis (Paper III).

The so-called PNF stretch techniques have for the most part been shown to induce greater improvements in joint ROM than the SS techniques, for both acute and chronic stretching (see reviews Magnusson 1998; Gajdosik 2001). The assumption behind the effectiveness of PNF techniques is that they should, via spinal reflex mechanisms, promote muscle inhibition and thereby reduce the resistance of the stretched muscles. However, even though PNF techniques have proven more efficient than SS, they seem to cause greater EMG activity in the stretched muscles than does SS (Magnusson 1998; Gajdosik 2001). An alternative explanation may be that PNF techniques increase the stretch tolerance more strongly than does SS (Magnusson et al. 1996b), but the underlying mechanism is unknown.

The significance of contractile activity on the resistance during ‘passive’ muscle-length tests and on the ROM of healthy subjects has been questioned due to repeated findings of negligible EMG activity (e.g., McHugh et al. 1998). However, recent reports showing altered joint ROM in humans during anesthesia implicate neural contributions to “passive” muscle flexibility (Krabak et al. 2001; Dompier et al. 2001).

In conclusion, the importance of the neurophysiological effects of stretching is not clear. Neurophysiological effects of stretching may play a greater role in pathological than in normal conditions (see *The effects of stretching on muscle cramp*

and spasm below).

Effects of muscle stretching on blood flow

It has been suggested that muscle stretching promotes circulatory and trophic changes in the stretched muscle (Leivseth et al. 1989). However, during static muscle stretch the blood flow is most likely compromised through alterations in capillary geometry and luminal diameter consequent to increased muscle sarcomere length (Poole et al. 1997; Kindig and Poole 2001). Yet, this does not exclude reactive hyperaemia at the release of stretch (S. Egginton, personal communication).

In animal studies, an intense stretching regimen was shown to present a mechanical stimulus to capillary growth/angiogenesis (Hudlicka 1998; Egginton et al. 1998; Gustavsson and Kraus 2001). Whether similar effects could be attained by more intense stretching paradigms in humans is not known. Leivseth et al. (1989) treated hip osteoarthritis patients with 25 min/day of passive muscle stretching of the adductor muscles for 5 days/week for 4 weeks, and found increased ROM, decreased pain and increased daily activity. Muscle biopsies showed increased type I and II fiber cross-sectional area and glycogen content after treatment. Unfortunately, muscle biopsies from the control leg were only taken before, but not after treatment, making it impossible to assess how much the increased daily activity contributed to the changes.

Stretching effects on muscle performance

Currently, there is a growing interest in investigating the effects of stretching on muscle performance. For example, the effects of stretching on maximal voluntary torque production (Handel et al. 1997; Kubo et al. 2001; Nelson et al. 2001a), on jump height (Church et al. 2001; Knudson et al. 2001; Young and Elliot 2001; Cornwell et al. 2002) and on running economy (Nelson et al. 2001b; Jones 2002) were recently investigated. The general outcome is that long-term stretch training programs enhance the performance (Wilson et al. 1992; Worrell et al. 1994; Handel et al. 1997). Wilson and colleagues (1992) showed that 8 weeks of stretching training improved the rebound bench press performance, particularly the initial concentric portion of the lift. It was suggested that this was due to increased utilization of elastic strain energy at the rebound, caused by reduced stiffness of the series-elastic component. In support of the notion of stretch-induced increase of reused energy during the stretch-shortening cycle, Kubo and co-workers showed a reduced hysteresis for the calf tendon and aponeurosis structures, assessed by ultrasonography, following acute (Kubo et al. 2002a) as well as long-term stretching regimens (Kubo et al. 2002b,c). However, after acute episodes of stretching, several authors report diminishing effects on jump height (Church et al. 2001; Young and Elliot 2001; Cornwell et al. 2002). A decrease in passive muscle stiffness and/or a depression of muscle activation were proposed as possible mechanisms for these acute effects. The possibility that stretching may induce changes in proprioceptive acuity, which in turn may affect movement performance,

has not been considered until the present thesis (see Paper III). The controversial findings on this topic indicate a highly complex relation of stretch-shortening cycle performance and mechanical musculoskeletal stiffness-related properties (Ettema 2001).

Therapeutical muscle stretching

A decreased ROM, restricted by soft tissue around a joint, is associated with many types of pathology, e.g., posttraumatic contractures, inactivity, musculoskeletal pain disorders, etc. Therefore, it is not surprising that muscle stretching is used in different disciplines, such as sports medicine, physical rehabilitation of musculoskeletal disorders and neurological disorders, and also in psychiatry as a means of general relaxation and in alternative treatment adjuncts such as Yoga. The main reason for the stretching treatment is to enhance the ROM, reduce muscle tension and promote muscle relaxation. However, any attempt at evaluating the effects of muscle stretching is hampered by the fact that stretching often constitutes one treatment modality within a multimodal treatment approach.

Clinical application of muscle stretching related to muscle pain

Muscle stretching is used as a treatment tool in *manual therapy* as well as in the *rehabilitation of muscle pain disorders*. Stretching on musculoskeletal pain patients may be indicated for different reasons, e.g., when a reduced ROM hampers necessary movements of daily life (see also the following sections below). Disorders in which muscle-stretch treatment may not be advocated include whiplash-associated disorders, acute disc herniations, infections, inflammatory and fibroblastic phases of soft tissue healing, malignancy, etc. Also, if the patient has severe muscle pain, stretching may be inappropriate or may require special techniques (see *Muscle stretching in myofascial pain syndrome* below).

The effects of stretching on muscle cramp and spasm

As suggested by Simons and Mense (1998), a muscle spasm can be defined as increased muscle activity, as reflected in increased EMG activity, which is not under voluntary control and is not dependent upon posture. It may or may not be painful. A muscle cramp is commonly considered to be a painful muscle spasm. Muscle cramps may occur in normal subjects under certain conditions (e.g., during a strong voluntary contraction-especially when the muscle is in shortened position, during sleep, during intensive exercise, during pregnancy) and in several pathological conditions, such as myopathies, neuropathies, motoneuron diseases, metabolic disorders or endocrine pathologies (Parisi et al 2003).

The ability of stretching to abolish muscle cramps is well known. Accordingly, muscle stretching has been suggested to prevent nocturnal leg cramps (Leclerc and Landry 1996; Kanaan and Sawaya 2001), cramps associated with other disorders and systemic diseases (Eaton 1989; McGee 1990; Riley and Antony 1995; Luther 2002), as well as exercise-induced muscle cramps (Bentley 1996). However, the mechanisms by which stretching relieves cramp are not clear. Ross and Thomas (1995) demonstrated an initial increase of motor unit activity, followed by a cessation, when a cramping muscle was stretched. The authors proposed the response pattern to be caused by a stretch-induced group Ia excitation of the motor units, followed by autogenic motoneuron inhibition exerted by increased activity of Ib afferents from Golgi tendon organs. The most effective way to abolish muscle cramp may be to assist the stretch by agonist contraction (AC) (Norris et al. 1957).

Muscle stretching in treatment and rehabilitation of muscle pain syndromes

The three concepts described below are common working hypothesis connected to the use of muscle stretching in the clinical setting. However, these concepts do not show a full picture of the use of stretching in disorders involving muscle pain. Also, the concepts somewhat overlap.

The muscle-imbalance concept

A common clinical finding in chronic muscle pain syndromes is an agonist-antagonist imbalance, where some postural muscles are tight, strong and hyperexcitable (without increased resting activity) and their antagonists are weakened and inhibited (e.g., Janda 1978). Suggested causes for the muscle imbalance pattern are poor posture and painful muscles with trigger points (Mense et al. 2001) and static work postures with asymmetric shortening of muscles due to prolonged contraction (Novak and Mackinnon 1997; Novak and Mackinnon 2002). For the latter suggestion, some support exists for adaptive shortening (see *Structural adaptations* above) as well as for the induction of pain or cramp of muscles that are exposed to prolonged contractions in shortened positions (see *The effects of stretching on muscle cramp and spasm* above). The proposed management of muscle imbalance is multi-factorial and depends on the underlying etiology of each specific case, but to reduce tightness via some stretching technique constitutes one of its cornerstones (e.g., Mackinnon et al. 1994; Mense et al. 2001). According to Jull and Janda (1987), the strength of the antagonistic weak muscles may be restored simply by treating and releasing the tight muscle, but experimental support for this notion seems to lack behind. Also, when it comes to deviations from normal posture, such as excessive lumbar lordosis, scoliosis, kyphosis, and abducted scapulae, there is a lack of experimental data to support the contention that exercise will correct such deviations (Hrysomallis and Goodman 2001).

Muscle stretching in myofascial pain syndrome

Myofascial pain syndrome in its specific meaning involves a syndrome supposedly caused by trigger points in the muscle (for references see Mense et al. 2001). The hypothesis behind the syndrome includes the *energy crisis hypothesis*: An initial insult, caused by, e.g., muscle overload, such as a mechanical rupture of the sarcolemma would release calcium that maximally triggers actin - myosin contractile activity. By way of hypothesized mechanisms, a maximum contracture in the vicinity of the motor endplate could be sustained without motor unit action potentials. This sustained contracture would increase the metabolic demand (Bruckle et al. 1990) and choke off local circulation. The local ischemia hinders the energy supply to the calcium pump, thus completing a *vicious circle* with a sustained endogenous contracture of the involved sarcomeres – a trigger point.

According to Mense et al. (2001), the energy crisis hypothesis also accounts for the observed effectiveness of stretch-treatment. Continued activity of the actin-myosin interaction depends on the physical contact between the molecules. Upon stretch to full muscle length, the molecules do not overlap anymore, and the contractile actin-myosin activity ceases, which may relieve the compression of capillaries and reduce the energy demand. Even though muscle stretching has a prominent role in the handling of myofascial pain with trigger points, the basis of its effectiveness has not been firmly established in experimental investigations. Stretching is believed to be especially effective in newly activated trigger points caused by a moderate overload, when used on its own or together with different augmentation techniques such as intermittent cold (“spray and stretch”) (for more reading on the topic see Simons et al. 1999; Mense et al. 2001).

In a study on 28 chronic low back pain patients diagnosed with myofascial syndrome, subjects were randomized to two groups, both receiving 2 weeks of a multimodal rehabilitation program, but the experimental group also receiving lumbar and thigh muscle stretching as an “add-on therapy” (Khalil et al. 1992). The stretching group showed significantly greater increases in back extensor strength, lumbar paraspinal EMG muscle activity during back extension and significant decreases in self-reported pain levels compared to the treatment group not receiving stretch-treatment. The lumbar EMG activity during back extension was increased immediately after each stretch-treatment and was cumulative in nature. For myofascial neck pain patients, stretching has been reported effective in increasing the pressure pain threshold, reducing the pain intensity and increasing the cervical ROM (Jaeger and Reeves 1986; Hanten et al. 2000; Hou et al. 2002). For the two latter studies the stretch was one part of two or more treatment adjuncts, which makes the relative importance of the stretch treatment in these studies hard to discern.

Optimizing the biomechanical condition

A further rationale for using stretching in the treatment of musculoskeletal disorders is to reduce the strain on painful joints by optimizing the biomechanics. For example,

the pain-reducing effect of stretching ilio-crural muscles on low back pain patients may be attributed to the reduction of the mechanical strain on hyperreactive segments of the low back (Blomberg 1993). However, this explanation is purely hypothetical, and the importance of flexibility in coping with chronic low back pain for subjects whose functional limitations are not severe has been questioned (Kuukkanen and Malkia 2000).

Stretching in short rest breaks

The introduction of short rest breaks to prevent monotonous loading of muscles during repetitive work in occupational settings has been of interest for decades. Breaks for rest may be used in e.g. computer work in order to change the temporal pattern of the work task and allow for periods of recovery from the monotonous load (van den Heuvel et al. 2003). The breaks can be passive or active, where active stretching breaks may be more advantageous in promoting worker productivity and well-being, as reported from a computer work place (Henning et al. 1997). Other studies also point out the benefits of active breaks, showing their ability to change muscle activity pattern in computer work, as assessed by EMG (Sundelin and Hagberg 1989), and to reduce the level of discomfort during the course of the working day in meatpacking plants (Genaidy et al. 1995). However, these studies are far from unequivocal, and the results of this kind of occupational intervention studies should be interpreted with caution, since they may suffer from low internal validity with problems, such as large drop-out rates (van den Heuvel et al. 2003) and compliance problems (Monsey et al. 2003).

Also, the ability to recover from muscle fatigue is of interest. An experimental animal model has shown that muscles held at shortened position fatigue faster upon stimulation than muscles held at optimum length (Jones 1996). This effect was attributed to the movement restriction and accumulation of K^+ in the lumen of the t-tubules. The recovery from fatigue was accelerated by muscle lengthening. The reason to why muscle lengthening augmented the recovery was suggested to an enhancement of the K^+ diffusion out of the t-tubules (Jones 1996). To what extent this applies for human occupational fatigue is not known.

Pain alleviation through endogenous antinociceptive systems

One way to alleviate pain is to reinforce the endogenous antinociceptive systems of the CNS. The CNS pain-modulating systems can either suppress or enhance the transmission of nociceptive information. The suppression of nociception engages several levels of the CNS, involving supraspinal descending inhibition, propriospinal heterosegmental inhibition and segmental spinal inhibition (for review see Sandkühler 1996). The latter two concern spinal inhibitory systems referred to as *Gate Control* and *Diffuse Noxious Inhibitory Control*, while the former involves several *descending pain modulating systems* distributed throughout the forebrain, diencephalon, brainstem and spinal cord (Windhorst 2003). The gate-control theory, originally proposed by Melzack and

Wall (1965), posits that the activation of large diameter primary sensory afferents may inhibit the transmission of nociceptive signals through wide dynamic range projection neurons. For example, pain alleviation following transcutaneous electrical stimulation can be explained by the gate-control theory. Diffuse noxious inhibitory control (Le Bars et al. 1979) is based on a propriospinal heterosegmental inhibitory system, by which “counterirritation” on a distant part of the body may inhibit the pain evoked by nociceptive stimuli in another part.

Studies on the effects of cutaneous afferent stimulation on spinal nociceptive transmission are abundant (e.g., De Koninck and Henry 1992; Garrison and Foreman 1996). In contrast, much less is known about the ability of muscle afferents to contribute to endogenous antinociception on the level of the spinal cord. Pain alleviation through muscle stretching is usually explained by peripheral actions against factors underlying the stimulation of nociceptors, such as breaking local sarcomere contractures of painful muscles (see *Muscle stretching in myofascial pain syndrome*), or by reflex inhibition of α -motoneurons, such as stretch-induced autogenic motoneuron inhibition in muscle cramps (see *The effects of stretching on muscle cramp and spasm*). Rather surprisingly, the possibility of muscle-stretch induced pain inhibition through spinal inhibitory mechanisms is seldom considered. Therefore, in Paper VI an experimental animal model was used to check for the possibility of interactions between mechanical (stretch) innocuous and chemically induced noxious muscle afferent inputs on discharge behavior of nociceptive dorsal horn neurons. The chemical chosen for the noxious muscle afferent input was bradykinin, an endogenous algescic substance known to accompany tissue damage and inflammation (Dray and Perkins 1993).

AIMS

Even though exposure-response relations revealed by epidemiological studies have pointed towards possible underlying mechanisms of CWRNDs, a basic science approach is necessary to confirm and validate them. Once established, they could significantly contribute to the advances in prevention, treatment and rehabilitation of CWRNDs. The present thesis attempts at expanding the knowledge on the proprioceptive effects of prolonged repetitive low-intensity work, an exposure that could induce CWRNDs. The thesis also explores the effects of muscle stretching on sensory mechanisms and nociception. Before the importance of stretching for the prevention, alleviation and/or treatment of work-related neuromuscular pain can be adequately assessed, a better understanding of the mechanisms of stretching and the pathophysiological mechanisms behind the work-related disorders are needed.

General objectives:

- To test the impact of repetitive work exposure on the position sense.
- To examine effects of muscle stretching (especially sensory effects and effects on muscle nociception) and to relate its application to the prevention, alleviation and/or treatment of CWRND.

Specific aims of the thesis:

Paper I

To investigate, the effect of repetitive low-intensity arm work to fatigue on the position sense acuity of the shoulder, in a simulated occupational laboratory setting.

Paper II

To test if there is a relation between exposure time to repetitive low-intensity arm work to subjective fatigue and the retention time of the subjective fatigue. Also, to test (i) if working time to subjective fatigue predicts the extent of changed position sense acuity of the shoulder and (ii) if retention time of the subjective fatigue predicts the extent of changed position sense acuity of the shoulder.

Paper III

To investigate the effect of acute muscle stretching on position sense acuity of the shoulder.

Papers IV and V

To compare the reliability and validity of two methods to test the stretchability of the RFM (Paper IV), and to evaluate the effects of an RFM stretching regimen on knee

flexion ROM and subjective stretch sensation for the anterior aspect of the thigh (Paper V).

Paper VI

To investigate interactions between innocuous muscle stretch and nociceptive chemical stimulation on discharge behavior of nociceptive dorsal horn neurons.

METHODS

Position sense studies (Papers I-III)

All experiments were performed on healthy subjects and were approved by the Ethical Committee at the faculty of Medicine at the University of Umeå, Sweden. The experiments were performed after obtaining informed consent from each subject.

Subjects

In Paper I, 26 subjects (24.6 ± 3.1 years) participated. Seventy two subjects (26 ± 6.6 years) participated in Paper II and 18 subjects (24.2 ± 2.6 years) in Paper III. For all studies, males and females were equally represented in both number and age.

Study design and experimental protocol

Paper I

The study had a repeated measures design with two position sense tests before and one after the intervention (repetitive work). The position sense tests were performed for the right shoulder.

The subjects were divided into a primary group (18 subjects) and a supplemental group (8 subjects). The primary group performed the position sense test procedure three times – twice before and once after the repetitive work task. The time intervals between the tests were the same. After having assured reliability for the position sense test for the primary group (pre test 1 versus pre test 2), the first position sense test was omitted for the supplemental group. Another addition was that subjects of the supplemental group performed the work task while shoulder EMG was monitored throughout and furthermore these subjects performed MVC and static test contractions before and after the work task.

Paper II

The study design was a randomized experimental design with a matched control group. The subjects were assigned into pairs, matched for age and gender. Each of the subjects of a pair was randomly assigned to either a work or a control group. The experimental protocol for the work group consisted of position sense testing before and after performing a repetitive work task to fatigue. The protocol for the control group was the same as for the work group, with the exception that the controls were resting while those of the experimental group worked.

Paper III

Subjects were tested for position sense acuity of the right shoulder before and after two different stretch procedures, and before and after a control procedure.

A prospective 3x3-crossover design was used. The subjects were tested on three

	<u>A</u>	<u>B</u>	<u>C</u>
Test occasion 1:	CON	AG-STRETCH	ANTAG-STRETCH
Test occasion 2:	AG-STRETCH	ANTAG-STRETCH	CON
Test occasion 3:	ANTAG-STRETCH	CON	AG-STRETCH

Figure 2. A schematic of the study design. For all three groups of subjects (A, B, and C), position sense tests of the shoulder were done before and after stretching of agonist muscles (AG-STRETCH), stretching of antagonist muscles (ANTAG-STRETCH) and resting as a control procedure (CON).

occasions with each occasion accounting for a different test condition. The conditions were passive stretching of agonist muscles (AG-STRETCH), passive stretching of antagonist muscles (ANTAG-STRETCH), and a control procedure (CON) (for explanation of each condition, see *Intervention: Muscle stretching (paper III)* below). Subjects were randomized to group A, B or C in designation of the sequence of the test conditions. Figure 2 shows a schematic illustration of the study design.

Position sense apparatus and testing procedure

In Papers I, II and III the same position sense apparatus was used (see Figure 3 to the left), but the testing procedure differed slightly. Subjects were seated blindfolded in the testing apparatus wearing headphones. The system was composed of a steady chair and a motorized rig for the arm. A receiver attached to the rig and a stationary electromagnetic transmitter were used to monitor limb position. A switch in the subjects' left hand signaled the PC to stop rotation of the rig when pressed by the subject.

In this thesis all position sense tests were conducted from specific start positions to pre-determined target positions. Figure 3 (right diagrams) demonstrates the angular orientations for Papers I, II and III, respectively. The tests were performed as follows: From the starting position, the subject actively moved the arm horizontally until a command to "Stop" was given. The rig was then locked and the arm remained at this target position for five seconds. Then the subject actively returned to the starting position. Next the subject was instructed to actively move the arm to match the target position. When the subject considered the arm to be at the target position he/she pressed the switch in the left hand. The number of trials to each target position for the respective study is indicated in the legend of Figure 3. The presented order of the target positions was randomized.

EMG, MVC and static test contractions (Paper I)

For the supplemental group EMG electrodes were placed on the anterior and middle and posterior deltoid muscles, biceps, triceps, and descending trapezius muscles. MVC and consequently, maximal voluntary electrical activity (MVE), were measured in the

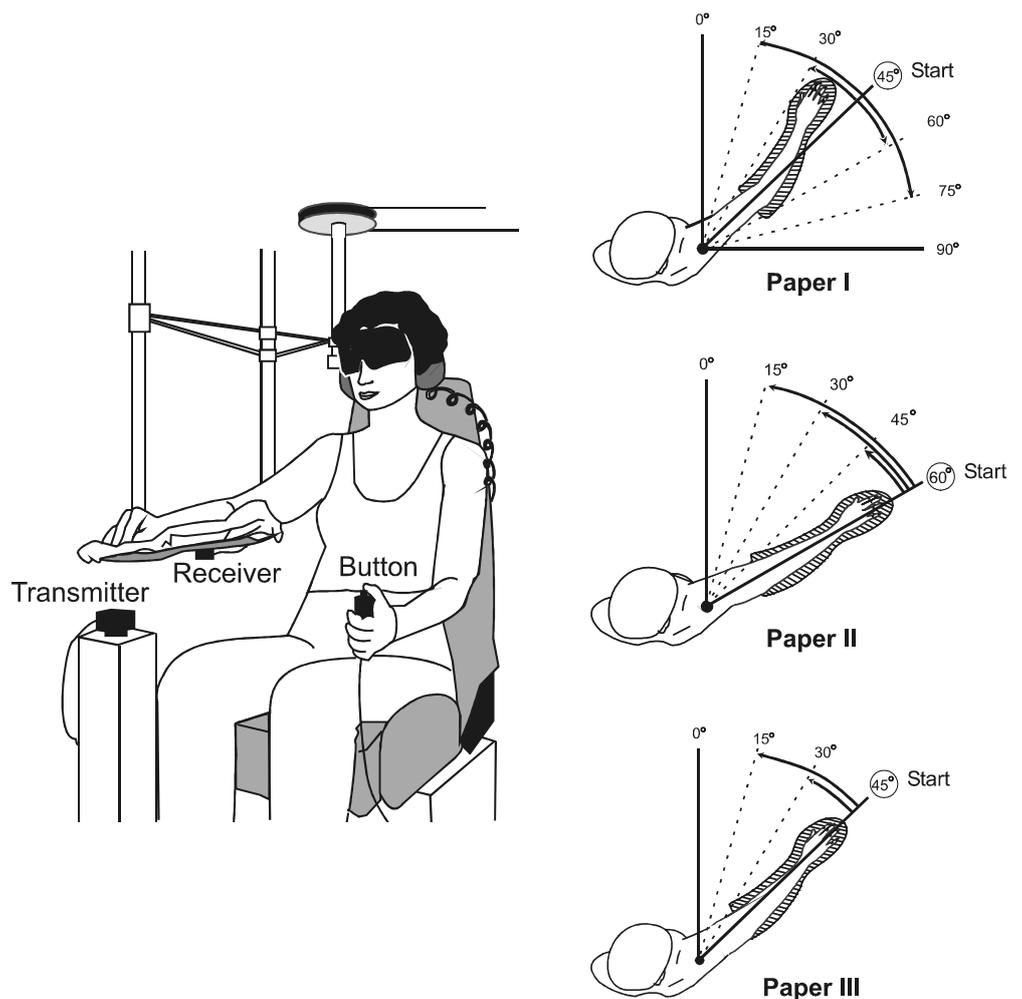


Figure 3. Schematic of a blindfolded subject seated in the position sense testing device with the arm resting on the motorised rig (left diagram). Refer to text for a detailed description of other components of the testing device. The right diagrams depict respective start positions and range of motions for target positions (extent of curved arrows) for Papers I-III. The number of trials for each target position was 6 for Paper I, 8 for Paper II, and 6 for Paper III.

and consequently, maximal voluntary electrical activity (MVE), were measured in the beginning and at the end of the test. While seated with the arm at 90° abduction the subject maximally lifted the arm in a vertical plane. The wrist was connected via a strap to a force transducer located on the floor. In addition, a static test contraction was performed immediately before and after the repetitive work task by holding out the right arm in 90° abduction in the scapular plane for 15 sec.

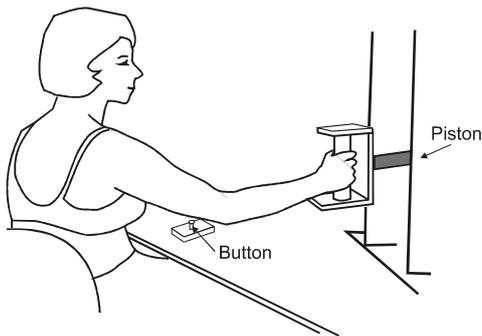


Figure 4. A schematic illustrating the simulated occupational work station and task. While seated subjects were required to push the piston and press the button with the use of a hand held manipulandum. These actions were performed in a continuous movement and to a designated time point according to the criteria set forth in Papers I and II, respectively.

Intervention: Repetitive work task (Papers I and II)

The subjects sat at a table and performed a repetitive work task consisting of pushing a piston and pressing a button with the use of a hand-held manipulandum weighing 300 grams (Paper I), and 220 grams (Paper II) (Figure 4). Subjects were required to work for at least 10 min and to continue until a certain level of fatigue in the area of the neck/shoulder/arm was reached. The criterion used for fatigue was based on subjective rating of 7 or greater on a category rating scale (0 = no fatigue, 10 = extreme fatigue; Borg 1982). In Paper II, the work task was also stopped if the critical level of fatigue was not reached within 59 min (4 subjects). Another assessment of fatigue was registered directly following the position sense test performed after the repetitive work task. This last rating was acquired in order to assess retention of the subjective fatigue (RFS)(Paper II).

Intervention: Muscle stretching (Paper III)

The stretching method used was the CR method (see *Introduction, Different kinds of muscle stretching* above). Figure 5 demonstrates AG-STRETCH and ANTAG-STRETCH. The stretching time was 3x20 sec with each 20-sec period preceded by 5 sec submaximal isometric contraction of the target muscles. In the control condition (CON), subjects rested for 5 minutes.



Figure 5. (a) Agonist (AG-STRETCH) shoulder muscle stretching in the direction of horizontal abduction. (b) Antagonist (ANTAG-STRETCH) shoulder muscle stretching in the direction of horizontal adduction.

Outcome variables of the position sense test

The difference between the reproduced position and the target position was determined for each trial (algebraic errors). To assess the response variability of the position sense, the standard deviation of algebraic errors, i.e. the variable error (VE), was calculated for each position sense test (before and after each test condition separately) and for each target position (Papers II and III). To estimate the overall accuracy of the position sense, the absolute error (AE, the mean of the absolute values of the algebraic errors) was determined (Papers I-III).

Effects of muscle stretching – Rectus femoris muscle (Papers IV and V)

The experiments were performed on healthy subjects and were approved by the Ethical Committee at the faculty of Medicine at the University of Uppsala, Sweden. The experiments were performed after obtaining informed consent from each subject. In Paper IV, intratester reliability and validity were determined for two methods for testing the stretchability of the RFM – a common clinical method (CCM), and a newly developed method (NDM) (Figure 6a and b). In Paper V, the NDM was used to evaluate the effect of a stretching regimen on passive knee flexion ROM and on subjective stretch sensation.

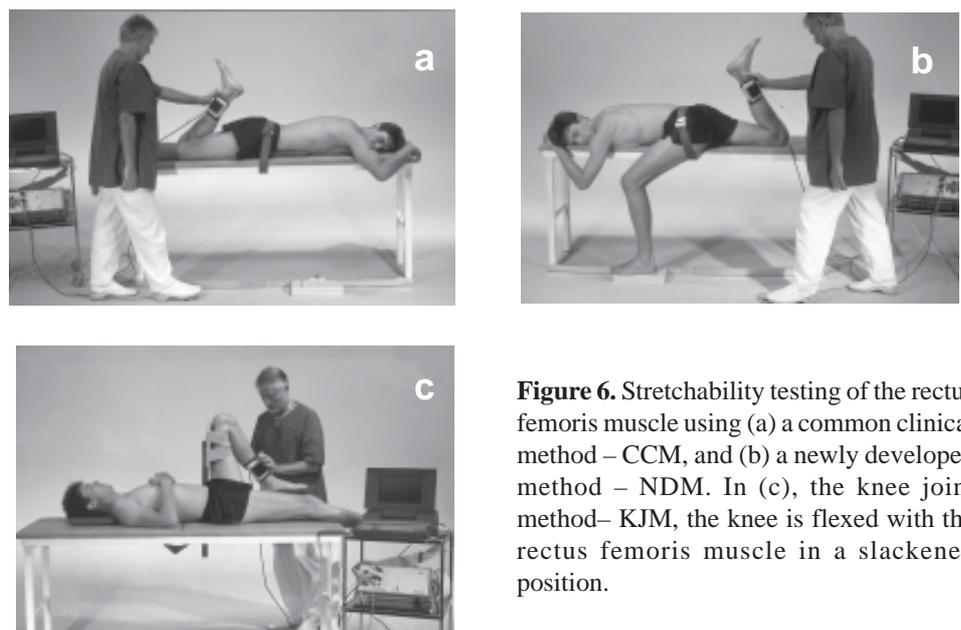


Figure 6. Stretchability testing of the rectus femoris muscle using (a) a common clinical method – CCM, and (b) a newly developed method – NDM. In (c), the knee joint method– KJM, the knee is flexed with the rectus femoris muscle in a slackened position.

Subjects

In Paper IV, a random sample of 71 subjects (35 males and 36 females), born in 1970 and registered in Uppsala, participated in the test-retest of the RFM stretchability, whereas 3 males and 3 females (mean age 30, range 19 to 45) participated in the X-ray investigation (a part of the validity assessment). Thirty one male military conscripts (20.8 ± 0.6 years) participated in Paper V.

Study design and experimental protocol

Paper IV

A test-retest design (test-interval 3.6 ± 3.3 days for the RFM assessment and 5 days for the X-ray assessment) was used to determine intratester reliability of two methods to assess stretchability of the RFM. Three validity criteria, based on anatomical and biomechanical principles, and could therefore together be looked upon as content validity, were also set up for comparison between the methods. The criteria were;

- i) **specific**: the method should isolate the movement to the knee joint with the pelvic stabilized, tested in X-ray.
- ii) **restrictive**: the movement imposed by the method should ideally only be constrained by the soft tissues tested, i.e., knee flexion ROM in the method should differ from the knee flexion ROM of the joint as tested when the RFM was slackened (knee joint method-KJM, see Figure 6c)
- iii) **sensation creative**: the ability of the method to create a sensation of stretch confined to the anterior aspect of the thigh, when testing knee flexion ROM with the same applied torque in both methods. The stretch sensation was quantified by subjective ratings of the stretch sensation on a Borg scale (Borg 1982).

Paper V

The study was arranged as a 2 x 2 crossover design comprising 2 treatment paradigms (experimental and control/sham treatment) and 2 intervention periods. Subjects were divided into 2 groups and data were acquired on 5 test occasions extending over 9 ½ weeks. The measurements on test occasions 1 and 2 were used to assess the test-retest reliability. Figure 7 shows a schematic of the study design.

Method to assess stretchability of the RFM (Papers IV and V)

Passive knee flexion ROM, as a quantitative measure of the stretchability of the RFM, was determined with the same applied torque that was specific for each subject at all tests. Prior to the tests, the specific applied torque was determined with the NDM at a rating of 5 on the Borg scale, and subsequently stored in the computer. An electronic goniometer and a pressure transducer were connected to the computer so that the angle of knee flexion was registered when a passive resistance equal to the specific

Test occ:	1	2	3	4	5
Activity:	<i>No intervention</i>	<i>Intervention period 1</i> Group A: Experimental treatment Group B: Control treatment	<i>Wash out</i>	<i>Intervention period 2</i> Group A: Control treatment Group B: Experimental treatment	
Time (weeks):	0	2.5	4.5	7.5	9.5

Figure 7. A description of the experimental design for Paper V, evaluating the effects of a 2-week stretching regimen on passive knee flexion ROM and on subjective stretch tolerance.

applied torque was reached. The test leader was blinded regarding the ROM measurements.

Test procedure Paper IV

Three trials of ROM during knee flexion were performed in each method, with the previously determined specific applied torque. Subjects were first tested in KJM - knee joint method, whereas the test order of CCM and NDM was randomized. The same test order was applied at the second test occasion (retest). Simultaneously with the measurements of knee flexion, subjects rated the stretch sensation at the anterior aspect of the thigh on the Borg scale. In the X-ray assessment, the inclination of the sacrum in the sagittal plane was determined from the X-ray film at the start and end position of each method.

Test procedure Paper V

The NDM with the same specific applied torque for each subject was used at each test occasion. In total, 6 measurements of knee flexion (3 on each leg) were acquired per subject. Simultaneously with the knee flexion measurements, subjects rated the stretch sensation at the anterior aspect of the thigh on the Borg scale. The mean was calculated to represent a single knee flexion value and a single Borg scale value per subject and per test occasion.

Intervention: Muscle stretching (Paper V)

The experimental treatment consisted of CR stretching of the RFM performed as supervised group training 4 times a week during the 2-week long intervention period. The control treatment consisted of stretching the calf muscles with the same frequency and duration as the experimental treatment.

Effects of muscle stretching – The animal model (Paper VI)

Animals, anaesthesia and surgery

All procedures were performed in accordance with principles of laboratory animal care, Swedish laws, and approved by the Ethical Committee on animal experiments, Umeå University. Experimental data were obtained from 11 adult cats. Initially, the cats were anaesthetized with i.p. injection of pentobarbital sodium supplemented by additional i.v. doses as required to maintain a full surgical anaesthesia. Anaesthesia was discontinued after decerebration. The gastrocnemius medialis and lateralis muscles were dissected free, their distal tendons detached and connected to an electromagnetic puller. The innervation of both muscles was preserved, while the rest of the hind limb was completely denervated. A branch of the sural artery was cannulated to permit i.a. injection of test solutions into the gastrocnemius muscles. A laminectomy was performed between L2 and S2. All animals were paralyzed (Gallamine Triethiodide, Wellcome, 10 mg/kg) and three animals were also spinalised at the T8 level.

Recording procedure

High impedance glass microelectrodes were used for single-unit recordings of superficial dorsal horn neurons (SDHNs) located within the L6–S1 spinal segments, from a depth of up to approximately 1000 µm. SDHNs were discerned from the activity in primary afferents on the basis of the amplitude and shape of the action potentials as well as the inability to follow high-frequency stimulation and the number of spikes evoked by a single electrical stimulation pulse. The selected SDHNs were classified as nociceptive, specific or multireceptive neurons on the basis of their responses to an identification procedure that included innocuous, physiological muscle stretch and light pressure and noxious pressure with serrated forceps applied by hand to the gastrocnemius muscle and tendon.

Experimental protocol; chemical and mechanical stimulation

The SDHNs were tested with innocuous mechanical (muscle stretch) and noxious chemical (i.a. bradykinin injection) stimulation, and the combination of the two (bradykinin injection immediately followed by stretch). At least 30 min elapsed between the bradykinin injections.

(I) Innocuous mechanical stimulation—trapezoidal muscle stretch:

The overall amplitude of the trapezoidal stretch was 14 mm divided into three levels (at 12, 13 and 14 mm, respectively). The third level reached 1 mm below the maximal physiological length (determined in situ). The passive tension at the third level never exceeded 3 N. Each of the three levels was kept for 5 sec, creating a complete stretching-cycle of 23 sec (including 8 sec for the ramp and release phases).

(II) Noxious chemical stimulation—bradykinin injection:

Bradykinin (50 μ g/ml) dissolved in Tyrode's solution was injected into the arterial supply of the gastrocnemius muscles (0.5–1 ml). Each test injection was preceded by a control injection of Tyrode's solution.

(III) Combination of noxious chemical and innocuous mechanical stimulation:

Bradykinin injection immediately followed by two trapezoidal stretching cycles.

Data processing

The response profile of SDHNs to different stimuli was evaluated by constructing time histograms with bin width of 1 sec. Subsequently, on the time histogram, the duration of a response was determined as the period during which the cell activity differed from the preceding mean discharge rate calculated over 30 sec before the test stimuli. A minimum of 10 sec of steady cell discharge had to elapse in order to be considered that the cell resumed baseline activity. The magnitude of SDHN response to bradykinin alone or in combination with stretch was estimated by calculating and comparing the area of the histograms in the different test procedures.

RESULTS

Paper I

All subjects endured the work task and thereby satisfied the criteria of the experiment without experiencing severe discomfort. Nineteen of the 26 subjects had reached a Borg scale rating = 7 at the end of the 10 min work task, whereas for the remaining 7 subjects (4 females, 3 males) the work continued to between 11 and 28 min.

Position sense test

In the following presentation, the incorrectness of the originally reported results concerning the overall gender difference of the position sense test, has been rectified (see Paper I and the appendix to Paper I). In the re-appraisal, the overall gender difference was the single factor that changed substantially, i.e., became non significant from originally being significant. The outcome of all other statistical calculations remained essentially the same. Therefore, the p-value for “gender” reported below is the only factor that is changed from the originally reported results in Paper I.

Figure 8 shows pre and post fatigue comparisons for AE for males and females. A repeated-measures two-way analysis of variance revealed an overall significant increase in AE for post as compared to pre fatigue ($p < 0.001$). The overall difference between gender and the interaction between the factors “occasion x gender” was not significant ($p = 0.15$ and $p = 0.38$, respectively). This indicates that AE for both males and females were similarly increased after fatigue.

EMG and MVC (workload)

Relative to MVE recordings, workloads were 15.5% (females 17.0%, males 14.0%) for the middle deltoid and 15.5% (females 12.0%, males 19.0%) for the descending

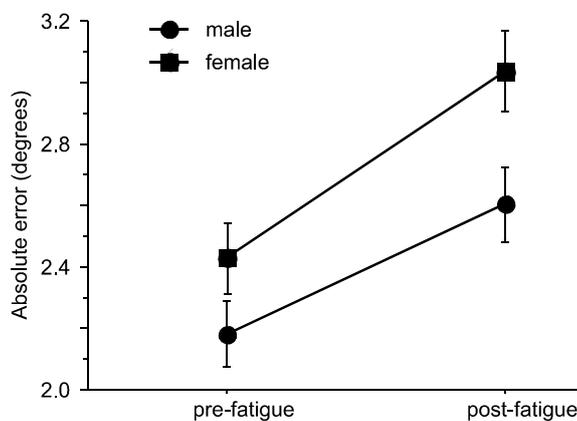


Figure 8. Absolute errors (AE) for males and females before (pre-fatigue) and after (post-fatigue) the repetitive work task.

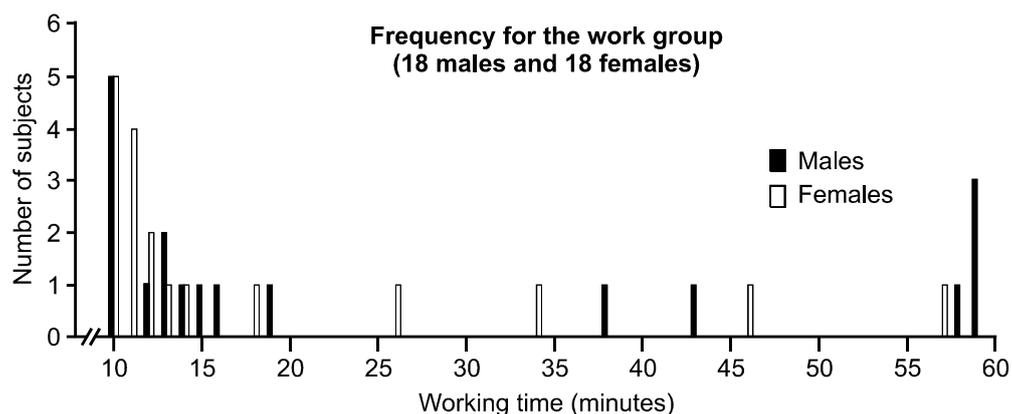


Figure 9. Histograms illustrating frequency distribution of working time for males and females.

trapezius. Mean power frequency during test contractions decreased after the repetitive work for all muscles tested. In accordance with the area of most subjective discomfort, the percentage decrease was $21.4 \pm 9.2\%$ ($p < 0.001$), $18.7 \pm 10.7\%$ ($p < 0.01$) for the anterior and middle deltoid muscles, respectively. The corresponding value for the posterior deltoid was $16.0 \pm 11.2\%$ ($p < 0.01$), for the biceps $10.9 \pm 18.6\%$ ($p = 0.09$), for the triceps $8.8 \pm 10.1\%$ ($p < 0.05$) and for the descending trapezius muscle $1.9 \pm 5.3\%$ ($p = 0.33$). The changes for the biceps and the descending trapezius muscles were not significant.

Paired t-test showed that the MVC decreased significantly from 59.9 ± 23.8 Nm before to 57.2 ± 23.9 Nm after the repetitive work task ($p < 0.05$).

Paper II

Working time for the subjects (Figure 9) ranged between 10-59 min (median (q1-q3); 13.0 (10.0-32.0) min). The spread of working times were greater amongst males (median (q1-q3); 14.5 (10.0-46.8) min) than females (median (q1-q3); 11.5 (10.0-20.0) min), but the difference was not significant ($p = 0.21$, two-sample Wilcoxon rank sum test).

Effect on retention of subjective fatigue from working time

The results of the regression analyses for retention of the subjective fatigue (RSF) with working time as main predictor, for the whole group and for both genders separately are displayed in Table 1. A longer working time to fatigue predicted a greater RSF for the whole group. The separate regressions for males and females revealed that this effect was present only for males.

Table 1.

Main predictor	Response	Adj. R^2	P -value model	P -value predictors
WORKING TIME	RSF-total (N=36)	0.36	< 0.001*	< 0.001* 0.27 (gender)
	RSF-males (N=18)	0.57		< 0.001*
	RSF- females (N=18)	-0.06		0.74

Table 2. Associations tested by multiple regression analyses of main predictors and the position matching response variability. Significant P -values are indicated with *.

Main predictor	Response	Adj. R^2	P -value model	P -value predictors
WORKING TIME	15°-total (N=27)	0.086	0.129	0.066 0.605 (gender)
	15°-males (N=15)	0.271		0.027*
	15°- females (N=12)	-0.085		0.715
RSF	15°-total (N=27)	0.150	0.055	0.024* 0.669 (gender)
	15°-males (N=15)	0.247		0.034*
	15°- females (N=12)	0.050		0.237
WORKING TIME	30°-total (N=36)	0.019	0.276	0.132 0.386 (gender)
	30°-males (N=18)	0.042		0.205
	30°- females (N=18)	-0.043		0.595
RSF	30°-total (N=36)	-0.044	0.768	0.616 0.521 (gender)
	30°-males (N=18)	-0.051		0.675
	30°- females (N=18)	-0.062		0.942
WORKING TIME	45°-total (N=36)	-0.019	0.514	0.529 0.281 (gender)
	45°-males (N=18)	-0.010		0.376
	45°- females (N=18)	-0.058		0.804
RSF	45°-total (N=36)	0.018	0.281	0.208 0.195 (gender)
	45°-males (N=18)	0.046		0.197
	45°- females (N=18)	-0.062		0.977

Effect on position matching from retention of subjective fatigue and working time

For the position matching, some dropouts occurred for the short target. This was due to a tendency for the criterion movements to exceed the set limit for this target position, which reduced the number of valid trials. Thus, six females and three males were excluded from the analysis for the short target position.

Change in position matching response variability (VE)

Table 2 displays the results for the regression analyses for relative change in position matching response variability (VE) for each target position separately (main predictors “working time” and “RSF” in separate regressions). For the short target position (15°), a longer working time predicted an increase in position matching VE, but only for males. Also for the short target position, a greater RSF predicted an increase in position matching VE for the whole work group and for males, but not for females. Neither of the regressions for the intermediate nor for the long target positions revealed any significant predictors.

Relative change in position matching overall acuity (AE)

Table 3 displays the results for the regression analyses for relative change in the absolute error (AE) of the position matching for each target position separately (main predictors “working time” and “RSF” in separate regressions). For the short target position (15°), the results for AE resembled the VE results. Thus, for this target position, a longer working time predicted increased AE, but only for males. Also for the short target position, greater RSF predicted increased AE for the whole group and for males, but not for females. For the intermediate target position, working time predicted increased AE for the whole work group. Neither of the regressions for the long target position revealed any significant predictors.

Paper III

In Paper III, the effect of stretching was assessed on both the response variability (analyses of VE) as well as the overall accuracy (analyses of AE) of the position sense tests.

Table 4 shows the mean VE and AE of the position sense tests *before* and *after* the stretch-interventions for each target position. The relative change *before* to *after* the stretch interventions were not different to the control, as assessed with one-sample t-tests.

For the response variability, a multivariate repeated measures two-way analysis of variance revealed no overall difference between interventions ($F_{4,10} = 1.36, p = 0.31$), test sequences ($F_{4,24} = 0.50, p = 0.73$) or in the interaction “intervention x sequence” ($F_{8,20} = 0.92, p = 0.52$) in relatively changed VE of the position sense test *before* to *after* the interventions.

Table 3. Associations tested by multiple regression analyses of main predictors and the position matching overall acuity. Significant P-values are indicated with *.

Main predictor	Response	Adj. R^2	P-value model	P-value predictors
WORKING TIME	15°-total (N=27)	0.052	0.201	0.174 0.164 (gender)
	15°-males (N=15)	0.544		0.001*
	15°- females (N=12)	0.120		0.145
RSF	15°-total (N=27)	0.186	0.032*	0.020* 0.092 (gender)
	15°-males (N=15)	0.331		0.015*
	15°- females (N=12)	-0.045		0.501
WORKING TIME	30°-total (N=36)	0.145	0.028*	0.050* 0.161 (gender)
	30°-males (N=18)	0.120		0.087
	30°- females (N=18)	-0.013		0.388
RSF	30°-total (N=36)	0.119	0.046*	0.090 0.190 (gender)
	30°-males (N=18)	0.081		0.133
	30°- females (N=18)	-0.035		0.521
WORKING TIME	45°-total (N=36)	0.056	0.147	0.436 0.113 (gender)
	45°-males (N=18)	-0.057		0.783
	45°- females (N=18)	-0.010		0.373
RSF	45°-total (N=36)	0.038	0.199	0.923 0.083 (gender)
	45°-males (N=18)	-0.062		0.975
	45°- females (N=18)	-0.060		0.857

For the overall acuity, the analysis revealed no overall difference between interventions ($F_{4,10} = 0.26, p = 0.90$), test sequences ($F_{4,24} = 0.54, p = 0.71$) or in the interaction “intervention x sequence” ($F_{8,20} = 1.61, p = 0.19$) in relatively changed AE of the position sense test *before* to *after* the interventions.

Table 4. Mean VE (top) and AE (bottom) for target positions from position sense tests before, after and the relative change for the interventions AG-STRETCH and ANTAG-STRETCH.

		Mean VE ($\pm 1SD$)			After/Before ^{intervention} minus After/Before ^{control}
		Before	After	After/Before	
AG-STRETCH	15°	1.23 \pm 0.52	1.48 \pm 0.69	1.36 \pm 0.86	0.28 \pm 1.12 (NS, $P = 0.32$)
	30°	1.97 \pm 1.10	1.93 \pm 0.87	1.51 \pm 1.72	0.27 \pm 1.80 (NS, $P = 0.93$)
ANTAG-STRETCH	15°	1.34 \pm 0.67	1.64 \pm 0.73	1.61 \pm 1.29	0.53 \pm 1.38 (NS, $P = 0.15$)
	30°	1.99 \pm 0.81	1.93 \pm 0.66	1.08 \pm 0.48	-0.16 \pm 0.62 (NS, $P = 0.51$)
		Mean AE ($\pm 1SD$)			After/Before ^{intervention} minus After/Before ^{control}
		Before	After	After/Before	
AG-STRETCH	15°	2.46 \pm 1.58	3.04 \pm 1.60	1.40 \pm 0.60	0.13 \pm 0.81 (NS, $p=0.51$)
	30°	3.18 \pm 1.34	3.28 \pm 1.78	1.12 \pm 0.53	-0.08 \pm 0.73 (NS, $p=0.66$)
ANTAG-STRETCH	15°	2.30 \pm 0.93	2.89 \pm 1.41	1.41 \pm 0.66	0.15 \pm 0.90 (NS, $p=0.52$)
	30°	2.85 \pm 1.39	3.42 \pm 2.07	1.34 \pm 0.86	0.14 \pm 1.04 (NS, $p=0.59$)

Paper IV

Two methods, CCM and NDM, to test the stretchability of the RFM were compared for reliability and validity.

Reliability

Test-retest reliability (test-interval of 3.6 ± 3.3 days) of the CCM and the NDM, assessed by Pearson's product moment correlation coefficient, were highly significant for both methods ($r=0.95, p < 0.001$ and $r=0.92, p < 0.001$ for CCM and NDM, respectively).

Validity

Specific

Before using the X-ray to compare the methods on the criterion *specific*, the test-retest reliability for the X-ray measurements was determined with the Pearson's product moment correlation coefficient, and found to be high ($r = 0.97, p < 0.001$ and $r = 0.96, p < 0.001$ for measurement of the start position of CCM and NDM, respectively).

The validity criterion *specific* meant that during the test of stretchability of the RFM, the method should isolate the test-movement to the knee joint with as little movement of the pelvic as possible. X-ray measurements showed that the pelvic tilted forwardly approximately 8° during both methods (NS, paired t-test). Thus, the pelvic moved, i.e., was forward tilted, equally in both methods meaning that CCM and NDM could not be discerned on the criterion *specific*.

X-ray measurements of the *start positions* of the methods revealed the pelvic tilt of the CCM to be on average 23.4° more anteriorly tilted compared to the NDM ($p < 0.001$, paired t-test).

Restrictive

Restrictive meant that the range of passive knee flexion obtained in the method should differ to the highest possible degree from the joint ROM when the RFM was slackened (KJM), i.e., be constrained by the soft tissue as much as possible.

On average, compared to KJM, the range of knee flexion differed 15.1° and 29.5° in CCM and NDM, respectively. Thus, NDM was clearly more restrictive than CCM ($p < 0.001$, paired t-test). Table 5 shows the knee flexion values for each method. Note the increasing standard deviation from KJM to CCM to NDM. By calculating the relative spread of distributions from SD and means (coefficient of variation, i.e., $CV = SD/mean \times 100\%$), CVs were calculated at 3.7%, 5.5% and 9.6% for KJM, CCM and NDM, respectively. This implies that the sample tested showed a greater spreading of the stretchability in NDM. This was confirmed by a F-test (see discussion section of the original study).

Note that the calculations of CV as well as the inference on the range of knee flexion means comparison, based on paired t-tests, were not shown in the original study.

Sensation creative

Sensation creative denotes the ability of the method to give rise to a sensation of stretch when testing passive knee flexion with the same applied torque in both methods. The stretch sensation was quantified by subjective ratings on a Borg scale (Borg 1982).

Table 5. Knee flexion (degrees) for testing and retesting for the three methods.

	Test		Retest	
	X ± SD	95% Confidence Interval	X ± SD	95% Confidence Interval
CCM	132.7± 7.3	131.0 to 134.4	132.7± 7.3	131.0 to 134.4
NDM	118.3±11.3	115.7 to 120.9	118.5±11.3	115.9 to 121.1
KJM	147.8± 5.4	146.5 to 149.1	148.4± 5.3	147.8 to 149.0

n = 71

The means and SD of the Borg ratings at the first measurement, on the first test occasion were 2.1 ± 1.3 (2 on the scale = “Weak (light)”) and 5.5 ± 1.5 (5 of the scale = “Strong (heavy)”) for the CCM and the NDM, respectively. The difference was significant ($p < 0.001$, paired t-test). Thus, the stretch sensation was clearly higher for NDM compared to CCM.

Paper V

In Paper V, the NDM was used to evaluate the effect of a 2-week RFM stretching regimen on knee flexion ROM and subjective stretch sensation.

To determine the test-retest reliability, paired t-tests and Pearson’s product moment correlation coefficient were calculated from the measurements obtained from test occasion 1 and 2 (see also schematic of the experimental design, Figure 7). There was no systematic variation of the ratings of stretch sensation from test occasion 1 and 2 ($p = 0.21$), and the data between occasions showed good correlation ($r = 0.71$, $p < 0.001$). The range of passive knee flexion decreased by 2.3° from test occasion 1 to 2 ($p < 0.01$) and the data between occasions were highly correlated ($r = 0.97$, $p < 0.001$).

Subjective rating of stretch sensation

Table 6a shows the average category scale ratings before and after control and experimental treatments. An additive 3-way analysis of variance revealed a significantly decreased category scale rating after experimental treatment as compared to the control treatment ($p < 0.01$). No difference was seen for results obtained in the first intervention period as compared to the second intervention period ($p = 0.83$, factor “intervention period”), or for differences between subjects in their responses to treatments ($p = 0.06$, factor “subject”).

Range of passive knee flexion

Table 6b shows the average range of passive knee flexion before and after control and experimental treatments. The three-way analysis of variance showed no significant

Table 6. (a) Subjective ratings of stretch sensation, and **(b)** range of passive knee flexion before and after control and experimental treatments.

	Treatment	Before	After
a	Control treatment:	5.1 ± 1.19	5.0 ± 1.22
	Experimental treatment	5.2 ± 1.20	4.3 ± 1.36
NOTE. Values are means ± SDs. ANOVA detected a significant decrease after the experimental treatment compared with the control treatment ($p < 0.01$).			
	Treatment	Before	After
b	Control treatment	124.1 ± 13.50	124.4 ± 13.47
	Experimental treatment	121.5 ± 13.80	123.0 ± 14.42
NOTE. Values are means ± SDs. ANOVA showed no significant change after the experimental treatment compared with the control treatment ($p = 0.42$).			

change in knee flexion (degrees) after the experimental treatment compared to the control treatment ($p = 0.42$). Also, no difference was observed between results obtained in the two intervention periods ($p = 0.73$), or between subjects in their responses to treatments ($p = 0.32$).

Paper VI

A total of 16 nociceptive superficial dorsal horn neurons (SDHNs) from 11 cats were recorded from. Changes in SDHN activity obtained after the spinalisation were not different from those obtained in non-spinalised animals and were therefore grouped together. Seven SDHNs responded to innocuous muscle stretch and two to light pressure of the tendon, implying that nine out of the 16 SDHNs responded to both the innocuous mechanical and the noxious chemical stimuli. These nine cells were denoted as multireceptive neurons (See also *Methods, Recording procedure*).

Response characteristics

The responses of SDHNs to individual as well as combined stimuli were complex (Table 7). With the combined stimuli, the bradykinin-response was modulated by stretch in six out of 12 neurons. The modulation was either a reduction of the bradykinin-induced activation or re-excitation of the neurons after the bradykinin had totally inhibited them.

Responses to bradykinin alone

Out of the 16 nociceptive SDHNs, five cells showed excitatory, four inhibitory and three mixed responses to the bradykinin injections (Table 7). Four SDHNs were unresponsive to the bradykinin injections.

The duration of excitatory and inhibitory effects were not significantly different ($p = 0.18$; two-sample Wilcoxon rank sum test).

Table 7. Responsiveness of nociceptive SDHNs to bradykinin injections. Left column denotes the individual cells.

Cell no	Dept (µm)	Cord level	BK doses (ml)	Response to BK-injection	Response to stretch	BK-response modulated by stretch
Multireceptive						
A 1	200	L7	0.7	Excitatory	X	X
A 2	200	L7	0.7	Excitatory	X	X
G 3	1000	High L7	1.0	Excitatory	X	X
K 1	1000	L7-S1	1.0	Excitatory	X	X
F 1	400	L7	1.0	Mixed	X	X
G 1	900	L7	1.0	Mixed	X	X
H 1	900	Low L7	1.0	Inhibitory		
I 1	700	High L7	1.0	Inhibitory		
G 2	600	L7	1.0	No response	X	
Nociceptive specific						
G 4	900	High L7	1.0	Excitatory		
J 1	700	High L7	1.0	Mixed		
C 1	600	L7	0.5	Inhibitory		
D 1	600	L7	1.0	Inhibitory		
B 1	400	L7	1.0	No response		
E 1	500	L7-L6	0.7	No response		
K 2	200	L7-S1	1.0	No response		

Typical tracing of excitatory and mixed responses to bradykinin are shown in Figure 10 a and b. The mixed responses (three cells) consisted of a small excitation followed by inhibition, during which the cells ceased firing completely.

Responses to stretch alone

Seven of the 16 SDHNs were responsive to muscle stretch. Out of these seven cells, four belonged to the group that showed excitatory responses to bradykinin injection, two belonged to the mixed-response group and one was unresponsive to bradykinin (Table 7).

Stretch modulation of the bradykinin response

In order to test the response of SDHNs to combined stimuli, we applied two consecutive stretches shortly after the bradykinin injection. In six out of the nine multireceptive neurons, the stretch stimuli modulated the bradykinin-induced response. However, none of the nociceptive specific neurons showed any modulation by the subsequent mechanical stimuli (Table 7). Four of the five SDHNs that exhibited excitatory

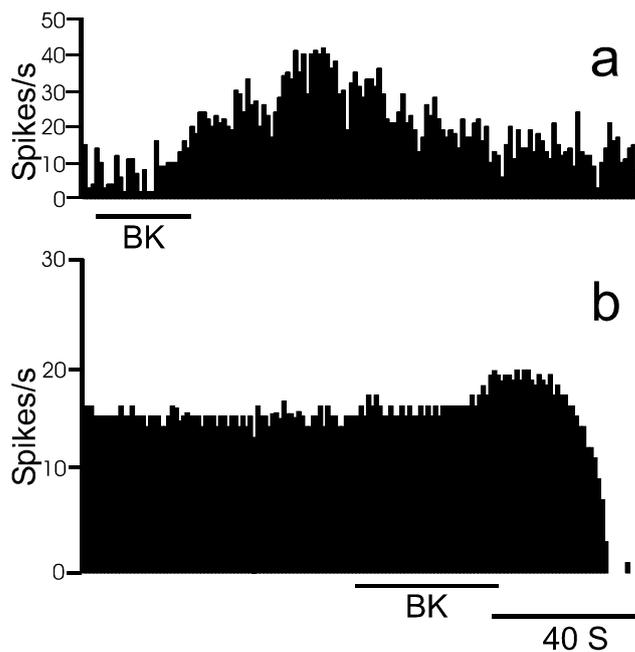


Figure 10. Typical time histograms of SDHN response to bradykinin injection. (a) SDNH with an excitatory response to 0.7 ml of injected bradykinin. (b) SDNH with a mixed response to 1 ml of injected bradykinin. The horizontal bar marks the time of injection.

responses to bradykinin were influenced by the stretch that followed the injection: in three cells the peak-excitation was reduced (on average by 37%) as compared to the responses to bradykinin, while in one cell the bradykinin-induced excitation was completely abolished by subsequent stretches. In two cells the excitatory responses, as compared to the bradykinin responses, were shortened (31 and 32%, respectively). An example of the response behavior of a cell from this group is shown in Figure 11. In the mixed-response group, two of the three SDHNs were influenced by the stretch that followed the bradykinin injection. Bradykinin initially excited the cells followed by an inhibition and eventual cessation of firing. In the inhibited state, the stretch re-excited the cells. An example of this is shown in Figure 12. All cells in the inhibitory response group were unaffected by the stretch that followed the bradykinin injection. Note that the cells in the inhibitory group were also unresponsive to stretch alone.

Summary of results

Paper I

The position sense acuity, as assessed by an arm-repositioning test, was significantly reduced after a repetitive low-intensity arm work to fatigue performed in a simulated occupational setting.

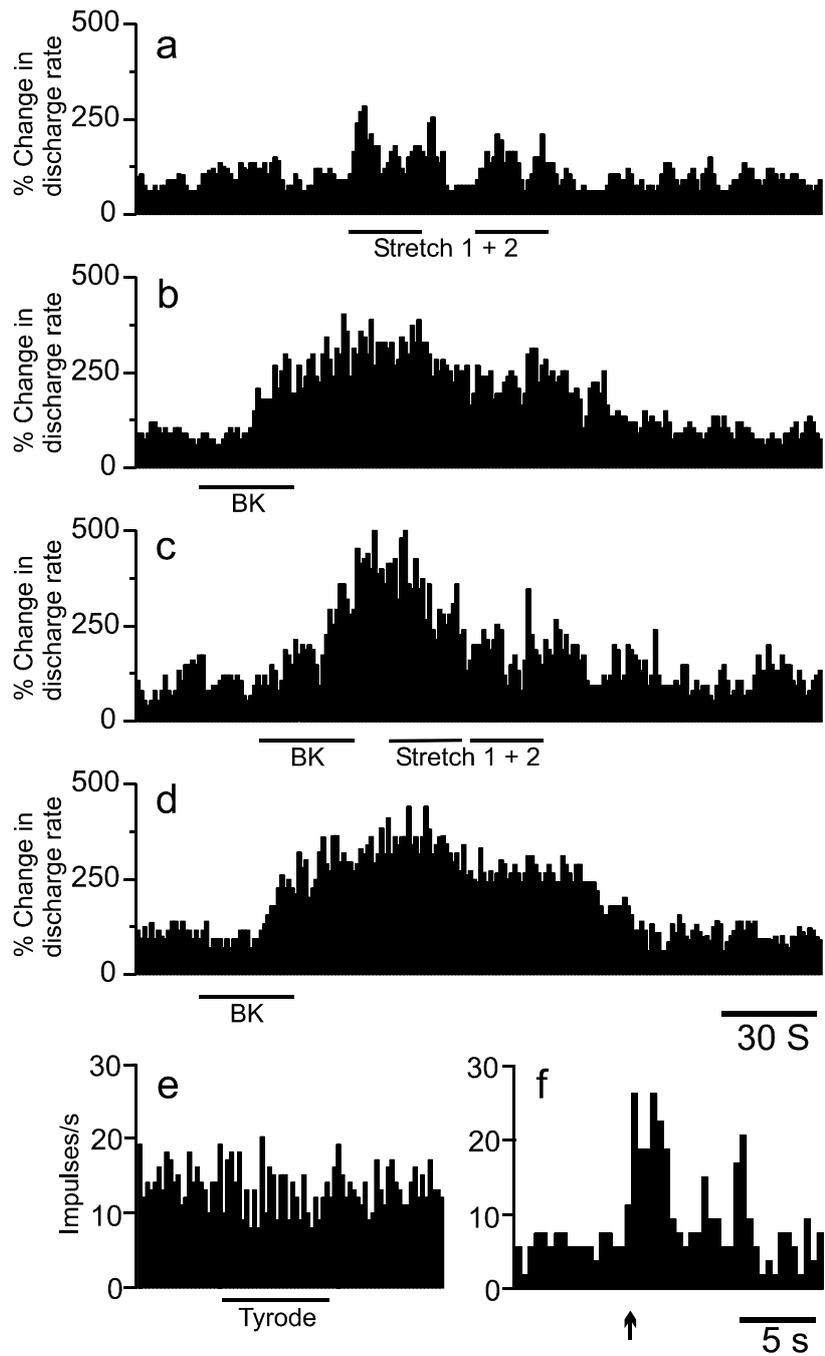


Figure 11. Stretch modulation of a cell exhibiting excitatory response to bradykinin. (a) response to stretch alone; (b) response to bradykinin injection alone; (c) response to combined stimuli; (d) response to repeated bradykinin injection 30 min after combined stimuli; (e) response to tyrode injection; (f) response to noxious muscle pinch, arrow indicates the start of pinch.

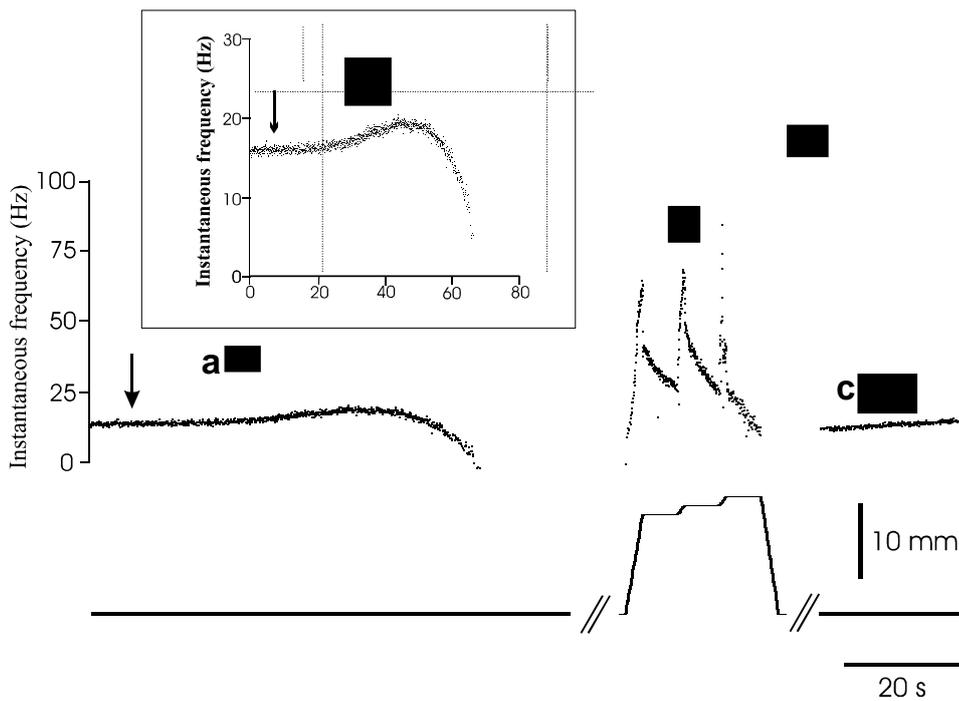


Figure 12. Instantaneous frequency of a cell exhibiting a mixed response to bradykinin with subsequent stretch modulation. The arrow indicates the start of bradykinin injection. *Inset:* The same response as in (a) with enlarged ordinate scale. The stretch counteracted the bradykinin-induced cessation of firing by evoking substantial cell activity (b). Spontaneous baseline firing (c) was resumed after a second stretch had been applied one minute after the first (not shown in figure). The lower trace shows changes in muscle length.

Paper II

The results revealed that working time predicted the retention of the subjective fatigue for males but not for females. Also, both working time and retention of fatigue predicted increased response variability (VE) and reduced accuracy (AE) of the position matching of short target position for males but not for females. For the intermediate target position, working time predicted increased AE for the whole work group.

Paper III

An acute bout of stretching of the shoulder muscles did not affect the shoulder position sense, as assessed by an arm-repositioning test. Neither stretching of agonistic nor antagonistic shoulder muscles changed the response variability (VE) or the overall acuity (AE) of the position sense test.

Paper IV and V

The intratester reliability of both a common clinical (CCM) and the newly developed method (NDM) to assess the stretchability of the RFM was high. Two out of three validity criteria favored the new method, and the third pointed out the two methods as equal (Paper IV).

In the follow up study (Paper V), a 2-week stretching regimen of the RFM resulted in a decreased stretch sensation for the anterior aspect of the thigh, whereas the knee flexion ROM, tested at an indicated applied torque, remained the same. The results imply that passive stiffness of the RFM did not change.

Paper VI

Interactions between afferent inputs induced by innocuous muscle stretching of the gastrocnemius muscles and noxious-chemically induced activation of muscle receptors (i.a. injections of bradykinin) were demonstrated as evidenced by changes of discharge behavior of nociceptive SDHN of the feline spinal cord. The majority of the neurons that showed excitatory and mixed responses to bradykinin were also influenced by stretches alone. In these neurons, the stretches when applied directly after the bradykinin injections, counteracted the bradykinin-induced response, i.e., shortened and/or reduced the bradykinin-induced excitation, or re-excited the cells that were inhibited by bradykinin.

DISCUSSION

The following discussion is organized according to the sequence of papers presented in this thesis.

Effects of repetitive low-intensity work on position sense (Papers I and II)

One of the main objectives of this thesis was to test the impact of repetitive work exposure on position sense. Papers I and II were set to investigate this issue. Overall, the results of Papers I and II support the hypothesis of a reduced proprioceptive acuity following repetitive low-intensity work to fatigue, even though the hypothesized relations of paper II, i.e., that position sense acuity depends on working time and the retention of subjective fatigue, were only partly confirmed.

Origin of effects

It is not easy to relate our findings to previous studies of fatigue effects on position sense, since most of these previous reports were concerned with fatigue induced by static muscular contractions above 20% of maximal force or high-intensity dynamic work. Also, these previous reports are not conclusive, even though there is an abundance of reports showing a reduction in position sense following muscle fatigue (for details, see *Introduction, Effects of fatigue on proprioception*).

Since position sense acuity is to a large extent dependent on muscle spindle activity (e.g., Roll and Gilhodes 1995), the effect that fatigue may have on the γ -motoneuron-muscle spindle system can provide a plausible mechanism for our findings. In acute animal preparations, muscle fatigue (Pedersen et al. 1998) as well as metabolites and inflammatory substances injected into muscles (e.g., Djupsjöbacka et al. 1995; Pedersen et al. 1997; Hellström et al. 2000) have been shown, via reflex effects on γ -motoneurons, to alter the activity of MSAs. Such reflex effects could potentially diminish the information transmitted by ensembles of MSAs resulting in reduced proprioceptive acuity. However, this explanation may be more applicable to fatigue regimes of high-intensity work that are known to produce metabolites and inflammatory substances. In contrast, the accumulation of these substances during low-intensity work is more uncertain. However, evidence has recently been obtained for inflammatory tissue responses to repetitive low-intensity work (Barbe et al. 2003). Also, a stereotypic constrained movement pattern, such as the work task of Papers I and II, may increase the risk of selective muscle fiber overloading due to sustained recruitment of a certain population of motor units (van Dieën et al. 2003). This in turn would increase the likelihood of an activation of chemosensitive group III and IV muscle afferents, mediated by inflammatory substances.

Based on the nature of the position sense test (i.e., reproduction of a previously presented target position), memory likely plays a role. Thus any effect on memory

from the work exposure could have influenced the position matching. Obviously, some type of memory test could have shed light on this issue. Also of concern is that the repetitive work tasks may have introduced boredom and thus affected the level of concentration (i.e., arousal), which may have influenced subjects' position sense performance after the work task.

Methodological considerations

Although changes in the γ -motoneuron-muscle spindle system are presumed to explain our findings in Papers I and II, other factors may be considered. Ideally, direct measurements of spindle activity would have been best for addressing the presumption of disturbances in the muscle spindle activity; however, such recordings are not that easy in human subjects. One method for directly measuring spindle activity is microneurography, which has been used, albeit with limited success. Disadvantages are that microneurography is invasive and may be deemed unreliable for repeated measurements due to sensitivity in electrode positioning.

In Paper I, the subjective rating of fatigue was used as a criterion to stop working, but EMG and MVC assessments also indicated that physiological muscle fatigue was reached. Accordingly, the MVC and mean power frequency of the EMG power spectrum were decreased significantly, as assessed during test contractions before and after the repetitive work. These manifestations may not be very typical for low-intensity dynamic work leading to low-frequency fatigue (LFF) (see *Introduction*), but a decreased mean power frequency has indeed been shown for low-intensity work, such as dynamic overhead activity performed for up to 3 hours (Nussbaum 2001) and intermittent static elbow flexions at 10% MVC (Madeleine et al. 2002). Also, after a static jaw closing activity at 10% MVC for 60 min, a slight but significant decrease in MVC and EMG changes (decrease in mean frequency and increase in root mean square amplitude) correlated well with the subjective feeling of fatigue (Svensson et al. 2001).

The estimated work loads for the middle deltoid muscle and for the descending trapezius ranged between 12% and 19% of MVE in Paper I. Thus, the work load was somewhat high in relation to occupational low-intensity repetitive work exposure. This was also reflected in quite a short working time, where most of the subjects reached the set level for subjective fatigue already after 10-11 min. However, it should be reiterated that the level for subjective fatigue was not set at maximum but at 7 on the 0 - 10 Borg scale. Nevertheless, the external validity for lower-level exposures is not straightforward in Paper I (see also below). In an attempt to increase the working times to subjective fatigue, the work load was reduced by lowering the weight of the manipulandum from 300 g to 220 g in Paper II. To some extent the lighter load had the desired effect by increasing the maximum work time from 28 to 59 min. However, the distribution was still largely skewed with a median work time of only 13 min.

A further development from Paper I to Paper II was that not only the response accuracy (AE) but also the response variability (VE) was assessed. While AE often is used to measure the overall accuracy in performance, VE represents the spread of

responses, which may reflect the noise in the sensory signal and in the processing of the sensory signal (van Beers et al. 1996).

The results of paper II, in which the hypothesized effects for males and for short target positions were principally verified, while no effect was found for females, are difficult to interpret. This striking gender difference could partly depend on the tendency toward a more skewed distribution of working times for females, making an effect easier to detect in males. However, since the working-time differences did not reach statistical significance, it is unlikely that they could account for a major part of the findings. Another hypothetical explanation lies in the rating of fatigue. In general, the rating of the subjective feeling of fatigue has been suggested to entail five independent factors (Åhsberg 2000). Thus, it cannot be excluded that gender differences in the relative weighting of such factors (e.g., *physical exertion*, *physical discomfort* and *lack of motivation*) resulted in females discontinuing the work at different states of, e.g., physical exertion than males. A further possibility that might account for the gender difference is that, for the short target position, a larger number of females than males dropped out (33% of females *vs.* 17% of males). In general, females had a higher tendency for the criterion movements to exceed the set limits of the short-target positions, thus reducing the number of valid trials. The power of the analyses concerning position matching for the short target was therefore lower for females than for males.

There could be several reasons why mainly the short-target position showed the hypothesized relation. Firstly, the response variability (VE) has frequently been reported to be lower for shorter than for longer movements (Keele and Eills 1972; Marteniuk 1973; Semler and Simmons 1979; Neufeld 1981), which also was the case in the present study. Thus, the outcome for the “longer” target positions (30 and 45 degrees) likely contained more noise. Hence, a larger impairment of the position sense would have been required to detect effects for these target positions. Secondly, the cognitive processes accompanying the task may differ for short and long target positions. Different cues for recalling movements, representing location and distance information, have been associated with different movement lengths of limb re-positioning tests. Accordingly, short movements appear to rely more heavily on distance cues involving dynamic information (Walsh 1981), whereas longer movements seem to be more reliant on location cues (Roy 1977; Semler and Simmons 1979). However, it is not known whether this distinction of cues was of any importance in the present study.

Regardless of the origin of this discrepancy between the target positions, the results motivate further studies on the proprioceptive mechanisms behind this effect.

Extrapolation to real working situations

The characteristics of the work task used, including repetitive horizontal dynamic arm movements with short cycle times, enhance the external validity of our findings (Sundelin and Hagberg 1992; Mathiassen 1994; Hermans and Spaepen 1997). An important question in this context is how to design laboratory work-exposure models

in order to best simulate real working situations. The ultimate goal is to control for extraneous variables in order to retain a high internal validity, and at the same time make the model as applied as possible to attain external validity. These two goals are hard to attain in the same study, often necessitating compromises. In Papers I and II, the subjects were subjected to the same absolute work load, irrespective of gender or individual physical capacity. This indifference was in line with real assembly line work, which seldom makes allowances for individual characteristics. On the other hand, the fact that subjects worked with the same absolute weight (same manipulandum) within each of the respective studies, makes it probable that they were exposed to different relative work loads. This restrained the internal control of the studies with regard to physiological muscle fatigue, which could have been important for paper II, where the work load was lower than in Paper I and the results were more differentiated. Also, it is likely that psychological factors like boredom have a greater impact when monotonous work simulations are prolonged and the end-point criterion of the work task is based on subjective ratings of the fatigue felt (even though care was taken to ensure that the subjects were unaware of the length of time required for performing the work task or the critical Borg scale level).

Finally, a work-place factor of importance but difficult to assess in laboratory simulations is the influence of psychological stress on occupational fatigue and proprioception. To be able to get a grip on this influence, careful experimental study designs aimed at evaluating the impact of specific stressors are needed. This was, however, not an objective in Papers I and II.

Functional implications

The proprioceptive information from muscle spindles is used by the CNS both for feedback control of movements as well as for the recalibration of internal models used for fine tuning motor commands. This implies that a precise motor control is heavily dependent on proprioceptive information, a notion proven particularly for the precision and coordination of multi-joint movements (Ghez and Sainburg 1995; Sainburg et al. 1999; Lackner and DiZio 2000). In a repetitive work task, the deranged motor control could cause perturbations of movement trajectories and positional disturbances.

A consequence of the gradual derangement in motor control is an increase in muscle co-activation of proximal muscles (Sainburg et al. 1995; Ghez and Sainburg 1995). The increased co-contraction increases joint stiffness, which in the short perspective will help to solve the work task. However, in the long run, the compensatory co-contraction may initiate a disadvantageous chain of events at several levels, events with the potential to contribute to vicious circles of importance for the development of CWRND. For example, the increased co-contraction will increase the overall work load, thus adding to the development of fatigue. This scenario is particularly likely to occur if the work is performed under stressful conditions since the sympathetically induced vasoconstriction may impede the washout of the intramuscular chemicals

accumulated.

The changed motor behavior due to the deranged motor control increases the risk of a more constant activation of muscle fibers, which, in the manifestation of the absence of EMG-gaps, has been shown to predict myalgia (Veiersted et al. 1993).

Future studies of low-intensity repetitive work exposure

One interesting research line to follow up on is the relation between increased work time to fatigue and increased retention of subjective fatigue, and the association between retention time of subjective fatigue and the extent of changed position sense acuity, as seen in Paper II. These findings fit well into the framework of LFF, with its hypothesized accumulation of inflammatory substances within the muscle. The technique of microdialysis may be of help to test for such a mechanism. A first step would be to verify the findings of Paper II, with a closer control of the fatigue induced by low-intensity work and its persistence after work. Modifications of the fatigue model used to simulate prolonged work exposure will also be necessary. One way may be to implement instruments for monitoring of the subjective fatigue level in both physical and mental dimensions (Åhsberg 2000). This may also shed some light on the intriguing gender difference observed in Paper II.

Erratum

The conclusions originally drawn in Paper I, that females had a significantly poorer position sense than men, was incorrect and was therefore rescinded in a Letter to the Editor of the same journal (Björklund et al. 2003, appendix to Paper I in this thesis). The incorrectness had to do with the way the statistics were run in regard to the experimental design. When recalculating and re-appraising the data of the study, all findings originally reported were still valid except for the reported gender difference, which was shown not to be significant ($p = 0.15$ at the reappraisal instead of the $p < 0.01$ as originally reported).

Conclusions

Based on the findings reported in Papers I and II, it can be concluded that low-intensity repetitive arm work to fatigue reduces the position sense acuity of the shoulder. To our knowledge, Papers I and II are the first studies to report on the effect of low-intensity repetitive work on proprioception. The origin of the effect is suggested to lie in the activation of chemosensitive group III and IV muscle afferents through the accumulation of inflammatory substances. Furthermore, the findings of Paper II indicate that, the longer one works to reach subjective fatigue, the longer the sensation is

retained, and the greater the impairment of the position sense acuity. The fact that this effect was only found for the male group raises important questions as to possible gender differences.

Effects of acute muscle stretching on position sense (Paper III)

Paper III demonstrated that acute stretching of the shoulder muscles, with a stretch duration and number of repetitions recommended for achieving muscle-tendon unit lengthening (Taylor et al. 1990; American College of Sports Medicine Position Stand 1998), did not affect the shoulder position sense. This pertained to both agonistic as well as antagonistic muscle stretches, performed on different test occasions in order to test whether the outcome would differ due to their relative contributions for encoding position sense. Thus, the findings of Paper III do not support the notion that the decrement in performance following acute stretching, as reported especially for jump height (Young and Elliot 2001; Cornwell et al. 2002), might be mediated by alterations in proprioception. However, in order to draw a firm conclusion on the particular case of jump height decrement, one would need to test the effect of lower limb stretching on both proprioception and jump height on the same subjects.

Speculations about the absence of effect

The rationale for assuming that muscle stretching might impair the position sense was that the observed stretch-induced increases in ROM or reductions in passive muscle stiffness (see *Introduction*) might influence MSA activity/sensitivity and thus indirectly proprioception. The experimental protocol chosen here was “applied” in the sense that the stretching performed resembled a bout of stretching as often employed in sporting activities (American College of Sports Medicine Position Stand 1998). This intervention may have been too small to reduce the stiffness significantly, even though acute transient viscoelastic responses are likely to occur after such a bout of stretching (Taylor et al. 1990; Toft et al. 1989; Magnusson et al. 1995) and may even be significant after repeated movements to the end-point of motion, such as when assessing the passive ROM (see discussion of Paper V below). An alternative explanation may be that the CNS is able to compensate for transient changes in passive muscle properties. In general, negative feedback systems are able to compensate not only for external disturbances, but also for changes in internal system properties, and this may also hold for the stretch reflex circuit (Houk and Rymer 1981). This ability might be enhanced by additional system properties, such as the intricate control of muscle-spindle behavior. The output of the muscle spindle reflects the integrated influences of direct mechanical muscle perturbations and the prevailing γ -motoneuron drive. This drive in turn constitutes the net effect of descending commands from central structures and reflex effects from peripheral sensory receptors (see *Introduction*). Hence, this complex system involving muscle spindles might be tuned to restrain

small transient viscoelastic changes of the muscle-tendon unit during normal conditions so as to ensure that the CNS be provided with persistent adequate proprioceptive information. This speculative idea requires experimental verification.

Future studies

Paper III shows that the position sense is not influenced by a bout of CR stretching under normal conditions, i.e., in the absence of deviating conditions, such as muscle fatigue or pain. Fatigued or painful muscles present with altered muscle spindle activity and possibly altered stretch reflex activity. The effect of muscle stretching on position sense may be different under these conditions. Also, stretching fatigued or painful muscles could exert indirect influences on the position sense through stretching-induced alteration of the pain itself (see *Introduction, Therapeutical muscle stretching* above).

Therefore, the next step of importance for both occupational and sports medicine would be to investigate the effects of stretching on the position sense after experimentally induced muscle fatigue.

Conclusions

The findings of Paper III indicate that acute stretching of the shoulder muscles, resembling a bout of stretching employed in sports activities, does not have any immediate effect on the shoulder position sense. The results suggest a minimal risk of distorted precision and coordination performance via altered position sense after a bout of stretching.

Effects of muscle stretching - Rectus femoris muscle (Papers IV-V)

Before studying the effects of muscle stretching in an applied study (Paper V), a new method (NDM) to assess passive stretchability of the RFM was developed and compared with a common clinical method (CCM) for content validity and intratester reliability (Paper IV).

The methods CCM and NDM have different starting positions (see Figure 6a and b). The X-ray analysis showed that the starting position in the NDM tilted the pelvic to a position 23° more posterior than that in the CCM. This had the consequence that the origin and insertion of the 2-joint RFM were more separated already in the starting position of NDM. Thus, the end-point ROM would be reached at a lower knee flexion in the NDM, which was confirmed in Paper IV. Based on three criteria, it was determined that the NDM improved the validity compared to the CCM. More specifically, the NDM could be evaluated as more sensitive in disclosing small differences in stretchability. With both methods showing similar reliability, the finding of a larger CV for the NDM implies a better ability of the NDM to detect differences in the stretchability of the RFM between subjects. The larger CV for CCM,

and especially for NDM compared to KJM, indicates that the muscle stretchability differs more between subjects than does the maximum joint ROM with muscle slackened. The NDM was also shown to give rise to more stretch sensation confined to the area of the RFM when applying the same torque with both methods. Thus, the NDM provided an improved validity and a reliable tool for evaluating effects of muscle stretching on changes of ROM.

In paper V, the NDM was used to detect changes in passive knee flexion ROM, determined in each test with the same applied torque specific for each subject, following a 2-week stretching regimen of the RFM. Simultaneous changes in stretch sensation for the anterior aspect of the thigh were evaluated with ratings on a category ratio scale (Borg 1982). The results revealed an increased tolerance to stretch but an unchanged knee flexion ROM after the stretch intervention, indicating that the stretching did not alter the passive stiffness of the RFM. To our knowledge, this is the first time sensory adaptation after a stretching regimen of the RFM has been demonstrated. Thus, the study expands our knowledge on responses to stretching of a muscle susceptible to tightness (Gajdosik 1985; Norris 1995; McDonald 1998), which might contribute to low back pain (Norris 1995; Lewit 1999), altered movement patterns (Lenart and Kullmann 1974) and anterior knee pain (Arnold et al. 1988; Smith et al. 1991).

Origin of effect

The explanation for the demonstrated sensory adaptation in Paper V is not readily apparent. The location of the effect could be in the peripheral soft tissue or in the CNS, or both. Adaptive mechanisms might occur for sets of peripheral receptors in muscle, skin or the fasciae around the muscles. In this respect, a role for nociceptive nerve endings in joints and muscles has been proposed (Magnusson et al. 1996a). However, joint receptors are not likely to contribute to any great extent since extreme joint positions were avoided with the stretching techniques applied. Also, animal research has shown that activity in muscle nociceptors is only elicited when the stretch is unphysiological, i.e., tissue-threatening or painful, whereas other fine muscle afferents are responsive to physiological muscle stretching (Mense and Meyer 1985). Furthermore, the subjects were instructed not to stretch at an intensity that could elicit pain, making muscle nociceptors unlikely candidates for the sensory adaptation. As much as 51% of group III and 12% of group IV muscle afferents have been reported to respond to muscle stretching (Kaufman and Rybicki 1987). These afferents adapted in the course of a static stretch of 20-30 sec, but whether they would exhibit long-term changes in response profiles after repeated stretches is not known. However, whether stretch-responsive non-nociceptive fine muscle afferents, or any other kind of mechanosensitive afferent fibers, were responsible for the long-term change of sensory adaptation seen in Paper V is not known. Changed sensory perception due to altered processing in the CNS may be an alternative explanation for the effects described in

Paper V.

Note also the observation that, concomitant with an increased subjective stretch tolerance, the onset of EMG at end-ROM appeared at a greater applied torque after stretching (e.g., Gajdosik 1991). Thus, sensory adaptation after stretching is corroborated with EMG-data.

Method discussion

Evaluation of stretching-induced changes in ROM requires objective measurements of both the passive and the active movement range. In Papers IV and V, passive ROM measurements were applied. However, because the EMG was not measured, we cannot state that the passive knee flexion was entirely passive. However, a plethora of studies suggests that passive ROM tests to an end-point below a pain-eliciting end-point will not evoke significant electric activity from the stretched muscle (see *Introduction*). In addition, the velocity with which the subjects were tested for knee flexion was probably well below that needed to stimulate stretch reflexes (cf. Davidoff 1992).

To make inferences about mechanisms behind increases in ROM acquired after stretching (e.g., changes in passive muscle stiffness), passive measurements with controlled torques are necessary. Even though measurements of active ROM are of functional importance, they have certain drawbacks when it comes to evaluating treatment effects. Subject blinding is practically impossible in studies of the effects of stretching, which may introduce a bias, especially when evaluating the effects with active ROM. The readiness of the subject to generate stretch-torque (varying effort), and hence a potential treatment effect, cannot be controlled during measurements of active ROM. These potential sources of bias in active ROM measurements are minimized when torque-controlled measurements of passive ROM are used (Harvey et al. 2002).

Test-retest reliability reported for an active knee-flexion test of RFM tightness with a 30 min test-interval (Gajdosik 1985) was not different from the reliability demonstrated in Paper IV and V, in spite of a remarkably longer test-retest interval for Papers IV (3-4 days test-interval) and V (2.5 weeks test-interval). Thus, Papers IV and V show that careful standardization of the measurement method and control of the applied torque can make test-retest reliability of passive as accurate as that of active ROM measurements, even though the latter is usually considered to show less variability (for references see Gajdosik and Bohannon 1987).

In future studies, it would be of interest to record the full joint angle – torque curve for a more elaborate assessment of the passive muscle stiffness.

Importance of the definition for the end-point of ROM

There are several examples of long-term effects of stretching on ROM (for review see Harvey et al. 2002), but in most of these studies the definite criterion for end-

ROM was the subjects' or the assessors' perception of the end-point, without any knowledge of the applied torque during the passive measurement. It is likely that the stretching regimen used in Paper V also would have shown an effect on ROM with a subjective stretch sensation, i.e., a maximal tolerated torque as the end-point criterion. In fact, this assumption was tested in a subgroup of 12 of our subjects. After the original measurement procedure, the subjects were re-tested but this time with the same magnitude of stretch sensation as that perceived before the stretch-intervention as the criterion for end-ROM. The outcome of this test was an increased ROM of about 15°, a magnitude in line with that found by others (Hardy 1985; Magnusson et al. 1996a).

Re-appraisal

In Paper V, we were surprised to find a decrease in knee-flexion ROM between test occasions 1 and 2 (2.5 weeks interval) of 2.3°, without any intervention between the tests. At the time of publication, we had no explanation for this finding. After later re-evaluation of the data, however, a possible explanation emerged. Only on the first test occasion did the subjects go through a training session to get acquainted with the testing- and rating procedures. Thus, 4 knee flexions per leg preceded the baseline measurements on test occasion 1. This could have evoked an acute viscoelastic response of the RFM. To test this assumption, we compared the knee-flexion ROM of measurement 1 with measurement 3 on each subject within each test occasion. On average, the ROM of measurement 3 was 2.1° larger than that of measurement 1 (123.0 ± 17.7 ; 120.9 ± 17.5 , $p < 0.001$, paired t-test), supporting the assumption that repeated knee flexions could induce acute viscoelastic deformations that resulted in decreased passive muscle stiffness and increased ROM. Thus, the contention that the observed difference in knee-flexion ROM between test occasions 1 and 2 was due to the training session on the first test occasion is supported. In future studies, possible acute changes of ROM due to testing procedures should be considered.

Conclusion

Based on the results of Paper IV, it is concluded that the NDM provided an improved validity, compared to the CCM, and was a reliable tool for evaluating effects of muscle stretching on changes in ROM.

The follow-up study (Paper V) showed that a 2-week stretching regimen reduced the stretch sensation for the anterior aspect of the thigh without any change in ROM, when tested with the same torque. This indicates that no long-lasting viscoelastic deformation or structural adaptation of the muscle was induced. This, however, does not exclude the possibility that stretching paradigms could induce persisting changes in muscle mechanical properties, such as reduced passive stiffness, when using more intensive stretching regimens (Toft et al. 1989; Chan et al. 2001; Kubo et al. 2002b). It is suggested that increased stretch tolerance is an important mechanism behind

increases in ROM acquired by stretching, and that these changes are more easily achieved than changes of the passive stiffness (see also Chan et al. 2001).

Sensory adaptation might also explain the gradual increase in pain-free ROM in myalgic patients subjected to stretch treatment (Sölveborn 1997; Hou et al. 2002), and perhaps contributes to alleviate tiredness and tenderness of muscles in these patients. In order to confirm this supposition, further studies are needed.

Effects of muscle stretching on noxiously activated dorsal horn neurons (Paper VI)

The mechanisms hypothesized to underlie the effects of stretching in the course of treatment and rehabilitation of painful musculoskeletal disorders usually implicate peripheral events, such as reductions in tension or changes in muscular energy and ionic dynamics (Simons et al. 1999; Mense et al. 2001). Another potential mechanism, rarely considered, might be the modulation of nociceptive processing in the CNS. In this study we explored the neuronal correlates underlying the effects of muscle stretching on nociceptive transmission in the superficial dorsal horn.

The results of Paper VI demonstrated interactions between afferent inputs induced by innocuous muscle stretching of the gastrocnemius muscles and chemically induced noxious activation of muscle receptors (i.a., injections of bradykinin) on nociceptive SDHN of the feline spinal cord.

The stretches used in our study were kept within physiological limits and did not exceed forces of 3 N, thus most probably not activating muscle nociceptors (Kniffki et al. 1978; Mense and Meyer 1985; Wilson and Engbretson 2000; also see Mense 1993). However, it is well established that other non-nociceptive fine muscle afferents respond to physiological stretching (Mense and Meyer 1985; Kaufman and Rybicki 1987). Group III muscle afferents are reported to be more stretch sensitive than group IV afferents, and could therefore constitute a part of the afferent ensemble activated by the stretches in Paper VI (Kaufman and Rybicki 1987). The major portion of large-diameter sensory fibers activated by the stretch most probably consisted of muscle spindle afferents and non-spindle group II afferents, e.g., slowly adapting spray endings (Ruffini) and fast adapting Paciniform endings (for references see Mense 1993). However, a direct action of these afferents on the SDHNs was unlikely since they are known to project to deeper dorsal horn laminae (Brown, 1981; Jankowska, 1992).

The study was not specifically designed to enable a precise assignment of effects to different types of receptors. However, the location of the SDHNs combined with the fact that only physiological stretch was used, suggest that the stretch-induced input derived mainly from non-nociceptive group III afferents, although input from other mechanically sensitive afferent fibers (i.e., non-spindle group II) relayed by interneurons cannot be excluded.

The experiments were performed on decerebrated cats and on three spinalized cats, and only peripheral stimuli with input to the same spinal segments that were

investigated for SDHNs were applied. Handwerker and co-workers (1975) showed that input from electrically activated thick myelinated axons, originating in cutaneous mechanoreceptors, interacted with nociceptive afferent input at the spinal segmental level. The interaction suppressed the nociceptive response of dorsal horn neurons, which would be in line with the gate-control theory (see *Introduction, Pain alleviation through endogenous antinociceptive systems*). This suppressive effect was not any different between reversibly spinalised and decerebrated animals. Chung et al. (1984a,b) showed that stimulation of the tibial nerve at group III strength inhibited group IV fiber-evoked effects on spinothalamic tract cells, regardless of whether the animals were anaesthetized, unanesthetized, decerebrate or spinalized. The authors concluded that the effects were mediated through spinal neuronal pathways. Likewise, in our study, no difference in effects was seen in non-spinalized and spinal animals. Thus, the experimental approach and the observation that the responses of the SDHNs were alike in spinal and un-spinalized decerebrate animals render it likely that the segmental inhibitory system was recruited.

Methodological considerations

Some important limitations of the study should also be acknowledged, especially when it comes to interpreting the findings and their functional implications.

The animal model

The study was conducted on an acute animal model, which inherently has important limitations. The decerebrate preparation used implied that the neurons recorded from were devoid of physiological descending control. Also the extensive denervation of the hind limb, with only the innervation to the gastrocnemius muscles being intact, effectively removed other afferent inputs (i.e., cutaneous, joint etc.), which could have altered the response characteristic of the examined neurons (for references see Mense 1993). Finally, the experimental model used is more apt to reflect the acute pain rather than chronic pain condition, the two forms of pain probably being differently processed in the CNS.

On the other hand, while the decerebration and the restriction of afferent inputs enhanced the stability of the recordings, which was crucial for obtaining a controlled and reproducible experimental situation especially with regard to the lengthy protocol of the present study, they also allowed confining the conclusions to *muscle* afferent inputs and their reflex effects at the spinal level.

The significance of the restrictions of the preparation used is difficult to evaluate. Therefore, the results of Paper VI should be interpreted with caution and cannot easily be extrapolated to human conditions. Nevertheless, the results of Paper VI suggest that the prerequisite for muscle-stretch effects on nociceptive spinal processing, namely the existence of required circuitry, is present.

Identification and number of SDHN

A further limitation of the study concerns the identification and the overall sample of SDHNs. Inclusion criteria for neurons to be recorded were that they a) were localized within a depth of 1000 μm from the cord dorsum and b) showed a clear response to noxious pinch of the gastrocnemius muscle or tendon. No additional histological characterization of the SDHNs or electrophysiological determination of their output targets was employed. In other words, we cannot say whether they were non-projecting interneurons or neurons projecting to supraspinal structures of the CNS. Therefore, we cannot say anything about the kind of sensation these neurons might mediate, or whether they are involved in eliciting subjective sensations at all. However, due to the location of the neurons in the dorsal horn and their clear responsiveness to peripheral noxious stimulation, it may be suggested that the neurons recorded from were involved in deep nociceptive processing.

Also, the low number of SDHNs recorded made it difficult to provide a broad, statistically safe picture of the processes occurring in the dorsal horn under the selected experimental conditions. Thus, the findings of the study were presented in a rather descriptive way and should be regarded as preliminary. With these reservations in mind, it should be reiterated that the results of Paper VI provide indications for the very existence of spinal circuitry required for an anti-nociceptive effects of muscle stretching. This was an important goal of the study and thus a starting point for further investigations.

Functional implications

A number of studies have investigated the modulation of nociceptive transmission in the spinal cord (Handwerker et al. 1975; Wall 1978; Tsuruoka et al. 1990; De Koninck and Henry 1992; Garrison and Foreman 1996; for review see Besson and Chaouch 1987). However, in these studies, only modulatory effects of cutaneous afferent inputs were tested, with muscle afferent inputs being largely neglected. Yet, muscle pain is prevalent among somatic pain syndromes (for references see Mense 1993; Johansson et al. 2003), and effective therapeutical interventions include different means of activation and stimulation of muscles (see Mense et al. 2001). Therefore, to investigate the ability of muscle stimulation to modify the spinal transmission of muscle nociceptive signals is of great interest. Muscle stretching is commonly used in clinical rehabilitation in order to alleviate muscle tenderness and tension as well as to enhance the pain-free ROM (Jaeger and Reeves 1986; Khalil et al. 1992; Sölveborn 1997; Hanten et al. 2000; Hou et al. 2002). (see *Introduction, Muscle stretching in myofascial pain syndrome*).

For healthy subjects, acute (Halbertsma et al. 1996; Magnusson et al. 1996b; Wiemann and Hahn 1997) and chronic (Halbertsma and Göeken 1994; Magnusson et al. 1996a) effects of stretching have been shown to increase the tolerance to stretch (see also Paper V in this thesis). This effect has even been designated as an analgesic

effect (Shrier 2000). The increase in stretch tolerance could be an important mechanistic factor in partly explaining the effect of stretching on the ROM.

Based on the results of Paper VI, a hypothesis is put forward, which implicates the segmental control of nociceptive transmission as a mechanism underlying the pain-alleviating effect of stretching. This hypothesis complements rather than contradicts the more peripherally oriented hypotheses. It has to be emphasized, though, that Paper VI does not prove the existence of such a mechanism in humans, but rather suggests that interactions between mechanical stretch-sensitive and nociceptive muscle afferent inputs at the level of the spinal cord are possible and therefore worthy of further investigation.

Future studies

The next step in examining the effects of muscle stretch on nociceptive processing in SDHNs should aim at identifying and characterizing the neurons modulated by stretch.

Conclusion

Based on the findings of Paper VI, it is concluded that interactions between mechanical stretch-sensitive and nociceptive muscle afferent inputs at the level of the spinal cord are possible. Furthermore, the study suggests that the mechanical input, here induced by physiological static muscle stretch, has the ability to counteract the initial response of the nociceptive dorsal horn neurons to the bradykinin-induced noxious input.

MAIN CONCLUSIONS OF THE THESIS

The present thesis shows that repetitive low-intensity arm work reduces the position sense acuity of the shoulder. It also indicates that the longer one works to reach fatigue, the longer the sensation of fatigue is retained. Furthermore, a greater retention of the fatigue sensation is related to a greater detrimental effect on proprioceptive acuity.

Since proprioceptive information is of crucial importance for motor control, the reduced proprioceptive acuity that may result from repetitive work exposure can lead to an increased muscle co-activation while working, thus reducing muscle relaxation periods and increasing the risk of muscle fiber overload.

This suggests one plausible mechanism linking long-term stereotypic repetitive work exposure to muscle pain disorders.

The present thesis also shows that acute bouts of shoulder muscle stretching in healthy subjects do not affect shoulder position sense.

It also shows that stretch training for two weeks can increase the subjective tolerance to stretch torque, while not affecting the range of motion (ROM) or passive muscle stiffness. Increased tolerance to stretch torque may be a mechanism explaining increases in ROM associated with stretch training. The increase in tolerance to stretch torque, likely due to sensory adaptation, might also explain the gradual increase in pain-free ROM in myalgic patients subjected to stretch treatment, and perhaps contributes to alleviate tenderness of muscles in these patients.

Finally, in an acute animal model, interactions between stretch-sensitive and nociceptive muscle afferent inputs at the level of the spinal cord were demonstrated. This finding indicates a possible spinal mechanism involved in stretching-induced pain alleviation.

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REFERENCES

- Akazawa K, Milner TE, Stein RB (1983) Modulation of reflex EMG and stiffness in response to stretch of human finger muscle. *J Neurophysiol* 49: 16-27
- Alter MJ (1996) *Science of Flexibility*. 2. ed. Human Kinetics, Champaign, USA, pp 1-373
- American College of Sports Medicine Position Stand (1998) The recommended quantity and quality of exercise for developing and maintaining cardiorespiratory and muscular fitness, and flexibility in healthy adults. *Med Sci Sports Exerc* 30: 975-991
- Arbetsmiljöverket och SCB (2001) *Arbetsjukdomar och Arbetsolyckor*. Statistiska centralbyrån, Stockholm, Sweden
- Ariëns GA, van Mechelen W, Bongers PM, Bouter LM, van der Wal G (2000) Physical risk factors for neck pain. *Scand J Work Environ Health* 26: 7-19
- Armstrong TJ, Buckle P, Fine LJ, Hagberg M, Jonsson B, Kilbom Å, Kuorinka IAA, Silverstein BA, Sjøgaard G, Viikari-Juntura ERA (1993) A conceptual model for work-related neck and upper-limb musculoskeletal disorders. *Scand J Work Environ Health* 19: 73-84
- Arnold MP, Baumann JU, Koch HG (1988) Kontrakturen von pelvicuralen muskeln und femoropatellares schmerzsyndrom bei velofahrern. Effekte von muskeldehnungsübungen. *Schweiz Z Sportmed* 36: 187-190
- Barbe MF, Barr AE, Gorzelany I, Amin M, Gaughan JP, Safadi FF (2003) Chronic repetitive reaching and grasping results in decreased motor performance and widespread tissue responses in a rat model of MSD. *J Orthop Res* 21: 167-176
- Bentley S (1996) Exercise-induced muscle cramp. Proposed mechanisms and management. *Sports Med* 21: 409-420
- Bergenheim M, Johansson H, Pedersen J (1995) The role of the "gamma"-system for improving information transmission in populations of Ia afferents. *Neurosci Res* 23: 207-215
- Bergenheim M, Johansson H, Pedersen J, Öhberg F, Sjölander P (1996) Ensemble coding of muscle stretches in afferent populations containing different types of muscle afferents. *Brain Res* 734: 157-166
- Bernard BP (1997) *Musculoskeletal Disorders and Workplace Factors. A Critical Review of Epidemiologic Evidence for Work-Related Musculoskeletal Disorders of the Neck, Upper Extremity, and Low Back*. Department of Health and Human Services, National Institute for Occupational Safety and Health, Cincinnati, USA
- Besson J-M, Chaouch A (1987) Peripheral and Spinal Mechanisms of Nociception. *Physiol Rev* 67: 67-186
- Björklund M, Crenshaw AG, Djupsjöbacka M, Johansson H (2003) Position sense acuity is diminished following repetitive low-intensity work to fatigue in a simulated occupational setting. A critical comment. *Eur J Appl Physiol* 88: 485-486
- Blair S, Djupsjöbacka M, Johansson H, Ljubisavljevic M, Passatore M, Windhorst U, Punnett L (2003) Neuromuscular mechanisms behind chronic work-related myalgias: An overview. In: Johansson H, Windhorst U, Djupsjöbacka M, Passatore M (eds) *Chronic Work-Related Myalgia. Neuromuscular Mechanisms behind Work-Related Chronic Muscle Pain*

- Syndromes. Gävle University Press, pp 5-46
- Blair SJ (1995) Cervicobrachial disorders in repetitive motion disorders of the upper extremity. In: Gordon SL, Blair SJ, Fine LJ (eds) Repetitive motion disorders of the upper extremity. American Academy of Orthopaedic Surgeons, Rosemont, USA, pp 507-515
- Blomberg S (1993) A pragmatic approach to low-back pain including manual therapy and steroid injections. A multicentre study in primary health care. Almqvist & Wiksell, Uppsala University, Sweden, pp 1-146
- Bongers PM, de Winter CR, Kompier MA (1993) Psychosocial factors at work and musculoskeletal disease. *Scand J Work Environ Health* 19: 297-312
- Bonutti PM, Windau JE, Ables BA, Miller BG (1994) Static progressive stretch to reestablish elbow range of motion. *Clin Orthop* 303: 128-134
- Borg G (1982) A category scale with ratio properties for intermodal and interindividual comparisons. In: Geissler H-G, Petzold P (eds) Psychophysical Judgement and the Process of Perception. VEB Deutscher Verlag der Wissenschaften, Berlin, Germany, pp 24-34
- Brockett C, Warren N, Gregory JE, Morgan DL, Proske U (1997) A comparison of the effects of concentric versus eccentric exercise on force and position sense at the human elbow joint. *Brain Res* 771: 251-258
- Brown AG (1981) Organization in the spinal cord: the anatomy and physiology of identified neurones. Organization in the spinal cord: the anatomy and physiology of identified neurones. Springer-Verlag, New York, USA, pp 1-238
- Bruckle W, Suckfull M, Fleckenstein W, Weiss C, Muller W (1990) Gewebe-pO₂-Messung in der verspannten Rückenmuskulatur (m. erector spinae). *Z Rheumatol* 49: 208-216
- Buckle B, Devereux J (1999) Work-related neck and upper limb musculoskeletal disorders. European Agency for Safety and Health at Work ; Luxembourg : Office for Official Publications of the European Communities, Bilbao, Luxembourg
- Bureau of Labor Statistics (2001) Nonfatal Illnesses Cases by Selected Categories, Private Industry, 2000. U.S. Department of Labor, Bureau of Labor Statistics, Washington, USA
- Burton AK, McClune TD, Clarke RD, Main CJ (2004) Long-term follow-up of patients with low back pain attending for manipulative care: outcomes and predictors. *Man Ther* 9: 30-35
- Calvin-Figuiera S, Romaguere P, Gilhodes JC, Roll JP (1999) Antagonist motor responses correlate with kinesthetic illusions induced by tendon vibration. *Exp Brain Res* 124: 342-350
- Carli G, Farabollini F, Fontani G, Meucci M (1979) Slowly adapting receptors in cat hip joint. *J Neurophysiol* 42: 767-778
- Carpenter JE, Blaiser RB, Pellizzon GG (1998) The effects of muscle fatigue on shoulder joint position sense. *Am J Sports Med* 26: 262-265
- Chan SP, Hong Y, Robinson PD (2001) Flexibility and passive resistance of the hamstrings of young adults using two different static stretching protocols. *Scand J Med Sci Sports* 11: 81-86
- Chung JM, Fang ZR, Hori Y, Lee KH, Willis WD (1984a) Prolonged inhibition of primate spinothalamic tract cells by peripheral nerve stimulation. *Pain* 19: 259-275

- Chung JM, Lee KH, Hori Y, Endo K, Willis WD (1984b) Factors influencing peripheral nerve stimulation produced inhibition of primate spinothalamic tract cells. *Pain* 19: 277-293
- Church JB, Wiggins MS, Moode FM, Crist R (2001) Effect of warm-up and flexibility treatments on vertical jump performance. *J Strength Cond Res* 15: 332-336
- Clark FJ, Burgess RC, Chapin JW, Lipscomb WT (1985) Role of intramuscular receptors in the awareness of limb position. *J Neurophysiol* 54: 1529-1540
- Clark FJ, Horch KW, Bach SM, Larson GF (1979) Contributions of cutaneous and joint receptors to static knee-position sense in man. *J Neurophysiol* 42: 877-888
- Collins DF, Prochazka A (1996) Movement illusions evoked by ensemble cutaneous input from the dorsum of the human hand. *J Physiol (Lond)* 496: 857-871
- Cornwell A, Nelson AG, Sidaway B (2002) Acute effects of stretching on the neuromechanical properties of the triceps surae muscle complex. *Eur J Appl Physiol* 86: 428-434
- Davidoff RA (1992) Skeletal muscle tone and the misunderstood stretch reflex. *Neurology* 42: 951-963
- Day RK, Ashmore CR, Lee YB (1984) The effect of stretch removal on muscle weight and proteolytic enzyme activity in normal and dystrophic chicken muscles. *Muscle Nerve* 7: 482-485
- De Deyne PG (2001) Application of passive stretch and its implications for muscle fibers. *Phys Ther* 81: 819-827
- De Koninck Y, Henry JL (1992) Peripheral vibration causes an adenosine-mediated postsynaptic inhibitory potential in dorsal horn neurons of the cat spinal cord. *Neuroscience* 50: 435-443
- de Vries HA (1962) Evaluation of static stretching procedures for improvement of flexibility. *Res Q Exerc Sport* 33: 222-229
- Djupsjöbacka M, Johansson H, Bergenheim M (1994) Influences on the "gamma"-muscle spindle system from muscle afferents stimulated by increased intramuscular concentrations of arachidonic acid. *Brain Res* 663: 293-302
- Djupsjöbacka M, Johansson H, Bergenheim M, Wenngren BI (1995) Influences on the "gamma"-muscle spindle system from muscle afferents stimulated by increased intramuscular concentrations of bradykinin and 5-HT. *Neurosci Res* 22: 325-333
- Dompier TP, Denegar CR, Buckley WE, Miller SJ, Hertel J, Sebastianelli WJ (2001) The effect of general anesthesia on passive-knee-extension range of motion. *J Sport Rehabil* 10: 257-264
- Dray A, Perkins M (1993) Bradykinin and inflammatory pain. *Trends Neurosci* 16: 99-104
- Duong B, Low M, Moseley AM, Lee RY, Herbert RD (2001) Time course of stress relaxation and recovery in human ankles. *Clin Biomech* 16: 601-607
- Eaton JM (1989) Is this really a muscle cramp? *Postgrad Med* 86: 227-232
- Edin BB (1992) Quantitative analysis of static strain sensitivity in human mechanoreceptors from hairy skin. *J Neurophysiol* 67: 1105-1113
- Edin BB (2001) Cutaneous afferents provide information about knee joint movements in humans. *J Physiol (Lond)* 531: 289-297
- Edin BB, Johansson N (1995) Skin strain patterns provide kinaesthetic information to the hu-

- man central nervous system. *J Physiol (Lond)* 487: 243-251
- Egginton S, Hudlicka O, Brown MD, Walter H, Weiss JB, Bate A (1998) Capillary growth in relation to blood flow and performance in overloaded rat skeletal muscle. *J Appl Physiol* 85: 2025-2032
- Ekberg K, Karlsson M, Axelson O, Malm P (1995) Cross-sectional study of risk factors for symptoms in the neck and shoulder area. *Ergonomics* 38: 971-980
- Enoka RM (1994) Acute adaptations. *Neuromechanical Basis of Kinesiology* 2:nd ed. Human Kinetics, Champaign, USA, pp 271-293
- Etnyre BR, Abraham LD (1986a) Gains in range of ankle dorsiflexion using three popular stretching techniques. *Am J Phys Med* 65: 189-196
- Etnyre BR, Abraham LD (1986b) H-reflex changes during static stretching and two variations of proprioceptive neuromuscular facilitation techniques. *Electroencephalogr Clin Neurophysiol* 63: 174-179
- Ettema GJ (2001) Muscle efficiency: the controversial role of elasticity and mechanical energy conversion in stretch-shortening cycles. *Eur J Appl Physiol* 85: 457-465
- Ferguson D (1984) The "new" industrial epidemic. *Med J Aust* 140: 318-319
- Ferrell WR (1980) The adequacy of stretch receptors in the cat knee joint for signalling joint angle throughout a full range of movement. *J Physiol (Lond)* 299: 85-99
- Forestier N, Teasdale N, Nougier V (2002) Alteration of the position sense at the ankle induced by muscular fatigue in humans. *Med Sci Sports Exerc* 34: 117-122
- Forsman M, Birch L, Zhang Q, Kadefors R (2001) Motor unit recruitment in the trapezius muscle with special reference to coarse arm movements. *J Electromyogr Kinesiol* 11: 207-216
- Frankeny JR, Holly RG, Ashmore CR (1983) Effects of graded duration of stretch on normal and dystrophic skeletal muscle. *Muscle Nerve* 6: 269-277
- Gajdosik RL (1985) Rectus femoris muscle tightness: Intratester reliability of an active knee flexion test. *J Orthop Sports Phys Ther* 6: 289-292
- Gajdosik RL (1991) Effects of static stretching on the maximal length and resistance to passive stretch of short hamstring muscles. *J Orthop Sports Phys Ther* 14: 250-255
- Gajdosik RL (2001) Passive extensibility of skeletal muscle: review of the literature with clinical implications. *Clin Biomech* 16: 87-101
- Gajdosik RL, Bohannon RW (1987) Clinical measurement on range of motion. Review of goniometry emphasizing reliability and validity. *Phys Ther* 67: 1867-1872
- Gandevia SC, Burke D (1992) Does the nervous system depend on kinesthetic information to control natural limb movements. *Behav Brain Res* 15: 614-632
- Gareis H, Solomonow M, Baratta R, Best R, D'ambrosia R (1992) The isometric length-force models of nine different skeletal muscles. *J Biomech* 25: 903-916
- Garrison DW, Foreman RD (1996) Effects of transcutaneous electrical nerve stimulation (TENS) on spontaneous and noxiously evoked dorsal horn cell activity in cats with transected spinal cords. *Neurosci Lett* 216: 125-128
- Gelfan S, Carter S (1967) Muscle sense in man. *Exp Neurol* 18: 469-473

- Genaidy AM, Delgado E, Bustos T (1995) Active microbreak effects on musculoskeletal comfort ratings in meatpacking plants. *Ergonomics* 38: 326-336
- Ghez C, Sainburg R (1995) Proprioceptive control of interjoint coordination. *Can J Physiol Pharmacol* 73: 273-284
- Gissel H (2000) Ca²⁺ accumulation and cell damage in skeletal muscle during low frequency stimulation. *Eur J Appl Physiol* 83: 175-180
- Gleim GW, McHugh MP (1997) Flexibility and its effects on sports injury and performance. *Sports Med* 24: 289-299
- Godges JJ, MacRae H, Longdon C, Tinberg C, MacRae P (1989) The effects of two stretching procedures on hip range of motion and gait economy. *J Orthop Sports Phys Ther* 3: 350-357
- Goodwin GM, McCloskey DI, Matthews PBC (1972) The contribution of muscle afferents to kinaesthesia shown by vibration induced illusions of movement and by the effects of paralyzing joint afferents. *Brain* 95: 705-748
- Gossman MR, Sahrman SA, Rose SJ (1982) Review of length-associated changes in muscle. Experimental evidence and clinical implications. *Phys Ther* 62: 1799-1808
- Grigg P (1994) Peripheral neural mechanisms in proprioception. *J Sports Med* 3: 2-17
- Guissard N, Duchateau J, Hainaut K (1988) Muscle stretching and motoneuron excitability. *Eur J Appl Physiol* 58: 47-52
- Guissard N, Duchateau J, Hainaut K (2001) Mechanisms of decreased motoneurone excitation during passive muscle stretching. *Exp Brain Res* 137: 163-169
- Gustafsson T, Kraus WE (2001) Exercise-induced angiogenesis-related growth and transcription factors in skeletal muscle, and their modification in muscle pathology. *Front Biosci* 6: D75-D89
- Halbertsma JPK, Göeken LNH (1994) Stretching exercises: Effect on passive extensibility and stiffness in short hamstrings of healthy subjects. *Arch Phys Med Rehabil* 75: 976-981
- Halbertsma JPK, van Bolhuis AI, Göeken LNH (1996) Sport stretching: Effect on passive muscle stiffness of short hamstrings. *Arch Phys Med Rehabil* 77: 688-692
- Handel M, Horstmann T, Dickhuth H-H, Gülch RW (1997) Effects of contract-relax stretching training on muscle performance in athletes. *Eur J Appl Physiol* 76: 400-408
- Handwerker HO, Iggo A, Zimmermann M (1975) Segmental and supraspinal actions on dorsal horn neurons responding to noxious and non-noxious skin stimuli. *Pain* 1: 147-165
- Hansen J, Thomas GD, Harris SA, Parsons WJ, Victor RG (1996) Differential sympathetic neural control of oxygenation in resting and exercising human skeletal muscle. *J Clin Invest* 98: 584-596.
- Hanten WP, Olson SL, Butts NL, Nowicki AL (2000) Effectiveness of a home program of ischemic pressure followed by sustained stretch for treatment of myofascial trigger points. *Phys Ther* 80: 997-1003
- Hardy L (1985) Improving active range of hip flexion. *Res Q Exerc Sport* 56: 111-114
- Harvey L, Herbert R, Crosbie J (2002) Does stretching induce lasting increases in joint ROM? A systematic review. *Physiother Res Int* 7: 1-13
- Hellström F, Thunberg J, Bergenheim M, Sjölander P, Pedersen J, Johansson H (2000) Eleva-

- ted intramuscular concentration of bradykinin in jaw muscle increases the fusimotor drive to neck muscles in the cat. *J Dent Res* 79: 1815-1822
- Henneman E, Somjen G, Carpenter DO (1965) Excitability and inhibitability of motoneurons of different sizes. *J Neurophysiol* 28: 599-620
- Henning RA, Jacques P, Kissel GV, Sullivan AB, Alteras-Webb SM (1997) Frequent short rest breaks from computer work: effects on productivity and well-being at two field sites. *Ergonomics* 40: 78-91
- Herbert RD (1988) The passive mechanical properties of muscle and their adaptations to altered patterns of use. *Aust J Physiother* 34: 141-149
- Herbert RD, Moseley AM, Butler JE, Gandevia SC (2002) Change in length of relaxed muscle fascicles and tendons with knee and ankle movement in humans. *J Physiol (Lond)* 539: 637-645
- Hermans V, Spaepen AJ (1997) Muscular activity of the shoulder and neck region during sustained and intermittent exercise. *Clin Physiol* 17: 95-104
- Hill DK (1968) Tension due to interaction between the sliding filaments in resting striated muscle. The effect of stimulation. *J Physiol (Lond)* 199: 637-684
- Horch KW, Clark FJ, Burgess PR (1975) Awareness of knee joint angle under static conditions. *J Neurophysiol* 38: 1436-1447
- Hou CR, Tsai LC, Cheng KF, Chung KC, Hong CZ (2002) Immediate effects of various physical therapeutic modalities on cervical myofascial pain and trigger-point sensitivity. *Arch Phys Med Rehabil* 83: 1406-1414
- Houk JC, Henneman E (1967) Responses of golgi tendon organs to active contractions of the soleus muscle of the cat. *J Neurophysiol* 30: 466-481
- Houk JC, Rymer WZ (1981) Neural control of muscle length and tension. In: Brooks VB (ed) *Handbook of Physiology, Section 1, The Nervous system, vol II, part 1: Motor control*. American Physiological Society, Bethesda, pp 257-323
- Hrysomallis C, Goodman C (2001) A review of resistance exercise and posture realignment. *J Strength Cond Res* 15: 385-390
- Hudlicka O (1998) Is physiological angiogenesis in skeletal muscle regulated by changes in microcirculation? *Microcirculation* 5: 5-23
- Hulliger M (1984) The mammalian muscle spindle and its central control. *Rev Physiol Biochem Pharmacol* 101: 1-110
- Hutton RS (1993) Neuromuscular basis of stretching exercises. In: Komi PV (ed) *The Encyclopaedia of Sports Medicine. Vol 3. Strength and Power in Sport*. Blackwell Science, Oxford, pp 29-38
- Hägg GM (1991) Static work loads and occupational myalgia - A new explanation model. In: Anderson PA, Hobart DJ, Danoff JV (eds) *Electromyographical Kinesiology*. Elsevier Science Publishers B.V., pp 141-144
- Jaeger B, Reeves JL (1986) Quantification of changes in myofascial trigger point sensitivity with the pressure algometer following passive stretch. *Pain* 27: 203-210
- Jahnke MT, Proske U, Struppler A (1989) Measurements of muscle stiffness, the electromyogram

- and activity in single muscle spindles of human flexor muscles following conditioning by passive stretch or contraction. *Brain Res* 493: 103-112
- Janda V (1978) Muscles, central nervous motor regulation and back problems. In: Korr IM (ed) *The Neurobiologic Mechanisms in Manipulative Therapy*. Plenum Press, New York, pp 27-41
- Jankowska E (1992) Interneuronal relay in spinal pathways from proprioceptors. *Prog Neurobiol* 38: 335-378
- Johansson H, Djupsjöbacka M, Sjölander P (1993) Influences on the “gamma”- muscle spindle system from muscle afferents stimulated by KCl and lactic acid. *Neurosci Res* 16: 49-57
- Johansson H, Pedersen J, Bergenheim M, Djupsjöbacka M (1998) Peripheral afferents of the knee: their stiffness, joint stability, and proprioception and coordination. In: Lephard SM, Fu FH (eds) *Proprioception and Neuromuscular Control in Joint Stability*. Human Kinetics, USA, pp 5-22
- Johansson H, Windhorst U, Djupsjöbacka M, Passatore M (2003) In: Johansson H, Windhorst U, Djupsjöbacka M, Passatore M (eds) *Chronic Work-Related Myalgia. Neuromuscular Mechanisms behind Work-Related Chronic Muscle Pain Syndromes*. Gävle University Press, pp 1-310
- Jones AM (2002) Running economy is negatively related to sit-and-reach test performance in international-standard distance runners. *Int J Sports Med* 23: 40-43
- Jones DA (1996) High- and low-frequency fatigue revisited. *Acta Physiol Scand* 156: 265-270
- Jull GA, Janda V (1987) Muscles and motor control in low back pain: Assessment and management. In: Twomey LT (ed) *Physical therapy of the low back*. Churchill Livingstone, New York, USA
- Kabat H, Knott M (1953) Proprioceptive facilitation technics for treatment of paralysis. *Phys Ther Rev* 33: 53-64
- Kadi F, Waling K, Ahlgren C, Sundelin G, Holmner S, Butler-Browne GS, Thornell LE (1998) Pathological mechanisms implicated in localized female trapezius myalgia. *Pain* 78: 191-196
- Kanaan N, Sawaya R (2001) Nocturnal leg cramps. Clinically mysterious and painful-but manageable. *Geriatrics* 56: 34-34.
- Kaufman MP, Rybicki KJ (1987) Discharge properties of group III and IV muscle afferents: Their responses to mechanical and metabolic stimuli. *Circulation* 61: I60-I65
- Keele SW, Eells JG (1972) Memory characteristics of kinesthetic information. *J Mot Behav* 4: 127-134
- Kell RT, Bell G, Quinney A (2001) Musculoskeletal fitness, health outcomes and quality of life. *Sports Med* 31: 863-873
- Khalil TM, Asfour SS, Martinez LM, Waly SM, Rosomoff RS, Rosomoff HL (1992) Stretching in the rehabilitation of low-back pain patients. *Spine* 17: 311-317
- Kindig CA, Poole DC (2001) Sarcomere length-induced alterations of capillary hemodynamics in rat spinotrapezius muscle: vasoactive vs passive control. *Microvasc Res* 61: 64-74
- Klenerman L, Slade PD, Stanley IM, Pennie B, Reilly JP, Atchison LE, Troup JD, Rose MJ

- (1995) The prediction of chronicity in patients with an acute attack of low back pain in a general practice setting. *Spine* 20: 478-484
- Kniffki K-D, Mense S, Schmidt RF (1978) Responses of group IV afferent units from skeletal muscle to stretch, contraction and chemical stimulation. *Exp Brain Res* 31: 511-522
- Knudson D, Bennett K, Corn R, Leick D, Smith C (2001) Acute effects of stretching are not evident in the kinematics of the vertical jump. *J Strength Cond Res* 15: 98-101
- Kostyukov AI, Cherkassky VL (1992) Movement-dependent after-effects in the firing of the spindle endings from the de-efferented muscles of the cat hindlimb. *Neuroscience* 46: 989-999
- Kottke FJ, Pauley DL, Ptak RA (1966) The rationale for prolonged stretching for correction of shortening of connective tissue. *Arch Phys Med Rehabil* 6: 345-352
- Krabak BJ, Laskowski ER, Smith J, Stuart MJ, Wong GY (2001) Neurophysiologic influences on hamstring flexibility: a pilot study. *Clin J Sports Med* 11: 241-246
- Kubo K, Kanehisa H, Fukunaga T (2002a) Effects of transient muscle contractions and stretching on the tendon structures in vivo. *Acta Physiol Scand* 175: 157-164
- Kubo K, Kanehisa H, Fukunaga T (2002b) Effect of stretching training on the viscoelastic properties of human tendon structures in vivo. *J Appl Physiol* 92: 595-601
- Kubo K, Kanehisa H, Fukunaga T (2002c) Effects of resistance and stretching training programmes on the viscoelastic properties of human tendon structures in vivo. *J Physiol (Lond)* 538: 219-226
- Kubo K, Kanehisa H, Kawakami Y, Fukunaga T (2001) Influence of static stretching on viscoelastic properties of human tendon structures in vivo. *J Appl Physiol* 90: 520-527
- Kuukkanen T, Malkia E (2000) Effects of a three-month therapeutic exercise programme on flexibility in subjects with low back pain. *Physiother Res Int* 5: 46-61
- Lackner JR, DiZio PA (2000) Aspects of body self-calibration. *Trends Cogn Sci* 4: 279-288
- Larsson R, Öberg PA, Larsson SE (1999) Changes of trapezius muscle blood flow and electromyography in chronic neck pain due to trapezius myalgia. *Pain* 79: 45-50
- Larsson S-E, Bengtsson A, Bodegård L, Henriksson KG, Larsson J (1988) Muscle changes in work-related chronic myalgia. *Acta Orthop Scand* 59: 552-556
- Larsson S-E, Bodegård L, Henriksson KG, Öberg PÅ (1990) Chronic trapezius myalgia. Morphology and blood flow studied in 17 patients. *Acta Orthop Scand* 61: 394-398
- Lattanzio P-J, Petrella RJ, Sproule JR, Fowler PJ (1997) Effects of fatigue on knee proprioception. *Clin J Sports Med* 7: 22-27
- Le Bars D, Dickenson AH, Besson J-M (1979) Diffuse noxious inhibitory controls (DNIC). I. Effects on dorsal horn convergent neurones in the rat. *Pain* 6: 283-304
- Leclerc KM, Landry FJ (1996) Benign nocturnal leg cramps. Current controversies over use of quinine. *Postgrad Med* 99: 177-178
- Lee HM, Liao JJ, Cheng CK, Tan CM, Shih JT (2003) Evaluation of shoulder proprioception following muscle fatigue. *Clin Biomech* 18: 843-847
- Leivseth G, Torstensson J, Reikerås O (1989) Effect of passive muscle stretching in osteoarthritis of the hip. *Clin Sci (Colch)* 76: 113-117

- Lenart G, Kullmann L (1974) Isolated contracture of the rectus femoris muscle. *Clin Orthop* 99: 125-130
- Lewit K (1999) Manipulative therapy in rehabilitation of the locomotor system. 3rd ed. Butterworth-Heinemann, Oxford, UK
- Lindman R, Hagberg M, Ångqvist K-A, Söderlund K, Hultman E, Thornell L-E (1991) Changes in muscle morphology in chronic trapezius myalgia. *Scand J Work Environ Health* 17: 347-355
- Luther BL (2002) Congenital muscular torticollis. *Orthop Nurs* 21: 21-27
- Macefield G, Gandevia SC, Burke D (1990) Perceptual responses to microstimulation of single afferents innervating joints, muscles and skin of the human hand. *J Physiol (Lond)* 429: 113-129
- Mackinnon SE, Novak CB, Louis S (1994) Clinical commentary: Pathogenesis of cumulative trauma disorder. *J Hand Surg (Am)* 19A: 873-883
- Madeleine P, Jorgensen LV, Sogaard K, Arendt-Nielsen L, Sjogaard G (2002) Development of muscle fatigue as assessed by electromyography and mechanomyography during continuous and intermittent low-force contractions: effects of the feedback mode. *Eur J Appl Physiol* 87: 28-37
- Magnusson SP (1998) Passive properties of human skeletal muscle during stretch maneuvers. *Scand J Med Sci Sports* 8: 65-77
- Magnusson SP, Simonsen EB, Aagaard P, Gleim GW, McHugh MP, Kjaer M (1995) Viscoelastic response to repeated static stretching in the human hamstring muscle. *Scand J Med Sci Sports* 5: 342-347
- Magnusson SP, Simonsen EB, Aagaard P, Sorensen H, Kjaer M (1996a) A mechanism for altered flexibility in human skeletal muscle. *J Physiol (Lond)* 497: 291-298
- Magnusson SP, Simonsen EB, Aagaard P, Dyhre-Poulsen P, McHugh MP, Kjaer MAM (1996b) Mechanical and physiological responses to stretching with and without preisometric contraction in human skeletal muscle. *Arch Phys Med Rehabil* 77: 373-378
- Marks R, Quinney HA (1993) Effect of fatiguing maximal isokinetic quadriceps contractions on ability to estimate knee-position. *Percept Mot Skills* 77: 1195-1202
- Marteniuk RG (1973) Retention characteristics of motor short-term memory cues. *J Mot Behav* 5: 249-259
- Mathiassen SE (1994) On the validity of isometric exercise as a model of occupational shoulder-neck activity. Proceedings of the 12th Triennial Congress of the International Ergonomics Association 2: 189-191
- Matthews PB, Simmonds A (1974) Sensations of finger movement elicited by pulling upon flexor tendons in man. *J Physiol (Lond)* 239: 27P-28P
- Matthews PBC (1972) Mammalian muscle receptors and their central actions. Edward Arnold Ltd, London, UK, pp 1-630
- McCarthy PW, Olsen JP, Smeby IH (1997) Effects of contract-relax stretching procedures on active range of motion of the cervical spine in the transverse plane. *Clin Biomech* 12: 136-138

- McCloskey DI (1973) Differences between the senses of movement and position shown by the effects of loading and vibration of muscles in man. *Brain Res* 63: 119-131
- McCloskey DI, Cross MJ, Honner R, Potter E (1983) Sensory effects of pulling or vibrating exposed tendons in man. *Brain* 106: 21-37
- McDonald CM (1998) Limb contractures in progressive neuromuscular disease and the role of stretching, orthotics, and surgery. *Phys Med Rehabil Clin N Am* 9: 187-211
- McGee SR (1990) Muscle cramps. *Arch Intern Med* 150: 511-518
- McHugh MP, Kremenec IJ, Fox MB, Gleim GW (1998) The role of mechanical and neural restraints to joint range of motion during passive stretch. *Med Sci Sports Exerc* 30: 928-932
- Medeiros JM, Smidt GL, Burmeister LF, Soderberg GL (1977) The influence of isometric exercise and passive stretch on hip joint motion. *Phys Ther* 57: 518-523
- Melzack R, Wall PD (1965) Pain Mechanisms: A New Theory. *Science* 150: 971-979
- Mense S (1993) Nociception from skeletal muscle in relation to clinical muscle pain. *Pain* 54: 241-289
- Mense S, Meyer H (1985) Different types of slowly conducting afferent units in cat skeletal muscle and tendon. *J Physiol (Lond)* 363: 403-417
- Mense S, Simons DG, Russell IJ (2001) *Muscle Pain: Understanding its Nature, Diagnosis, and Treatment*. Lippincott Williams & Wilkins, Philadelphia, USA, pp 1-385
- Moberg E (1983) The role of cutaneous afferents in position sense, kinaesthesia, and motor function of the hand. *Brain* 106: 1-19
- Monsey M, Ioffe I, Beatini A, Lukey B, Santiago A, James AB (2003) Increasing compliance with stretch breaks in computer users through reminder software. *Work* 21: 107-111
- Morgan DL, Prochazka A, Proske U (1984) The after-effects of stretch and fusimotor stimulation on the responses of primary endings of cat muscle spindles. *J Physiol (Lond)* 356: 465-477
- Muir IW, Chesworth BM, Vandervoort AA (1999) Effect of a static calf-stretching exercise on the resistive torque during passive ankle dorsiflexion in healthy subjects. *J Orthop Sports Phys Ther* 29: 106-115
- National Research Council (1998) *Work-related Musculoskeletal Disorders: A Review of the Evidence*. National Academy Press, Washington, USA
- National Research Council (2001) *Musculoskeletal Disorders and the Workplace: Low Back and Upper Extremities*. National Academy Press, Washington, USA
- Nelson AG, Allen JD, Cornwell A, Kokkonen J (2001a) Inhibition of maximal voluntary isometric torque production by acute stretching is joint-angle specific. *Res Q Exerc Sport* 72: 68-70
- Nelson AG, Kokkonen J, Eldredge C, Cornwell A, Glickman-Weiss E (2001b) Chronic stretching and running economy. *Scand J Med Sci Sports* 11: 260-265
- Neufeld SD (1981) Reproducing movement in the lower extremity using kinesthetic cues of distance and location. *Phys Ther* 61: 1147-1151
- Norlund A, Waddell G (2000) Samhällets totala kostnader för ont i ryggen. In: Nachemson A, Jonsson E (eds) *Ont i ryggen, ont i nacken*. Vol 2. SBU, Stockholm, Sweden, pp 297-309
- Norris CM (1995) Spinal stabilisation. 4. Muscle imbalance and the low back. *Physiotherapy*

81: 127-138

- Norris Jr FH, Gasteiger EL, Chatfield PO (1957) An electromyographic study of induced and spontaneous muscle cramps. *Electroencephalogr Clin Neurophysiol Suppl* 9: 139-147
- Novak CB, Mackinnon SE (1997) Repetitive use and static postures: a source of nerve compression and pain. *J Hand Ther* 10: 151-159
- Novak CB, Mackinnon SE (2002) Multilevel nerve compression and muscle imbalance in work-related neuromuscular disorders. *Am J Ind Med* 41: 343-352
- Nussbaum MA (2001) Static and dynamic myoelectric measures of shoulder muscle fatigue during intermittent dynamic exertions of low to moderate intensity. *Eur J Appl Physiol* 85: 299-309
- Paoli P, Merllié D (2001) Third European survey on working conditions 2001. European Foundation for the Improvement of Living and Working Conditions
- Parisi L, Pierelli F, Amabile G, Valente G, Calandriello E, Fattapposta F, Rossi P, Serrao M (2003) Muscular cramps: proposals for a new classification. *Acta Neurol Scand* 107: 176-186
- Passatore M, Roatta S (2003) Sympathetic nervous system: Interaction with muscle function and involvement in motor control. In: Johansson H, Windhorst U, Djupsjöbacka M, Passatore M (eds) *Chronic Work-Related Myalgia. Neuromuscular Mechanisms behind Work-Related Chronic Muscle Pain Syndromes*. Gävle University Press, pp 243-263
- Pedersen J, Ljubisavljevic M, Bergenheim M, Johansson H (1998) Alterations in information transmission in ensembles of primary muscle spindle afferents after muscle fatigue in heteronymous muscle. *Neuroscience* 84: 953-959
- Pedersen J, Lönn J, Hellström F, Djupsjöbacka M, Johansson H (1999) Localized muscle fatigue decreases the acuity of the movement sense in the human shoulder. *Med Sci Sports Exerc* 31: 1047-1052
- Pedersen J, Sjölander P, Wenngren BI, Johansson H (1997) Increased intramuscular concentration of bradykinin increases the static fusimotor drive to muscle spindles in neck muscles of the cat. *Pain* 70: 83-91
- Pincus T, Burton AK, Vogel S, Field AP (2002) A systematic review of psychological factors as predictors of chronicity/disability in prospective cohorts of low back pain. *Spine* 27: E109-E120
- Poole DC, Musch TI, Kindig CA (1997) In vivo microvascular structural and functional consequences of muscle length changes. *Am J Physiol* 272: H2107-H2114
- Prochazka A (1996) Proprioceptive feedback and movement regulation. In: Rowell L, Sheperd JT (eds) *Handbook of Physiology. Section 12. Exercise: Regulation and Integration of Multiple Systems*. American Physiological Society, New York, pp 89-127
- Proske U, Morgan DL, Gregory JE (1993) Thixotropy in skeletal muscle and in muscle spindles: a review. *Prog Neurobiol* 41: 705-721
- Punnett L, Herbert R (2000) Work-related Musculoskeletal Disorders: Is there a gender differential, and if so, what does it mean. In: Goldman MB, Hatch MC (eds) *Women and Health*. Academic Press, San Diego, USA

- Purslow PP (1989) Strain-induced reorientation of an intramuscular connective tissue network: implications for passive muscle elasticity. *J Biomech* 22: 21-31
- Rehn B, Bergdahl IA, Ahlgren C, From C, Jarvholm B, Lundstrom R, Nilsson T, Sundelin G (2002) Musculoskeletal symptoms among drivers of all-terrain vehicles. *J Sound Vib* 253: 21-29
- Riley JD, Antony SJ (1995) Leg cramps: differential diagnosis and management. *Am Fam Physician* 52: 1794-1798
- Robinson KL, McComas AJ, Belanger AY (1982) Control of soleus motoneuron excitability during muscle stretch in man. *J Neurol Neurosurg Psychiatry* 45: 699-704
- Roll JP, Gilhodes JC (1995) Proprioceptive sensory codes mediating movement trajectory perception: human hand vibration-induced drawing illusions. *Can J Physiol Pharmacol* 73: 295-304
- Rosenbaum D, Hennig E (1995) The influence of stretching and warm-up exercises on achilles tendon reflex activity. *J Sports Sci* 13: 481-490
- Ross BH, Thomas CK (1995) Human motor unit activity during induced muscle cramp. *Brain* 118: 983-993
- Roy EA (1977) Spatial cues in memory for movement. *J Mot Behav* 9: 151-156
- Sainburg RL, Ghez C, Kalakanis D (1999) Intersegmental dynamics are controlled by sequential anticipatory, error correction, and postural mechanisms. *J Neurophysiol* 81: 1045-1056
- Sainburg RL, Ghilardi MF, Poizner H, Ghez C (1995) Control of limb dynamics in normal subjects and patients without proprioception. *J Neurophysiol* 73: 820-835
- Sakamoto K, Aschenbach WG, Hirshman MF, Goodyear LJ (2003) Akt signaling in skeletal muscle: regulation by exercise and passive stretch. *Am J Physiol Endocrinol Metab* 285: E1081-E1088
- Sandkühler J (1996) The organization and function of endogenous antinociceptive systems. *Prog Neurobiol* 50: 49-81
- Saxton JM, Clarkson PM, James R, Miles M, Westerfer M, Clark S, Donnelly AE (1995) Neuromuscular dysfunction following eccentric exercise. *Med Sci Sports Exerc* 27: 1185-1193
- Schultz-Johnson K (2002) Static progressive splinting. *J Hand Ther* 15: 163-178
- Scott SH, Loeb GE (1994) The computation of position sense from spindles in mono- and multiarticular muscles. *J Neurosci* 14: 7529-7540
- Semler LM, Simmons RW (1979) Role of selected encoding strategies on short-term retention of kinesthetic information. *Percept Mot Skills* 48: 963-966
- Sharpe MH, Miles TS (1993) Position sense at the elbow after fatiguing contractions. *Exp Brain Res* 94: 179-182
- Shrier I (2000) Stretching before exercise: an evidence based approach. *Br J Sports Med* 34: 324-325
- Simons DG, Mense S (1998) Understanding and measurement of muscle tone as related to clinical muscle pain. *Pain* 75: 1-17
- Simons DG, Travell JG, Simons LS (1999) *Travell & Simons' Myofascial Pain and Dysfunction*

- : the Trigger Point Manual. 2. ed. Williams & Wilkins, Baltimore, USA
- Sittig AC, Denier van der Gon JJ, Gielen CCAM (1985) Separate control of arm position and velocity demonstrated by vibration of muscle tendon in man. *Exp Brain Res* 60: 445-453
- Sjøgaard G, Sjøgaard K (1998) Muscle Injury in Repetitive Motion Disorders. *Clin Orthop* 351: 21-31
- Sjölander P, Johansson H, Djupsjöbacka M (2002) Spinal and supraspinal effects of activity in ligament afferents. *J Electromyogr Kinesiol* 12: 167-176
- Smith AD, Stroud L, McQueen C (1991) Flexibility and anterior knee pain in adolescent elite figure skaters. *J Pediatr Orthop* 11: 77-82
- Sterner RL, Pincivero DM, Lephart SM (1998) The effects of muscular fatigue on shoulder proprioception. *Clin J Sports Med* 8: 96-101
- Sundelin G, Hagberg M (1989) The effects of different pause types on neck and shoulder EMG activity during VDU work. *Ergonomics* 32: 527-537
- Sundelin G, Hagberg M (1992) Electromyographic signs of shoulder muscle fatigue in repetitive arm work paced by the methods-time measurement system. *Scand J Work Environ Health* 18: 262-268
- Svensson P, Burgaard A, Schlosser S (2001) Fatigue and pain in human jaw muscles during a sustained, low-intensity clenching task. *Arch Oral Biol* 46: 773-777
- Sölveborn S-A (1997) Radial epicondylalgia ("tennis elbow"): treatment with stretching or forearm band. A prospective study with long-term follow-up including range-of-motion measurements. *Scand J Med Sci Sports* 7: 229-237
- Taimela S, Kankaanpää M, Luoto S (1999) The effect of lumbar fatigue on the ability to sense a change in lumbar position. A controlled study. *Spine* 24: 1322-1327
- Tardieu C, Tardieu G, Colbeau-Justin P, Huet de la Tour E, Lespargot A (1979) Trophic muscle regulation in children with congenital cerebral lesions. *J Neurol Sci* 42: 357-364
- Taylor DC, Dalton JDJ, Seaber AV, Garrett WEJ (1990) Viscoelastic properties of muscle-tendon units. The biomechanical effects of stretching. *Am J Sports Med* 18: 300-309
- Tock Y, Steinberg Y, Inbar GF, Ljubisavljevic M, Thunberg J, Windhorst U, Johansson H (2003) Estimation of muscle spindle information rate by pattern matching and effects of the fusimotor system. *Proceedings of the 1st International IEEE EMBS Conference on Neural Engineering* 51-54
- Toft E, Espersen GT, Kålund S, Sinkjær T, Hornemann BC (1989) Passive tension of the ankle before and after stretching. *Am J Sports Med* 17: 489-494
- Toft E, Sinkjær T, Andreassen S, Larsen K (1991) Mechanical and electromyographic responses to stretch of the human ankle extensors. *J Neurophysiol* 65: 1402-1410
- Tsuruoka M, Kang J-H, Matsui A, Matsui Y (1990) Nonsegmental inhibition of rat dorsal horn neurons by innocuous stimulation. *Brain Res Bull* 24: 861-864
- van Beers RJ, Sittig AC, Denier van der Gon JJ (1996) How humans combine simultaneous proprioceptive and visual position information. *Exp Brain Res* 111: 253-261
- van den Heuvel SG, de Looze MP, Hildebrandt VH, The KH (2003) Effects of software programs stimulating regular breaks and exercises on work-related neck and upper-limb disorders.

- Scand J Work Environ Health 29: 106-116
- van Dieën JH, Visser B, Hermans V (2003) The contribution of task-related biomechanical constraints to the development of work-related myalgia. In: Johansson H, Windhorst U, Djupsjöbacka M, Passatore M (eds) *Chronic Work-Related Myalgia. Neuromuscular Mechanisms behind Work-Related Chronic Muscle Pain Syndromes*. Gävle University Press, pp 83-93
- Van Roy P, Borms J, Haentjens A (1987) Goniometric study of the maintenance of hip flexibility resulting from hamstring stretches. *Physiother Pract* 3: 52-59
- Vasseljen O, Westgaard RH (1995) A case-control study of trapezius muscle activity in office and manual workers with shoulder and neck pain and symptom-free controls. *Int Arch Occup Environ Health* 67: 11-18
- Veiersted KB, Westgaard RH, Andersen P (1993) Electromyographic evaluation of muscular work pattern as a predictor of trapezius myalgia. *Scand J Work Environ Health* 19: 284-290
- Voight ML, Hardin JA, Blackburn TA, Tippet S, Canner GC (1996) The effects of muscle fatigue on and the relationship of arm dominance to shoulder proprioception. *J Orthop Sports Phys Ther* 23: 348-352
- Völlestad NK (1997) Measurement of human muscle fatigue. *J Neurosci Methods* 74: 219-227
- Von Holst E, Mittelstaedt H (1950) Das reafferenzprinzip (Wechselwirkungen zwischen Zentralnervensystem und peripherie). *Naturwissenschaften* 37: 464-476
- Voss DE (1967) Proprioceptive neuromuscular facilitation. *Am J Phys Med* 46: 838-899
- Wall PD (1978) The gate control theory of pain mechanisms. A re-examination and re-statement. *Brain* 101: 1-18
- Wallin D, Ekblom B, Grahn R, Nordenborg T (1985) Improvement of muscle flexibility. A comparison between two techniques. *Am J Sports Med* 13: 263-268
- Walsh WD (1981) Memory for preselected and constrained short movements. *Res Q Exerc Sport* 52: 368-379
- Weber S, Kraus H (1949) Passive and active stretching of muscles: spring stretch and control group. *Phys Ther Rev* 29: 407-410
- Westerblad H, Bruton JD, Allen DG, Lannergren J (2000) Functional significance of Ca²⁺ in long-lasting fatigue of skeletal muscle. *Eur J Appl Physiol* 83: 166-174
- Westgaard RH, de Luca CJ (1999) Motor unit substitution in long-duration contractions of the human trapezius muscle. *J Neurophysiol* 82: 501-504
- Wiemann K, Hahn K (1997) Influences of strength, stretching and circulatory exercises on flexibility parameters of the human hamstrings. *Int J Sports Med* 18: 340-346
- Williams PE (1988) Effect of intermittent stretch on immobilised muscle. *Ann Rheum Dis* 47: 1014-1016
- Williams PE (1990) Use of intermittent stretch in the prevention of serial sarcomere loss in immobilised muscle. *Ann Rheum Dis* 49: 316-317
- Willy RW, Kyle BA, Moore SA, Chleboun GS (2001) Effect of Cessation and Resumption of Static Hamstring Muscle Stretching on Joint Range of Motion. *J Orthop Sports Phys Ther* 31: 138-144

- Wilson GJ, Elliott BC, Wood GA (1992) Stretch shorten cycle performance enhancement through flexibility training. *Med Sci Sports Exerc* 24: 116-123
- Wilson LB, Engbretson J (2000) Dorsal horn administration of L-arginine accentuates the pressor response evoked by activation of muscle mechanoreceptors. *Auton Neurosci* 86: 135-139
- Windhorst U (2003) Neuroplasticity and modulation of chronic pain. In: Johansson H, Windhorst U, Djupsjöbacka M, Passatore M (eds) *Chronic Work-Related Myalgia. Neuromuscular Mechanisms behind Work-Related Chronic Muscle Pain Syndromes*. Gävle University Press, pp 207-224
- Wise AK, Gregory JE, Proske U (1996) The effects of muscle conditioning on movement detection thresholds at the human forearm. *Brain Res* 735: 125-130
- Worrell TW, Smith TL, Winegardner J (1994) Effect of hamstring stretching on hamstring muscle performance. *J Orthop Sports Phys Ther* 20: 154-159
- Yang H, Alnaqeeb M, Simpson H, Goldspink G (1997) Changes in muscle fibre type, muscle mass and IGF-I gene expression in rabbit skeletal muscle subjected to stretch. *J Anat* 190: 613-622
- Young W, Elliott S (2001) Acute effects of static stretching, proprioceptive neuromuscular facilitation stretching, and maximum voluntary contractions on explosive force production and jumping performance. *Res Q Exerc Sport* 72: 273-279
- Åhsberg E (2000) Dimensions of fatigue in different working populations. *Scand J Psychol* 41: 231-241