Psychophysiological reactions to experimental stress

Relations to pain sensitivity, position sense and stress perception

Marina Heiden
To my family
ABSTRACT

Stress and monotonous work contribute substantially to the development of chronic musculoskeletal disorders. Yet, the pathophysiological mechanisms underlying the process, particularly the involvement of autonomic regulation, remain unclear. It has been suggested that altered motor control resulting from distorted sensory information from fatigued muscles may be an important component in the development of musculoskeletal disorders. Animal studies have shown that sympathetic nervous system activation exerts actions in skeletal muscles, such as vasoconstriction and modulation of afferent information from muscle spindles. However, few attempts have been made to address this issue in humans. Therefore, the first aim of the thesis was to investigate the impact of repetitive computer work with and without additional stressors on muscle oxygenation and position sense in the upper extremity.

Assuming an important role of stress in the development of chronic musculoskeletal symptoms, one may expect open or latent manifestations of such symptoms in patients with non-specific stress-related illnesses. It is possible that sympathetic activation may influence pain perception, and that treatments aimed at reducing stress may also affect the pain experience. Thus, the second aim of the thesis was to evaluate the effects of a cognitive-behavioral training program and a physical activity program for patients with stress-related illnesses on autonomic reactivity, pain, and perceived health.

First, a laboratory model of computer mouse use was characterized in terms of biomechanical exposure of the wrist, and wrist position sense was determined before and after 45 minutes of continuous mouse use. Then, the effects of performing the computer mouse work under time pressure and precision demands were determined. Autonomic activity and muscle oxygenation in the upper extremity were measured during the work, and wrist position sense was assessed before and after the work. When patients with stress-related illnesses were compared to healthy individuals in autonomic reactivity to functional tests, pressure-pain thresholds, and ratings of health, indications of a relation between autonomic reactivity and symptoms of pain was found. Hence, in a subsequent evaluation of a cognitive-behavioral training program and a physical activity program for patients with stress-related illnesses, post intervention effects on autonomic reactivity to functional tests, pressure-pain
thresholds, ratings of health and return-to-work were studied during a period of 12 months after the intervention.

The main findings were the following. 1) Wrist kinetics data obtained during the computer mouse work showed similarities to previously presented data for mouse-operated design tasks. 2) When time pressure and precision demands were added to the computer work, increased autonomic activity paralleled with decreased muscle oxygenation in the upper extremity was found. Wrist position sense accuracy, however, did not decrease after the work as it did when the work was performed without the additional demands. The result is intriguing, as it does not appear to be in concordance with previous animal studies. 3) Patients with stress-related illnesses showed higher autonomic reactivity to cognitive and physical laboratory tests than healthy control subjects. They also had substantially lower pressure-pain thresholds in the back, and rated poorer health and health-related behavior than the control subjects. 4) We found little difference in effect of cognitive-behavioral training and physical activity, compared to usual care, for patients with stress-related illnesses. Patients in the control group showed an improvement of about the same magnitude as in the treatment groups over the 12-month follow-up period.

The present findings indicate a non-additive relation between autonomic activity during repetitive work and position sense inaccuracy. Furthermore, patients with stress-related illnesses often reported pain in the neck, shoulders, and lower back. This was associated with lower pressure-pain thresholds in the back and a modest increase in sympathetic reactivity to physical and mental tests, which might suggest a potential use of these methods in the clinical examination and rehabilitation of patients with stress-related illnesses.

**Key words:** Autonomic activity, cognitive-behavioral training, muscle oxygenation, physical activity, position sense, pressure-pain thresholds, sick leave, stress
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ABBREVIATIONS

ACTH  adrenocorticotropic hormone
AE    absolute error
CFS   chronic fatigue syndrome
CNS   central nervous system
CRH   corticotropin-releasing hormone
CRI   coping resources inventory
ECG   electrocardiogram
EDA   electrodermal activity
EMG   electromyographic
ES    m. erector spinae
HF    high frequency spectral density of heart rate variability spectrum
JAS   Jenkins activity survey
KSQ   Karolinska sleep questionnaire
LDT   less demanding task
LF    low frequency spectral density of heart rate variability spectrum
MDT   more demanding task
SF-36  short form 36 item health survey
VAS   visual analogue scale
VE    variable error
ORIGINAL PAPERS

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


IV Heiden M, Lyskov E, Nakata M, Sahlin K, Sahlin T, Barnekow-Bergkvist M. Evaluation of a cognitive-behavioral training program and a physical activity program for patients with stress-related illnesses – a randomized controlled study. (submitted)

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INTRODUCTION

Most people have an opinion of what stress is, and would probably agree that stress is a part of everyday life. Yet, a large number of people experience stress to the extent that they are no longer able to perform their work (Lidwall 2003). Attempts have been made to separate work related and non-work related stress (Wemme and Rosvall 2005), although these concepts seem likely to interact with each other, yielding a total stress load on the individual. The individual’s resources for coping with the stress will then determine its potential effects, and might explain the large variation often found in individuals’ susceptibility to stress.

Stress – the developing concept

Stress has been, and still is, defined in a variety of different ways. In the early 20th century, Walter Cannon demonstrated the “fight or flight” response of the sympathetic nervous system to threats (Cannon 1929). Hans Selye then attempted to distinguish between stressors, constituting environmental demands, and stress being “the non-specific response of the body to any demand for change” (c.f. Rosch 1999). Later, Lazarus and Folkman (1984) emphasized the importance of appraisal and coping in stress theory, arguing that it is the stimulus-response relationship that defines stress. Others have used the term allostasis to describe the process by which stability is achieved through change (McEwen 1998; Lundberg and Johansson 2000). Allostatic responses maintained active or inactive for long periods of time causes wear and tear of the mechanisms involved, and give rise to an allostatic load on the organism. In this thesis, stress will be considered as a stimulus-response relationship, where the stressors (i.e., the potential agents of stress) and the individual make-up (i.e., how a person responds to stressors) together will determine the stress response (Morse 1995).

Physiological responses to stressors

Acute physiological stress responses are regulated by the activation of primary stress effector systems such as the hypothalamic-pituitary-adrenocortical system, the sympathetic nervous system, the adrenomedullary system, and the parasympathetic nervous system (Goldstein 2000; Pacak and McCarty 2000). Upon exposure to a
stressor, corticotropin-releasing hormone (CRH) accumulates in the hypothalamus and triggers the release of adrenocorticotropic hormone (ACTH) from the anterior pituitary. This increase in ACTH causes glucocorticoids (e.g., cortisol) to be released from the adrenal cortex. At the same time, adrenaline is released from the adrenal medulla, and noradrenaline increases as a result of sympathetic activation, each giving rise to various responses in the target organs. These actions are intimately coupled. For example, the change in CRH concentration is affected by catecholamines (adrenaline and noradrenaline), whereas glucocorticoids suppress any excessive production of catecholamines resulting from exposure to acute stressors (Kalezic et al. 2003). The ultimate effects of these actions (e.g., increased blood pressure, heart rate and oxygen consumption) often result from the combined effects of glucocorticoids and catecholamines.

In addition to modulating cardiocirculatory and respiratory functions, sympathetic activation exerts a number of actions in skeletal muscles, such as vasoconstriction/vasodilatation, alteration of muscle contractility, and modulation of afferent information from muscle receptors. In particular, sympathetic activation reduces the sensitivity of muscle spindles to muscle length changes (Passatore and Roatta 2003).

The parasympathetic nervous system functions mainly to restore the actions of the hypothalamic-pituitary-adrenocortical system, the sympathetic nervous system, and the adrenomedullary system. However, in certain situations individuals may react to stressors with predominantly parasympathetic responses, such as decreased blood pressure, heart rate and respiration rate. The parasympathetic nervous system also tends to dominate in situations where low perceived control is experienced (Kalezic et al. 2003; Morse 1995).

**Chronic exposure to stressors – somatic consequences and clinical manifestations**

Long-term exposure to stressors without sufficient time for recovery may lead to a variety of symptoms, such as physical and emotional exhaustion, irritability, depressed mood, sleep disturbances, concentration difficulties and somatic symptoms such as musculoskeletal pain (Gockel et al. 1995; Lyskov et al. 2001). Schaufeli and Enzmann (1998) listed a number of symptoms associated with burnout, showing a
close resemblance to the effects of chronic exposure to stressors. Burnout, however, is usually defined as a psychological condition, encompassing emotional exhaustion, depersonalization, and reduced personal accomplishment (Maslach et al. 2001).

Once the symptoms have appeared, they may become more severe if no action is taken to reduce the exposure to stressors. Eventually, they may prevent individuals from performing their work or participating in daily activities. They may even lead to long-term sick leave from work.

**Exposure to stressors in laboratory settings**

When investigating the effects of exposure to stressors, it is of interest to emulate stressors in laboratory settings. By doing so, the stressors may be standardized, and known confounding factors may be better controlled for than in real life situations. There is, however, a limitation with this type of research in that people’s behavior in the laboratory may differ from their behavior in everyday life. Furthermore, the duration of the stressor may be of crucial importance for the stress response, and chronic stressors may be difficult to simulate in a laboratory. This potential lack of ecological validity in laboratory studies is often debated (Linden et al. 1998; Schwartz et al. 2003).

Within the field of laboratory stress research, a variety of stressors are used. Some stressors could be considered mainly cognitive stressors, such as color-word tests where the subjects indicate whether the color of a color word matches the meaning of the color word, and mental arithmetic tasks. Other stressors are more physically oriented, such as static handgrip tests and certain types of repetitive work tasks. In general, large individual differences in physiological reactivity to the tasks are found.

**Physiological arousal and musculoskeletal pain**

Pain is a multidimensional sensation, involving sensory, affective, cognitive, behavioral and social components. Recognizing the sensory as well as the emotional aspect of pain, the International Association for the Study of Pain (Merskey and Bogduk 1994) defined pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage”.

Although, in some situations, intense physiological arousal may cause imme-
mediate alleviation of pain, it is possible that sustained activation of the stress effector systems may influence the perception of pain differently. In fact, sustained activation of the systems may even have the opposite effect, thus increasing pain sensitivity.

Muscle pain is signaled to the central nervous system (CNS) mainly through unmyelinated but also through myelinated primary afferents (Schaible 2006). When potentially noxious stimuli are presented, such as muscle overload and inflammation, nociceptors are activated and signals are transmitted via fast-conducting Aδ and slow-conducting C fibers to the dorsal horn of the spinal cord, where they reach several spinal segments. Within the grey matter of the spinal cord, the nociceptive information is processed in neurons that receive input from deep tissue alone or in neurons that receive information from deep tissue and skin. These neurons convey the information to several supraspinal sites (e.g., thalamus and cortex) or to interneurons and motor neurons within the spinal cord. At the same time, descending inhibitory systems within the CNS tonically inhibit the spinal cord neurons that process nociceptive information from muscles. For example, signals from hypothalamus, which plays an important part in coordinating autonomic responses, inhibits the response of spinal neurons to noxious stimuli. If this inhibition is interrupted, the neurons’ excitation thresholds for mechanical stimulation may decrease, and their responses to stimulation above the threshold may increase (Kidd 2005; Millan 2002; Schaible 2006).

When tissue injury occurs, it causes a local release of numerous chemicals that may, directly or indirectly, activate nearby nociceptors. Some of the chemicals (e.g., bradykinin) may also lead to a sensitization of the nociceptors, whereby the nociceptors’ responses to natural stimuli are altered and pain hypersensitivity at the site of the injury is increased (Meyer et al. 2006). When primary nociceptive afferents increase their signalling to CNS, the excitation threshold of the dorsal horn neurons is lowered, and the neurons’ receptive fields expand. This may lead to a central sensitization causing pain and tenderness in normal tissues adjacent to the site of the injury. Increased signalling from nociceptive afferents may also lead to strengthened synaptic links between afferents conveying non-nociceptive information (e.g., touch or light pressure) and pain-signalling dorsal horn neurons, causing normally non-painful stimuli to be perceived as painful.
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**Pain assessment**

Due to the many dimensions underlying pain, the assessment of pain is challenging. In experimental studies of pain-free individuals, it is possible to expose the subjects to stimuli such as electrical or thermal stimulation in order to evaluate their pain reactions (Arendt-Nielsen and Graven-Nielsen 2005). Another possibility is to apply mechanical pressure to estimate the subjects’ pain thresholds and sensitivity in various body regions. Measures of pressure pain sensitivity are considered clinically relevant for fibromyalgia and myofascial pain syndromes, although they are subjective and may easily be biased (Gracely 2006).

Other measures of pain include the one-dimensional visual analogue scale (VAS) where subjects indicate their pain on a 10-cm line ranging from “no pain” to “worst possible pain”, and the multidimensional McGill Pain Questionnaire which assesses sensory, affective and evaluative dimensions of pain (Melzack and Katz 2006). The questionnaire Short Form 36 Item Health Survey also contains an index addressing pain during the last four weeks (Ware and Sherbourne 1992).

**Autonomic activity, pain, and motor control**

Considering the complexity of pain signaling, it is not surprising that the autonomic nervous system (notably the sympathetic nervous system) may influence the perception of pain. Studies have shown that, under pathological conditions such as tissue inflammation, sympathetic activity may excite nociceptors either directly by the release of noradrenaline or indirectly through the change of tissue blood flow (Roatta et al. 2003). However, the role of the sympathetic nervous system in the generation of inflammatory mediated pain is still debated (Jänig and Levine 2006).

It has been suggested that the sympathetic modulation of muscle spindle activity may contribute to altered motor control (e.g., reduced movement- and position sense and coordination), causing perturbations of required joint movements. In order to counteract these perturbations, increased co-activation of muscles will be needed to perform precise movements, thus increasing the workload and promoting fatigue in the muscles involved (Blair et al. 2003; Johansson et al. 2003a). This might imply that musculoskeletal pain is also associated with altered motor function (Madeleine et al. 2003a; Madeleine et al. 2003b).
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Treatments of stress-related illnesses

While this thesis was prepared, progress was made in the diagnosis of subjects with stress-related illnesses. In Sweden, there are now clearly stated criteria for diagnosing subjects with “Utmattningssyndrom” (Åsberg et al. 2003). However, the benefit of treatments for these subjects is still unclear.

Assuming the role of the autonomic nervous system in the maintenance of pain discussed above, treatments aimed at reducing stress could also affect the pain experience. Physical activity may alter autonomic function by increasing parasympathetic activity and decreasing sympathetic activity (Carter et al. 2003; Goldsmith et al. 2000). Cognitive behavioral training, on the other hand, may promote changes in the appraisal of stressors (Murphy 1996). Studies investigating the effects of cognitive-behavioral training programs on chronic pain patients have indeed shown promising results in helping the patients to control and decrease their pain, and to return to work (Eccleston et al. 2003; Marhold et al. 2001). Furthermore, positive effects of cognitive-behavioral interventions for patients with chronic fatigue syndrome have been found in physical functioning and ratings of fatigue (Deale et al. 1997; Sharpe et al. 1996).

There are also indications that regular physical activity may reduce stress-related symptoms (Carmack et al. 1999; Jennen and Uhlenbruck 2004). Mannerkorpi and Iversen (2003) concluded that pool exercise may alleviate symptoms and distress, and that aerobic exercise may improve physical functioning and reduce tenderness in patients with fibromyalgia and related syndromes. It is possible that appropriate physical activity may be beneficial to subjects with stress-related illnesses as well.
The overall aim of this thesis was to explore the relation between pain sensitivity, position sense, and autonomic reactivity in response to laboratory stressors. To that end, four studies were conducted on healthy subjects and subjects on sick leave due to stress-related illnesses. The specific aims of the thesis were:

- To determine the effects of a mouse-operated computer task on perception of fatigue and wrist position sense (paper I), and to evaluate their interrelations with autonomic activity and muscle oxygenation when the task is performed under time pressure and precision demands (paper II).

- To characterize subjects with stress-related illnesses by comparing autonomic activity, pressure-pain thresholds, and subjective assessments of health and behaviour between subjects with stress-related illnesses and healthy control subjects (paper III).

- To evaluate the effects of a cognitive-behavioral training program and a physical activity program for subjects with stress-related illnesses on autonomic activity, pressure-pain thresholds, subjective assessments of health and behaviour, and sick leave from work (paper IV).
METHODS

This thesis is based on four studies. Table 1 presents an overview of the study populations and measures used in these studies. In study I and II, physiological and psychological responses to a repetitive mouse-operated computer task were investigated in a group of healthy individuals. In addition, the effects of the task on wrist position sense were examined. In study III, subjects on sick leave due to stress-related illnesses were compared to age- and gender-matched healthy control subjects in terms of autonomic reactivity to laboratory stressors, pressure-pain thresholds in the upper and lower back, and subjective health measures of life quality, behavioral patterns, and pain. Study IV aimed at evaluating the effects of a cognitive-behavioral training program and a physical activity program for subjects on sick leave due to stress-related illnesses. Measures of autonomic reactivity to laboratory stressors, pressure-pain thresholds in the upper and lower back, and subjective health measures as well as the number of subjects returning to work were studied until 12 months after the intervention period.

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Methods

**Acute response to a computer-mouse task with and without time pressure and precision demands (Study I-II)**

**Subjects**

Fifty-one subjects (26 males and 25 females; age 19-33 years) volunteered to participate in study I, while twenty-four subjects (12 males and 12 females; age 19-28 years) participated in study II. All subjects were healthy, right-handed college students. They reported no history of musculoskeletal complaints in the upper extremities at the time of the studies.

**Study design and experimental protocol**

*Study I*

One group of subjects (16 males and 16 females) performed a 45-min mouse-operated computer task involving painting rectangles on the computer screen. The subjects were seated in front of a computer at a desk, which was adjusted so that subjects had full lower arm support. A Microsoft Intellimouse (Intellipoint v 5.1) with medium pointer speed and low pointer acceleration was positioned on the table so that the subjects’ right arm could be held close to the body while painting, thereby avoiding abduction and external rotation of the upper arm in an attempt to isolate the wrist movements. Throughout the painting task, rectangles were presented, one at a time, at random locations on the screen (15” resolution 1024×768 pixels), and subjects were instructed to paint approximately 2 rectangles per minute (cursor size 6 pixels). If required, they were told to increase or decrease their work pace during the task to maintain this work rate. Periodically throughout the task, the subjects were asked to rate their perception of fatigue in the arm and hand operating the computer mouse.

Before and after the painting task, the subjects performed position sense tests of the right wrist (see description below). The results were compared to those of a control group (6 males and 6 females), who performed wrist position sense tests before and after 45 minutes of seated rest. For a supplemental group consisting of 7 subjects (4 males and 3 females), wrist kinetics were assessed during 15 minutes of painting in order to quantify the movements during the task.
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Study II
All subjects performed the 45-min mouse-operated computer task (see study I) on two occasions, separated by 3-6 days. On one occasion, subjects performed the task as described in study I. This task version will be referred to in the text as the less demanding task (LDT). On the other occasion, time pressure was imposed on the task by limiting the time available for painting a rectangle, and a sound was used to alert the subjects when the time was running out (“AlarmClock”, Bradley and Lang 1999). Subjects were given no prior information of the allotted time for each rectangle, which was randomized between 15 and 25 s. In addition, painting performance scores were introduced. Subjects scored 1 point for every rectangle that was filled up to at least 80% of its area, and their cumulative score was displayed on the computer screen throughout the task. Whenever the subjects painted outside the rectangle, a buzzing sound was heard (“Buzzer”, Bradley and Lang 1999). This task version will be referred to as the more demanding task (MDT). The order of the two task versions was randomized so that half of the subjects (6 males and 6 females) started with LDT, and the other half of the subjects started with MDT.

On each occasion, subjects performed a position sense test of the right wrist (see description below). When completed, recording equipment for measuring local tissue oxygen saturation, heart rate, electrodermal activity, skin blood flow, respiration rate and blood pressure was attached to the subjects (see below). They were instructed to rest quietly for 5 minutes, while baseline recordings were obtained, and then to commence with the painting task. Throughout the task, painting performance measures were recorded, and subjects were asked to rate their perception of fatigue in the working arm as well as general tenseness. When the task was finished, the recording equipment was removed, and subjects repeated the position sense test.

Data collection and processing

Wrist kinetics (Study I)
Wrist movement data were sampled at 30 Hz using a 3Space FASTRAK (Polhemus Inc., Colchester, VT, USA) with 6 degrees of freedom. Four receivers were attached to the subjects’ right arm: one was placed over the acromion, one was placed on the
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dorsal upper arm close to the elbow joint, one was placed on the lower arm close to the wrist, and one was placed on the back of the hand over the third metacarpal bone. Before the mouse-operated computer task, the wrist position while resting the hand on the computer mouse was obtained. All subsequent data were normalized to this reference position by subtracting the reference position from the remaining positions.

From the angular positions of the wrist during the task, the range of motion (i.e., the difference between the 5th and the 95th percentile of wrist angles), mean angle position, mean velocity, and mean power frequency (i.e., the center of gravity for a Welch power spectrum with Hanning windowing) was calculated.

Position sense tests (study I-II)

Subjects were seated with their right arm placed in an adjustable rig, allowing flexion-extension movements about the right wrist joint while keeping the lower arm fixed at 90° of elbow flexion. They were equipped with goggles and earphones to minimize visual and auditory inputs. From a starting position of 30° of wrist extension, their hand was moved passively at 30°/s to a target position, where it remained for 6 s. It was then passively returned at 30°/s to the starting position. After 3 s, subjects were instructed via the headphones to actively move their hand in an attempt to match the target position. They marked the reproduced position by pressing a button held in their left hand. Each position sense test consisted of 15 position-matching trials, where target positions were randomized between 0° and 30° of flexion. To avoid confounding effects of target position order on the between-subjects variation, all subjects were given the same order of target positions. Prior to the first position sense test, a training session was given to each subject.

For each position matching trial, a position error was calculated by subtracting the target position from the reproduced position. The mean of the absolute values of the errors (Absolute Error, AE), as well as the standard deviation of the errors (Variable Error, VE) were computed for each subject, and used as outcome measures.

Oxygenation measurements (Study II)

Local tissue oxygenation in the right trapezius and extensor carpi radialis muscle was
measured non-invasively using a spectrometer (INSPECTRA Tissue Spectrometer – model 325, Hutchinson Technology Inc., The Netherlands). For trapezius, the 25-mm probe was placed so that the transmitter-detector position was paralleled with the muscle fibers, approximately half way between C7 and acromion. For extensor carpi radialis, the probe was placed over the muscle belly, also in the direction of the muscle fibers. The muscle belly was located by palpation during isometric contraction of the wrist. Probe positions were marked to ensure the same probe placement on both measurement occasions. Before placing the probes on the measurement sites, they were inserted in a light scattering calibrator to capture reference light intensities of all wavelengths. The tissue measurements were then related to the reference measurement, thereby converting light intensity measurements to optical absorbance. After processing the optical absorbance values in a scaled second derivative absorbance spectrum, a measure of hemoglobin and myoglobin oxygen saturation was obtained ($\%StO_2$). Tissue oxygen saturation was recorded at 0.3 Hz.

Oxygen saturation recordings during the 45-min mouse-operated computer task were divided into two parts, and a mean value for each part ($\approx 22.5$ min) was calculated. Reactivity indices were obtained by subtracting mean StO$_2$ during the initial rest period from mean StO$_2$ during the task.

**Autonomic activity recordings (Study II)**

Heart rate, respiration rate, skin blood flow and electrodermal activity were recorded simultaneously at 2 kHz using a multi-channel polygraph (LABLINC V System, Coulbourn Instruments, PA, USA). An electrocardiogram (ECG) was recorded from a wrist-thorax derivation with the ground electrode on the left elbow, while subjects’ respiration rate was monitored through a strain gauge wrapped around the chest. Blood flow in the left index finger was measured using photoplethysmography with the photo emitter and the photo sensor placed 3 mm apart. Electrodermal activity (EDA) was assessed by the skin-conductance method (AC 100 Hz, time constant 5 s, voltage 0.5 V) with electrodes that were placed on the thenar and hypothenar of the left hand.

Systemic arterial blood pressure was measured non-invasively using the oscillometric method before, in the middle of, and immediately after the task. An inflatable cuff was placed around the subject’s left upper arm, and controlled remotely.
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throughout the task (LABLINC V System, Coulbourn Instruments, PA, USA).

Autonomic activity recordings were analyzed in intervals of 250 consecutive heartbeats during the initial rest period, part 1 and part 2 of the task (see Oxygenation measurements). From the ECG signal, the QRS complexes were identified by a threshold and template method, and manually screened for artifacts and detection errors. Heart rate was calculated from the inter-beat intervals, and resampled at 5 Hz after cubic spline interpolation. After linear trend removal, spectral analysis was performed using autoregressive modelling with the least squares method. The spectral density of low frequency (LF, 0.04-0.15 Hz) and high frequency (HF, 0.15-0.40 Hz) components was calculated (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology 1996). Electrodermal responses were identified as any change in skin conductance higher than 3 times the standard deviation. Furthermore, the area under the rectified signal was calculated. Skin blood flow was quantified by the area under the rectified photoplethysmogram signal. The respiratory signal was re-sampled at the occurrence of each QRS complex, and spectral analysis was performed as described for heart rate. The peak frequency was used as an estimate of respiration rate. For each measure, reactivity indices were calculated by subtracting values at rest from values during the task.

Subjective ratings (Study I-II)

In study I, subjects were asked to rate their perception of fatigue in the arm and hand operating the computer mouse according to the Borg CR-scale (Borg 1982) while performing the computer task. In study II, ratings of physical fatigue in the working arm as well as ratings of general tenseness were obtained simultaneously using visual analogue scales (VAS), where subjects were asked to rate on a 10-cm scale how fatigued they felt in their right arm, and how tense they felt at the moment, respectively.

Statistical analysis

To determine the effect of the mouse-operated computer task on wrist repositioning accuracy, AE and VE were analyzed by repeated-measures analyses of variance. In study I, the within-subjects variable represented the first and second position sense test, respectively, and gender was included as between-subjects variable. In
study II, AE and VE change in response to LDT and MDT, respectively, were used as within-subjects variable. Gender and task sequence (the order in which the task versions were performed) were included as between-subjects variables. Whenever the sphericity assumption was not met, the Huynh-Feldt correction was used.

All oxygen saturation reactivity indices and autonomic reactivity indices were analyzed by multivariate repeated-measures analyses of variance with task version as within-subjects variable, and gender and task sequence as between-subjects variables. The multivariate tests were performed using Wilks’ Lambda. Ratings of perceived physical fatigue and general tenseness were analyzed by non-parametric tests. In all tests, p<0.05 was considered significant.

**Characteristics of stress-related illnesses (Study III)**

**Subjects**

Twenty cases (4 males and 16 females) and twenty healthy control subjects (also 4 males and 16 females) participated in the study. Cases were defined by the following inclusion criteria: 1) 25-60 years of age, 2) sick-listed for at least 50% more than 1 month and less than 2 years, and 3) stress-related diagnoses stated in their illness certificate as the cause of the sick leave. Cases were excluded from the study if the certificate indicated that they had any cardiovascular or neurological disease, thyroid disease, diabetes type 2, major depressive disorder, or if they were suffering from substance abuse (e.g., alcohol). The control subjects differed from the cases by working full time, not taking any medication, and reporting no health complaints.

**Study design and experimental protocol**

The cases were matched with control subjects of the same age (±1 year) and gender. All subjects performed tests of autonomic regulation and algometric tests (see description below), and completed questionnaires about physical and mental health and behavioral patterns, in randomized order. Each pair of subjects (a case and the matched control subject) was given the same order of measurements.
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Data collection and processing

Autonomic regulation tests
Subjects were seated in a desk chair in front of a computer screen, and recording equipment for measuring heart rate, blood pressure, respiration rate, skin blood flow, and electrodermal activity was attached to them. After a 5-min rest period, during which baseline recordings were obtained, three tasks were presented on the computer screen, with rest periods in between. The tasks were presented in randomized order and consisted of 1) mental arithmetic, where a mathematical problem involving multiple additions and subtractions of 1 and 2-digit numbers was presented for 2 min, and subjects were instructed to solve as much as possible of it within the time limit, 2) handgrip, where subjects performed a maximum handgrip with their right hand for 10 s, followed by a subjectively experienced 50% grip force for 1.5 min, and 3) deep breathing, where subjects were instructed to breathe at a prescribed rate of 6 breaths/min for 1.2 min. Each pair of subjects (a case and the matched control subject) was given the same order of tasks.

Autonomic activity was recorded and processed as in study II, with the exception of blood pressure, which was measured with finger cuffs continuously throughout the test using the volume clamp method (Penaz 1992). For each experimental stage (rest periods and tasks), intervals of ≥90 consecutive heartbeats were analyzed. Reactivity indices for the tasks were calculated as the value during the task minus the value during the rest period immediately before the task.

Algometric measurements
Algometric measurements on the right and left trapezius and erector spinae muscles were performed using a pressure algometer (Somedic Production AB, Sollentuna, Sweden). For trapezius, the algometer was applied approximately half way between C7 and acromion, while the subject was sitting in a relaxed upright position. For erector spinae, the algometer was applied on the muscle belly at the level of L3-L4, while the subject was lying in prone position. Pressure was increased at a rate of 50 kPa/cm²/s. Subjects were instructed to press a button as soon as the pressure sensation became a pain sensation, thereby registering the pressure-pain threshold. For each measurement location, five algometric recordings were obtained. They were
sorted by size, and the smallest and largest value were excluded from the analysis. A
mean value of the remaining three recordings was computed, and used as a measure
of the pressure-pain threshold.

Questionnaires
Subjects completed the Short Form 36 Item Health Survey (SF-36) (Ware and Sher-
bourne 1992) to assess quality of life, the Shirom-Melamed Burnout Questionnaire
(Melamed et al. 1992) for the assessment of different aspects of burnout, a short
version of the Jenkins Activity Survey (JAS) (Jenkins et al. 1967) containing ques-
tions about behavioral patterns, and the Karolinska Sleep Questionnaire (KSQ) (Ke-
cklund and Åkerstedt 1992) to assess sleep quality and sleep complaints. Subjects
also rated their pain intensity in different body regions (i.e., neck, shoulders/upper
back, and lower back) on a scale from 1 (no pain) to 6 (almost unbearable).

The SF-36 ratings were summarized in 8 indices (i.e., physical functioning,
physical role limitation, pain, general health, vitality, social functioning, emotional
role limitation and mental health), with higher values implying better perceived
health (SF-36® Health Survey: Manual & Interpretation Guide). For the Shirom-
Melamed Burnout Questionnaire, indices for burnout, tension, listlessness, cognitive
difficulties, and a total burnout score were calculated (Melamed et al. 1999; Soares
and Jablonska 2004). High values correspond to a high level of burnout. The 11
items in JAS were scored so that a higher value implied stronger type A behavioral
pattern, and a mean value of the items was calculated and used as a JAS index.
Two KSQ indices were computed by averaging the items of Disturbed sleep (“dif-
culties falling asleep”, “repeated awakenings”, “premature awakening”, “restless
sleep”) and Awakening (“difficulties awakening”, “not well rested”, “exhausted when
awakening”). Higher values imply lower sleep quality and more sleep complaints
(Åkerstedt et al. 2002).

Statistical analysis
The autonomic reactivity indices were analyzed in a multivariate repeated-measures
analysis of variance with task (i.e., mental arithmetic, handgrip and deep breathing)
and group of subjects (i.e., cases and control subjects) as within-subject variables. Al-
gomeric recordings and questionnaire indices were analyzed by multivariate repeat-
Methods

ed-measures analyses of variance with group of subjects as within-subject variable. All multivariate tests were performed using Wilks’ Lambda. Whenever the multivariate tests revealed significant differences (i.e., p<0.05), univariate analyses of variance on the dependent variables were employed, using the Huynh-Feldt correction if the sphericity assumption was not met. For the regional pain ratings, Wilcoxon’s signed rank test was used to test for differences between cases and healthy controls.

**Evaluation of treatments of stress-related illnesses (Study IV)**

**Subjects**

Seventy-five subjects with stress-related illnesses (15 males and 60 females) volunteered to participate in the study. The criteria for inclusion and exclusion of subjects were identical to those used in study III.

**Study design and experimental protocol**

When included in the study, the subjects performed tests of autonomic regulation and algometric tests, and completed questionnaires about physical and mental health and behavioral patterns (see study III). The subjects were then randomly allocated to one of three groups: group A participated in a cognitive-behavioral group training program, group B participated in a physical activity program, and group C constituted a control group thus receiving no treatment during the course of the study. After a 10-week intervention period, the tests were repeated in the same order as before. Follow-up tests were performed at 6 and 12 months after the intervention.

**Cognitive-behavioral training**

The cognitive-behavioral training program aimed at focusing on cognitive restructuring to improve participants’ self-care behavior (strategies for coping with negative emotions, daily routines with regular relaxation and physical activity, and eating and sleeping habits) and social support (building a supporting network) (Burell et al. 1994; Deale et al. 1997; Eccleston et al. 2003; Marhold et al. 2001; Ornish et al. 1990; Sharpe et al. 1996; Sundin et al. 1994). It consisted of two 3-hour group ses-
Methods

Sessions per week for 10 weeks, and was based on a manual (Sahlin and Hofvendahl 1998) that was given to all participants. The sessions contained educational elements in the form of seminars, group discussions, and required daily practice of skills. The sessions were led by a stress-management consultant, with experience of rehabilitation of subjects with stress-related illnesses. The cognitive-behavioral training group assembled at 1.5, 3, and 6 months after the intervention.

Physical activity
Subjects in the physical activity group were asked to participate in two exercise sessions per week for 10 weeks. One of the sessions followed a rehabilitation program involving low-intensity exercises in a warm water pool (32°C) (Mannerkorpi and Iversen 2003), emphasizing body awareness in terms of body stabilization and relaxation, but also including flexibility, strength and aerobics. Prior to this session, the participants met with the group leader – a physiotherapist with experience of rehabilitation of subjects with stress-related illnesses – to discuss their progress, and the difficulties they were facing during exercise. For the other session, the participants chose in consultation with the group leader what type of exercise to perform (e.g., strength training, swimming, aerobics and walks). The physical activity group assembled at 1.5, 3, and 6 months after the intervention.

Data collection and processing
Autonomic activity recordings and algometric measurements were obtained and processed as described in study III. Questionnaire ratings for Short Form 36 Item Health Survey, Shirom-Melamed Burnout Questionnaire, Jenkins Activity Survey, and Karolinska Sleep Questionnaire were summarized in indices as in study III, while ratings for an additional questionnaire Coping Resources Inventory (CRI) (Hammer and Marting 1988), measuring perceived resources during stressful situations, yielded indices for 5 domains: cognitive, social, emotional, spiritual/philosophical, and physical. High values indicated more resources.

Statistical analysis
For the autonomic reactivity indices, repeated-measures analyses of variance with
Methods

time (i.e., measurement occasions) and task (i.e., mental arithmetic, handgrip and deep breathing) as within-subjects variables, and group (i.e., cognitive-behavioral training group, physical activity group, and control group) and gender as between-subjects variables were employed to assess changes over time. Algometric recordings and questionnaire indices were analyzed by repeated-measures analyses of variance with time as within-subjects variable, and group and gender as between-subjects variables. Whenever the sphericity assumption was not met, the Huynh-Feldt correction was used.

Based on findings from study III, where cases and healthy control subjects differed substantially in ratings of burnout and quality of life, the number of subjects in this study whose ratings reached the 10th/90th percentile of the ratings for the healthy subjects (i.e., 3.0 on Shirom-Melamed Burnout Questionnaire and 71% on SF-36) was calculated. This number of subjects, together with the number of subjects working part-time or full-time throughout the study, was compared between groups with Chi-square tests. In all tests, \( p<0.05 \) was considered significant. Additional logistic regression analyses were then performed to investigate whether any of the initial measures could explain the prevalence of subjects returning to work by 12 months after the intervention.
RESULTS

Acute response to a computer-mouse task with and without time pressure and precision demands (Study I-II)

Angular data for wrist movements during the computer task showed that the subjects performed repetitive and constrained wrist movements (mostly below 30% of maximum voluntary range of motion) while painting the rectangles presented on the computer screen. Subjects also rated gradually increasing muscle fatigue in the arm and hand operating the computer mouse during 45 minutes of painting (p<0.001). The position sense tests revealed a significant increase in AE following the painting task (p=0.018, figure 1). However, no difference in VE was found (p=0.664, figure 1). For the control group, no difference in AE or VE was found after 45 minutes of seated rest (AE: p=0.746, VE: p=0.157, figure 1).

When time pressure and precision demands were added to the painting task, subjects increased their performance and rated more tenseness and physical fatigue than when they were painting without such demands (Tenseness: p=0.001, Fatigue: p=0.002). Furthermore, they exhibited increased electrodermal activity (p≤0.032).

Figure 1. Mean values of repositioning errors before and after seated rest (Rest), the less demanding task (LDT), and the more demanding task (MDT) in study I and II.
### Results

**Table 2. Autonomic activity during the less demanding task (LDT) and the more demanding task (MDT)**

<table>
<thead>
<tr>
<th></th>
<th>Rest</th>
<th>Work part 1</th>
<th>Work part 2</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EDA area</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDT</td>
<td>7.8 (8.6)</td>
<td>12.0 (9.2)</td>
<td>17.4 (15.0)</td>
<td></td>
</tr>
<tr>
<td>MDT</td>
<td>9.5 (12.1)</td>
<td>18.6 (14.0)</td>
<td>19.3 (14.4)</td>
<td>0.032</td>
</tr>
<tr>
<td><strong>EDA responses</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDT</td>
<td>5.5 (3.6)</td>
<td>6.1 (4.0)</td>
<td>6.4 (3.3)</td>
<td></td>
</tr>
<tr>
<td>MDT</td>
<td>4.6 (3.7)</td>
<td>8.2 (4.7)</td>
<td>7.9 (3.7)</td>
<td>0.001</td>
</tr>
<tr>
<td><strong>Respiration rate</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDT</td>
<td>14.4 (2.8)</td>
<td>17.4 (3.1)</td>
<td>16.8 (3.6)</td>
<td></td>
</tr>
<tr>
<td>MDT</td>
<td>15.3 (2.6)</td>
<td>17.6 (2.1)</td>
<td>17.4 (2.3)</td>
<td>0.729</td>
</tr>
<tr>
<td><strong>Skin blood flow</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDT</td>
<td>86.4 (50.0)</td>
<td>89.7 (58.6)</td>
<td>75.1 (39.5)</td>
<td></td>
</tr>
<tr>
<td>MDT</td>
<td>80.6 (47.6)</td>
<td>87.8 (53.6)</td>
<td>108.0 (60.0)</td>
<td>0.021</td>
</tr>
<tr>
<td><strong>Systolic BP</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDT</td>
<td>115.9 (11.3)</td>
<td>115.3 (8.7)</td>
<td>119.5 (14.2)</td>
<td></td>
</tr>
<tr>
<td>MDT</td>
<td>115.9 (9.2)</td>
<td>117.9 (11.6)</td>
<td>117.4 (9.2)</td>
<td>0.281</td>
</tr>
<tr>
<td><strong>Diastolic BP</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDT</td>
<td>68.4 (6.8)</td>
<td>70.6 (7.2)</td>
<td>71.0 (6.4)</td>
<td></td>
</tr>
<tr>
<td>MDT</td>
<td>69.8 (6.9)</td>
<td>70.3 (7.0)</td>
<td>71.2 (6.1)</td>
<td>0.518</td>
</tr>
<tr>
<td><strong>Heart rate</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDT</td>
<td>73.1 (8.9)</td>
<td>73.2 (8.2)</td>
<td>73.9 (9.3)</td>
<td></td>
</tr>
<tr>
<td>MDT</td>
<td>73.9 (9.4)</td>
<td>75.7 (10.5)</td>
<td>75.2 (10.4)</td>
<td>0.154</td>
</tr>
<tr>
<td><strong>LF</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDT</td>
<td>10.1 (7.3)</td>
<td>7.2 (4.3)</td>
<td>8.2 (5.5)</td>
<td></td>
</tr>
<tr>
<td>MDT</td>
<td>8.7 (4.8)</td>
<td>8.0 (4.6)</td>
<td>7.3 (4.0)</td>
<td>0.301</td>
</tr>
<tr>
<td><strong>HF</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDT</td>
<td>7.9 (4.5)</td>
<td>6.1 (3.1)</td>
<td>6.6 (4.7)</td>
<td></td>
</tr>
<tr>
<td>MDT</td>
<td>7.8 (4.4)</td>
<td>6.2 (3.0)</td>
<td>5.9 (2.8)</td>
<td>0.642</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDT</td>
<td>24.2 (15.4)</td>
<td>17.7 (8.7)</td>
<td>19.6 (12.9)</td>
<td></td>
</tr>
<tr>
<td>MDT</td>
<td>22.0 (11.0)</td>
<td>19.2 (10.0)</td>
<td>18.0 (8.7)</td>
<td>0.418</td>
</tr>
<tr>
<td><strong>Normalized LF</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDT</td>
<td>0.4 (0.1)</td>
<td>0.4 (0.1)</td>
<td>0.4 (0.1)</td>
<td></td>
</tr>
<tr>
<td>MDT</td>
<td>0.4 (0.1)</td>
<td>0.4 (0.1)</td>
<td>0.4 (0.1)</td>
<td>0.574</td>
</tr>
<tr>
<td><strong>Normalized HF</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDT</td>
<td>0.3 (0.1)</td>
<td>0.3 (0.1)</td>
<td>0.3 (0.1)</td>
<td></td>
</tr>
<tr>
<td>MDT</td>
<td>0.4 (0.1)</td>
<td>0.3 (0.1)</td>
<td>0.3 (0.1)</td>
<td>0.193</td>
</tr>
<tr>
<td><strong>LF/HF</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDT</td>
<td>1.2 (0.4)</td>
<td>1.3 (0.5)</td>
<td>1.4 (0.5)</td>
<td></td>
</tr>
<tr>
<td>MDT</td>
<td>1.2 (0.5)</td>
<td>1.3 (0.5)</td>
<td>1.3 (0.5)</td>
<td>0.538</td>
</tr>
</tbody>
</table>

Mean and standard deviation of electrodermal area (μS/min), electrodermal responses (responses/min), respiration rate (breaths/min), skin blood flow (a.u./min), blood pressure (mmHg), heart rate (beats/min), low frequency (LF), high frequency (HF) and total spectral density (s²), normalized spectral density of the low and high components (LF/Total and HF/Total), and the ratio between low and high spectral components during rest, part 1 and part 2 of work for LDT and MDT in study II. In all tests, p<0.05 was considered significant.
and skin blood flow (p=0.021) in response to the more demanding task (MDT) compared to the less demanding task (LDT) (table 2). While tissue oxygen saturation in m. extensor carpi radialis was significantly reduced during MDT than during LDT (p=0.022, figure 2), oxygen saturation reactivity in m. trapezius did not differ between the task versions (p=0.227, figure 2). The position sense tests revealed a significant increase in AE following LDT compared to MDT (p=0.033, figure 1), whereas there was no difference in VE between the task versions (p=0.128, figure 1).

No significant gender differences were found in performance or in ratings of tenseness or physical fatigue, with the exception of the ratings of fatigue that were obtained in study I after 5 minutes of painting, when males reported more muscle fatigue than females (p=0.010). In study II, males exhibited increased electrodermal activity (p=0.032) and skin blood flow (p=0.003) during MDT, compared to females. Although there were no gender differences in tissue oxygen saturation in response to the painting tasks, females had lower oxygen saturation in m. extensor carpi radialis as well as in m. trapezius than males throughout the experiment (Extensor carpi radialis: p<0.001, Trapezius: p<0.010, figure 3). For the position sense

![Figure 2](insert figure 2 here). Mean values of oxygen saturation in m. extensor carpi radialis and m. trapezius during rest, part 1 and part 2 of work for the less demanding task (LDT) and the more demanding task (MDT) in study II.
Figure 3. Mean values of oxygen saturation in m. extensor carpi radialis and m. trapezius during rest, part 1 and part 2 of work for males and females in study II.

tests in study I, no gender differences in AE or VE following the painting task were found. However, males in the control group had a higher AE than females before the rest period (p=0.018). In study II, no gender differences in AE were found. For VE, on the other hand, females showed an increase after the painting task, irrespective of the task version they performed (p=0.036).

Characteristics of stress-related illnesses (Study III)

Demographic characteristics of the cases and the control subjects are shown in table 3. Analyses of autonomic reactivity to mental arithmetic, handgrip and deep breathing showed that the cases’ skin blood flow was reduced during the handgrip, compared to the control subjects’ (p=0.001). Furthermore, electrodermal activity in the cases tended to increase in response to mental arithmetic, when compared to that of the control subjects (p=0.067, table 4).

In the analysis of algometric recordings on the right and left trapezius and erector spinae muscles, significantly lower pressure-pain thresholds were found in cases than in control subjects (p=0.001). Figure 4 depicts the pressure-pain thresholds for each measured muscle.
Results

Table 3. Demographic characteristics of cases (n=20) and healthy control subjects (n=20)

<table>
<thead>
<tr>
<th></th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (mean ± SD)</td>
<td>43 ± 9</td>
<td>43 ± 9</td>
</tr>
<tr>
<td>Height, cm (mean ± SD)</td>
<td>171 ± 11</td>
<td>170 ± 9</td>
</tr>
<tr>
<td>Weight, kg (mean ± SD)</td>
<td>74 ± 18</td>
<td>67 ± 11</td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present smoker</td>
<td>2 (10)</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Non-smoker</td>
<td>18 (90)</td>
<td>19 (95)</td>
</tr>
<tr>
<td>Smokeless tobacco use, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>5 (25)</td>
<td>6 (30)</td>
</tr>
<tr>
<td>No</td>
<td>15 (75)</td>
<td>14 (70)</td>
</tr>
<tr>
<td>Marital status, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unmarried</td>
<td>1 (5)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Married/Cohabiting</td>
<td>17 (85)</td>
<td>18 (90)</td>
</tr>
<tr>
<td>Divorced</td>
<td>2 (10)</td>
<td>2 (10)</td>
</tr>
<tr>
<td>Widowed</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Sick leave duration, months (mean ± SD)</td>
<td>9 ± 8</td>
<td>0 ± 0</td>
</tr>
</tbody>
</table>

Cases rated significantly poorer life quality in SF-36 than control subjects (p<0.001). Moreover, they rated a higher degree of burnout (p<0.001), sleep disturbances (p<0.001), and type A behavioral patterns (p=0.001) than their healthy counterparts. The regional pain ratings showed that cases reported stronger pain intensity

Figure 4. Mean values of pressure-pain thresholds in m. trapezius and m. erector spinae for cases and healthy control subjects in study III.
Results

Table 4. Autonomic activity in response to mental arithmetic, handgrip and deep breathing

<table>
<thead>
<tr>
<th></th>
<th>Initial rest</th>
<th>Mental arithmetic</th>
<th>Hand Grip</th>
<th>Deep Breathing</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EDA area</strong></td>
<td>Cases</td>
<td>3.5 (4.3)</td>
<td>5.3 (5.5)</td>
<td>2.1 (2.4)</td>
<td>4.1 (4.5)</td>
</tr>
<tr>
<td></td>
<td>Controls</td>
<td>3.3 (2.9)</td>
<td>3.1 (9.1)</td>
<td>3.2 (6.7)</td>
<td>7.1 (10.8)</td>
</tr>
<tr>
<td><strong>EDA responses</strong></td>
<td>Cases</td>
<td>5.7 (4.1)</td>
<td>5.3 (3.3)</td>
<td>2.2 (3.4)</td>
<td>3.6 (3.5)</td>
</tr>
<tr>
<td></td>
<td>Controls</td>
<td>4.4 (3.8)</td>
<td>5.4 (5.1)</td>
<td>2.9 (4.0)</td>
<td>4.6 (4.6)</td>
</tr>
<tr>
<td><strong>Respiration rate</strong></td>
<td>Cases</td>
<td>13.7 (2.6)</td>
<td>1.6 (4.0)</td>
<td>1.8 (2.7)</td>
<td>-6.3 (2.5)</td>
</tr>
<tr>
<td></td>
<td>Controls</td>
<td>13.2 (3.4)</td>
<td>3.1 (2.4)</td>
<td>2.2 (2.8)</td>
<td>-6.4 (3.2)</td>
</tr>
<tr>
<td><strong>Skin blood flow</strong></td>
<td>Cases</td>
<td>68.5 (53.9)</td>
<td>1.3 (26.9)</td>
<td>-52.7 (50.3)</td>
<td>-9.6 (23.9)</td>
</tr>
<tr>
<td></td>
<td>Controls</td>
<td>80.4 (59.8)</td>
<td>-5.0 (32.1)</td>
<td>10.1 (36.7)</td>
<td>0.5 (30.1)</td>
</tr>
<tr>
<td><strong>Heart rate</strong></td>
<td>Cases</td>
<td>72.5 (10.6)</td>
<td>4.6 (6.3)</td>
<td>1.9 (5.7)</td>
<td>3.6 (6.1)</td>
</tr>
<tr>
<td></td>
<td>Controls</td>
<td>73.2 (14.6)</td>
<td>5.7 (5.9)</td>
<td>-1.3 (4.3)</td>
<td>2.5 (6.5)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>31.4 (8.6)</td>
<td>33.5 (11.9)</td>
</tr>
<tr>
<td></td>
<td><strong>LF</strong></td>
<td>Cases</td>
<td>3.7 (3.3)</td>
<td>1.0 (6.8)</td>
<td>-1.4 (3.2)</td>
</tr>
<tr>
<td></td>
<td>Controls</td>
<td>5.2 (4.9)</td>
<td>-3.9 (8.3)</td>
<td>-1.3 (4.1)</td>
<td>35.6 (36.2)</td>
</tr>
<tr>
<td></td>
<td><strong>HF</strong></td>
<td>Cases</td>
<td>4.5 (4.6)</td>
<td>1.4 (5.6)</td>
<td>-0.5 (3.4)</td>
</tr>
<tr>
<td></td>
<td>Controls</td>
<td>5.5 (5.3)</td>
<td>-1.5 (4.6)</td>
<td>-0.8 (3.2)</td>
<td>21.1 (26.3)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>Cases</td>
<td>10.5 (9.4)</td>
<td>4.4 (16.2)</td>
<td>-1.8 (7.5)</td>
<td>48.6 (43.9)</td>
</tr>
<tr>
<td></td>
<td>Controls</td>
<td>13.6 (12.3)</td>
<td>-6.2 (16.2)</td>
<td>-2.4 (8.6)</td>
<td>67.5 (73.1)</td>
</tr>
<tr>
<td><strong>Normalized LF</strong></td>
<td>Cases</td>
<td>0.3 (0.1)</td>
<td>0.0 (0.1)</td>
<td>-0.1 (0.1)</td>
<td>0.1 (0.1)</td>
</tr>
<tr>
<td></td>
<td>Controls</td>
<td>0.4 (0.1)</td>
<td>-0.1 (0.1)</td>
<td>-0.1 (0.1)</td>
<td>0.1 (0.1)</td>
</tr>
<tr>
<td><strong>Normalized HF</strong></td>
<td>Cases</td>
<td>0.4 (0.1)</td>
<td>0.0 (0.1)</td>
<td>0.0 (0.1)</td>
<td>-0.1 (0.1)</td>
</tr>
<tr>
<td></td>
<td>Controls</td>
<td>0.4 (0.1)</td>
<td>0.0 (0.1)</td>
<td>0.0 (0.1)</td>
<td>-0.1 (0.1)</td>
</tr>
<tr>
<td><strong>LF/HF</strong></td>
<td>Cases</td>
<td>0.9 (0.3)</td>
<td>-0.1 (0.5)</td>
<td>-0.3 (0.6)</td>
<td>0.8 (0.6)</td>
</tr>
<tr>
<td></td>
<td>Controls</td>
<td>1.1 (0.7)</td>
<td>-0.3 (0.7)</td>
<td>-0.3 (0.7)</td>
<td>0.7 (0.5)</td>
</tr>
</tbody>
</table>

Mean and standard deviation (SD) of electrodermal area (μS/min), electrodermal responses (responses/min), respiration rate (breaths/min), skin blood flow (a.u./min), heart rate (beats/min), low frequency (LF), high frequency (HF) and total spectral density (s²), normalized spectral density of the low and high components (LF/Total and HF/Total), and the ratio between low and high spectral components during the initial resting period, as well as mean and SD of the variables when rest values prior to the task have been subtracted from values during the task for cases and control subjects in study III. For heart rate during deep breathing, mean and SD of the range (max-min) are also shown (R). In all tests, p<0.05 was considered significant.
Evaluation of treatments of stress-related illnesses (Study IV)

During the course of the study, 15% of the subjects (2 males and 9 females) chose to withdraw from it. Of these subjects, eight were allocated to the cognitive-behavioral training group, one to the physical activity group, and two to the control group. No differences in demographic characteristics were found between those subjects who completed the study, and those who did not (p>0.05).

Over time, subjects exhibited a relative decrease in autonomic reactivity to the tasks (Heart rate: p<0.001; Electrodermal activity: p≤0.001). For subjects in the cognitive-behavioral training group, heart rate variability in response to deep breathing was significantly reduced compared to before the intervention (p<0.05). However, this group had higher heart rate variability in response to deep breathing before the intervention period than the control group (p<0.05), which could partly explain the findings. Subjects’ autonomic activity during rest also changed significantly over

![Graphs](image_url)

**Figure 5.** Mean values of pressure-pain thresholds in m. trapezius and m. erector spinae for subjects in the cognitive-behavioral training group (CBT), the physical activity group (PA), and the control group (C) in study IV.
Figure 6. Mean values of Short Form 36 Item Health Survey (SF-36) ratings for subjects in the cognitive-behavioral training group (CBT), the physical activity group (PA), and the control group (C) in study IV. Dotted lines represent average values for healthy control subjects in study III.
Results

time: a decrease in electrodermal activity and an increase in skin blood flow were seen (p<0.05 and p=0.045, respectively). There were no differences in autonomic activity during rest between the intervention groups (p>0.05).

Immediately after the intervention period, subjects in the control group demonstrated lower pressure-pain thresholds in m. erector spinae (ES) than subjects in the other groups (Right ES: p=0.041). At 6 and 12 months after the intervention, however, this group difference was no longer present (p>0.05, figure 5). No differences between the intervention groups were found in pressure-pain thresholds before the intervention (p>0.05).

Throughout the study, subjects’ ratings of physical and mental health improved (p<0.05). Furthermore, they rated weaker type A behavioral pattern than before the intervention period (p=0.007). When intervention groups were compared, significant differences in the ratings of general health were found. Subjects in the cognitive-behavioral training group rated improved general health compared to subjects in the physical activity group (p<0.05, figure 6). No differences between the intervention groups were found in questionnaire ratings before the intervention.

Table 5. No. subjects satisfying criteria for working and ratings in the cognitive-behavioral training group (CBT), the physical activity group (PA), and the control group (C)

<table>
<thead>
<tr>
<th></th>
<th>Before</th>
<th>After</th>
<th>6 months</th>
<th>12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Part-time or full-time work</td>
<td>CBT 9</td>
<td>8</td>
<td>7</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>PA 4</td>
<td>6</td>
<td>9</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>C 4</td>
<td>9</td>
<td>11</td>
<td>12</td>
</tr>
<tr>
<td>Shirom-Melamed rating ≤ 3</td>
<td>CBT 2</td>
<td>1</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>PA 0</td>
<td>2</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>C 1</td>
<td>0</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>SF-36 rating ≥ 71%</td>
<td>CBT 1</td>
<td>4</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>PA 0</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>C 1</td>
<td>1</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>
(p>0.05).

The number of subjects working part-time or full-time did not change throughout the study, nor did it differ between the intervention groups (p=0.224, table 5). The number of subjects reporting burnout ratings below 3.0 or SF-36 ratings above 71% also did not differ between the intervention groups, but it increased significantly over time (p<0.033, table 5). There was no apparent overlap between the subjects returning to work and the subjects reporting improved health. Regression analyses showed that the subjects’ expectations of their health and their CRI ratings of perceived resources in the cognitive domain before the intervention significantly explained their return to work at 12 months after the intervention (Expectations: p=0.018; CRI cognitive: p=0.044). Higher ratings of expectation of health and cognitive resources increased the probability of returning to work.
DISCUSSION

The overall aim of this thesis was to explore the relation between pain sensitivity, position sense, and autonomic reactivity to laboratory stressors. The findings indicate a non-additive relation between autonomic activity during a repetitive work task and position sense inaccuracy. Furthermore, subjects with stress-related illnesses often reported pain in the neck, shoulders, and lower back. This was associated with lower pressure-pain thresholds in the back and a modest increase in sympathetic reactivity to physical and mental tests, which might suggest a potential use of these methods in the clinical examination and rehabilitation of subjects with stress-related illnesses.

Effects of a computer task with and without time pressure and precision demands

When performing the task without additional demands, the subjects rated increased muscle fatigue in the arm and hand operating the mouse, indicating an enhanced perceived physical load associated with the painting task. Analyses of wrist position sense data showed that the absolute repositioning error (i.e., the repositioning inaccuracy) increased following the task, but not following the control condition (rest). However, no such difference was seen for the variable repositioning error (i.e., the repositioning imprecision). Similar results were found in a study of shoulder position sense accuracy in response to repetitive arm work to fatigue (Björklund et al. 2000), where an increase in the absolute repositioning error of the shoulder in healthy subjects was found after performing a repetitive work task conducted in a simulated occupational setting. In a prospective laboratory study, Madeleine et al. (2003a) found that female industry workers who developed neck-shoulder pain during 6 months of employment exhibited sensory-motor changes that differed from workers that did not develop pain. These results tend to support hypotheses of altered motor control being a contributing factor in the development of musculoskeletal pain.

Adding time pressure and precision demands to the painting task gave rise to increased ratings of general tenseness as well as physical fatigue in the working arm and hand, compared to the ratings obtained when the subjects performed the task without these demands. This was paralleled by increased electrodermal activity and skin blood flow in the subjects during the more demanding task, as compared to
the less demanding task. Previous studies on mental and physical demands associated with computer work have yielded varying results. A reason for this may be the various tasks employed. Laursen et al. (2002) found an increased electromyographic (EMG) activity in the forearm, shoulder and neck muscles of healthy female subjects when performing the Stroop color word test\(^1\) compared to a reference task involving similar movements of the arm and hand. The same research group found no additional effect of the Stroop color word test on normalized spectral power of the heart rate variability spectrum than what was found for the reference task (Garde et al. 2002). Birch et al. (2000) investigated the effects of completing a computer drawing task under time pressure, precision and mental demands on the EMG activity in forearm and shoulder muscles. They found an increase in EMG responses in all measured muscles when high time pressure was imposed on the task, despite other demands being low. Similar results were found when a combination of time pressure and verbal provocations were added to a text editing task (Wahlström et al. 2002). In the latter study, they also found increased heart rate and blood pressure during the task. Finsen et al. (2001), in turn, studied heart rate, blood pressure and EMG activity in the upper extremity during a motion cycle involving lifting the fingers from, and resting the fingers on, the computer mouse. When memory demands were added to the task, an increase in these parameters was found. Finally, Hjortskov et al. (2004) found changes in heart rate variability as a result of introducing a combination of stressors (i.e., verbal provocation, surveillance, and memory tests) during a computer keying task.

An inherent difficulty in studies of mental and physical demands during computer work is ascribing potential physiological effects to either physical performance or mental load, since both elements are likely to be involved in the work. Kohlisch and Schaefer (1996) attempted to distinguish between effects related to mental load and motor demands, respectively, by examining cardiac and electrodermal activity during computer keyboard work with varying mental and motor demands. They

\(^1\) The Stroop Color Word test, or the Stroop Color Word conflict task (Stroop 1935) has appeared in many different forms in the literature. In the studies referred to in this text, color words were presented in different colors on the computer screen, and the subjects reported the color of the words using either the computer mouse or the keyboard.
found no effect of motor activity on the physiological measures unless the typing speed was very high, and concluded that, at lower levels of motor activity, physiological effects can be ascribed solely to mental load. Given the different computer tasks and performance measures used in the literature, it is difficult to compare the levels of motor activity used, and therefore to appreciate the contribution of motor activity to the physiological recordings.

**Muscle oxygenation**

During the painting task with time pressure and precision demands, oxygen saturation in m. extensor carpi radialis decreased, as compared to the oxygen saturation during the painting task without these demands. For the trapezius muscle, no differences in oxygen saturation between the task versions were found. As discussed above, the reduction in forearm oxygen saturation during the more demanding task might be attributed to increased mental load, higher work intensity, or a combination of these factors. The VAS ratings of tenseness and the electrodermal activity, that were both increased during the more demanding task compared to the less demanding task, indicate a higher mental load associated with the more demanding task. It is possible that such increased mental load could lead to a reduction in muscle oxygen saturation subsequent to sympathetically induced vasoconstriction. However, this could not be assessed in study II since no recordings of muscle sympathetic activity were made. Hansen et al. (1996) found that the ability of reflex-mediated sympathetic activation to reduce muscle oxygenation was abolished when the muscle was exercised at intensities above 10% of maximal voluntary contraction. Although EMG was not recorded in study II, previous studies of computer-mouse work with varying demands have reported lower levels of EMG activity (Birch et al. 2000; Finsen et al. 2001; B. Laursen et al. 2002). This would suggest that sympathetically induced vasoconstriction might contribute to the observed reduction in muscle oxygen saturation. Yet, it is not likely that mental load alone is responsible for the decrease in oxygen saturation in m. extensor carpi radialis. If this was the case, a similar decrease would reasonably be seen in the trapezius muscle as well. Furthermore, the increased performance and VAS ratings of fatigue indicate higher work intensity during the more demanding task. Based on the assumption that the work intensity imposed on the trapezius muscle was small compared to that of the extensor carpi radialis
Discussion

muscle, and on findings of decreasing muscle oxygenation with increasing work rate (Bhambhani et al. 1999; Chuang et al. 2002), one may conclude that the higher work intensity during the more demanding task contributed more to the oxygen saturation decrease than mental load. In support of this, studies have shown that muscular contractions may affect skin sympathetic activity (Leuenberger et al. 2003), and that relative muscular effort can influence exercise-induced skin sympathetic activity (Ray and Wilson 2004).

Position sense

In study II, no differences in variable repositioning error between the task versions were found. The absolute repositioning error, on the other hand, increased following the painting task without additional demands, as compared to the task when time pressure and precision demands were included. This result is intriguing, and might be interpreted in different ways.

1) That motor control is scarcely affected by the repetitive computer-mouse task as long as the work is performed under time pressure and precision demands. Assuming that the more demanding task gave rise to increased muscle sympathetic activity, and that this activity was still present during the position sense test following the task, this would contradict numerous previous findings (c.f. Johansson et al. 2003b). However, Matre and Knardahl (2003) found no evidence of reduced proprioception in the lower extremities when a cold pressor test and oral glucose ingestion was used to provoke muscle sympathetic activity. Similarly, Hjortskov et al. (2005) failed to show any difference in lumbar position sense accuracy when the threat of an electrical shock stressor was given to the subjects.

2) That moderate arousal may improve performance in the position sense test. During the more demanding task, we found modest increases in autonomic activity and VAS ratings of tenseness, suggesting heightened arousal when performing the task under time pressure and precision demands. According to the inverted U hypothesis of the relation between arousal and performance (Landers 1980; Schmidt 1988), increased arousal is paralleled by increased performance, but only up to a point. If arousal continues to increase beyond this point, the performance begins to decrease.
The fact that subjects improved their performance in the more demanding task may indicate that the level of arousal was high enough to improve performance also in the position sense test.

Reasonably, the performance on the position sense test used in these studies could be influenced by a number of factors, among which arousal may be of crucial importance. It should be mentioned, however, that the variable repositioning error may be a better estimate of the noise in the sensory signal and/or in the processing of the sensory signal than the absolute repositioning error, since it describes the variability in repositioning rather than overall repositioning accuracy (van Beers et al. 1996). If this is the case, the results indicate no effect of adding time pressure and precision demands to a computer task on position sense.

**Gender differences**

In study II, notably lower oxygen saturation in m. extensor carpi radialis and m. trapezius was found in females compared to males throughout the experiment. It is possible that gender differences in muscle mass or composition, or hematocrit, could give rise to such a difference. With males generally having thicker muscles, the penetration depth of the spectrometer probe might apply to the upper extremities of males and females differently.

**Characteristics of stress-related illnesses**

The cases exhibited a modest increase in autonomic reactivity to standardized laboratory stressors compared to the healthy control subjects. During the handgrip, the cases’ skin blood flow was reduced compared to the control subjects. Moreover, an indication of increased electrodermal activity was found in the cases during mental arithmetic. This may reflect a relatively high responsiveness of the sympathetic nervous system in the cases compared to healthy subjects. However, the results should be interpreted cautiously, since the inter-individual variability of these parameters is high, and clinically established normative values are lacking (Shields 2000). De Vente et al. (2003) found no difference in heart rate reactivity to a mental arithmetic task between burnout patients and healthy subjects, nor did we find any differences in heart rate or heart rate variability in response to the tasks between the cases and the
healthy control subjects.

Pain ratings as well as pressure-pain thresholds in m. trapezius and m. erector spinae differed significantly between the cases and the control subjects. This appears to be in accordance with the findings of Soares and Jablonska (2004), who reported that primary care patients with musculoskeletal pain scored higher on all the subscales (i.e., burnout, tension, listlessness and cognitive difficulties) of the Shirom-Melamed Burnout Questionnaire than patients with minor health problems (e.g., fever) who did not suffer from pain. Grossi et al. (1999) also showed that patients with musculoskeletal pain who had been on long-term sick leave (>30 days of 12 months) scored higher ratings of burnout than patients with shorter sick leave.

Conceivably, pain perception might be associated with autonomic regulation. When bivariate correlations were calculated between the cases’ pressure-pain thresholds and indices of their autonomic reactivity to the tasks, electrodermal reactivity was consistently negatively correlated with pressure-pain thresholds in m. trapezius as well as m. erector spinae (Pearson’s r ranged between -0.39 and -0.58). Similarly, cases’ ratings of listlessness were negatively correlated with pressure-pain thresholds in both muscles (-0.54<r<-0.36). For the healthy control subjects, however, no such associations were seen. Rather, their pressure-pain thresholds in m. erector spinae seemed to correlate with their heart rate reactivity to the tasks (0.52<r<0.56).

For the majority of the SF-36 indices, substantial differences between the cases and the control subjects were found. Cases’ scores of physical role limitation, general health, vitality and social functioning resembled those reported for patients with chronic fatigue syndrome (CFS) (Kennedy et al. 2004; Rakib et al. 2005). While the physical functioning scores were higher for our cases than for CFS patients, the mean scores obtained in the present study were comparable to the findings of Bergman et al. (2004), who reported ratings of high physical functioning for subjects with chronic pain. However, other studies on chronic pain patients have found lower levels of physical functioning (Dysvik et al. 2004; B. S. Laursen et al. 2005). The cases in this study also scored notably lower on the emotional role limitation index than patients with CFS or chronic pain.

**Effects of treatments for stress-related illnesses**

Throughout the evaluation period, subjects exhibited a relative decrease in aut-
nomic reactivity to the laboratory stressors, and the majority of their health ratings improved. However, subjects’ pressure-pain thresholds in the upper and lower back and their ratings of pain showed no such improvement over time. The results illustrate the complex interactions between these factors.

When comparing the effects of the cognitive-behavioral training program and the physical activity program, as compared to usual care, only minor differences were found. Subjects who received cognitive-behavioral training exhibited a reduction in heart rate variability in response to deep breathing, compared to the other intervention groups. However, these subjects had higher heart rate variability in response to deep breathing before the intervention than subjects in the control group, which may partly explain this difference in reactivity between the groups over time. For subjects who received either cognitive-behavioral training or physical activity, the pressure-pain thresholds in m. erector spinae were relatively unchanged immediately after the intervention, compared to subjects in the control group who showed decreased pressure-pain thresholds in m. erector spinae. At subsequent follow-up assessments, however, these differences were no longer present. Ratings of general health improved in the cognitive-behavioral training group compared to the physical activity group, although the ratings did not differ from those of the control group.

Taken together, the results show little difference in effects between physical activity attempting to modify autonomic regulation and cognitive-behavioral training attempting to change appraisal of stressful situations, compared to usual care, for subjects with stress-related illnesses. A reason for the marginal differences found between the intervention groups may be the improvement seen in the control group throughout the course of the study. It is possible that the attention given to these subjects by performing the measurements affected the results obtained for this group. However, this effect is likely to be equal between the three groups, since the same attention was given to all subjects.

Our results are in agreement with the findings of Granath et al. (2006), where subjects with self-reported stress-related problems improved regardless of whether they received cognitive-behavioral therapy or yoga. Jensen et al. (2001) found no effect of cognitive-behavioral therapy for sick-listed chronic pain patients on their absence from work, when compared to treatment as usual. However, other studies have shown that cognitive-behavioral therapy and physical exercise may be ben-
cial to patients with chronic fatigue syndrome as well as fibromyalgia (Afari and Buchwald 2003; Maquet et al. 2006; Pedersen and Saltin 2006). Linton and Ryberg (2001) found an improvement in subjects with neck and back pain who received a cognitive-behavioral group intervention compared to treatment as usual, despite the recovery over time seen for the control group. In particular, absenteeism from work was lower in the cognitive-behavioral intervention group. Yet, it is likely easier to reduce the number of sick leave days for patients with less severe symptoms and shorter sick leave history. Indeed, Marhold et al. (2001) found that pain patients who had been on short-term sick leave (2-6 months) were more likely to return to work after participating in a cognitive-behavioral return-to-work program than patients who had been on long-term sick leave (>12 months).

Although the number of subjects returning to work, or subjects with “healthy” ratings of burnout (i.e., Shirom-Melamed total score <3.0) or quality of life (i.e., SF-36 total score >71%) did not differ between the intervention groups, subjects’ ratings improved over time. Overall, the number of subjects reporting “healthy” levels of burnout or quality of life increased by 40% after the intervention. At 6 months after the intervention, the number had increased threefold, and it continued to grow until 12 months after the intervention. When regression analyses of SF-36 and Shirom-Melamed total scores were used to estimate the rate of improvement, the results showed that the subjects would reach “healthy” levels of ratings at approximately 34 months (SF-36) and 39 months (Shirom-Melamed) after the intervention. There was no increase in the number of subjects returning to work throughout the study, nor any apparent overlap between subjects returning to work and subjects reporting improved health.

Additional analyses revealed that the subjects’ pre-intervention ratings of cognitive resources and expectations of health were informative measures of their return to work at 12 months after the intervention. The result underlines the need to incorporate patients’ expectations of their health in the rehabilitation process.

**Methodological considerations**

In study I and II, the mouse-operated computer task lasted for 45 minutes. It is not clear whether similar results would be found for continuous long-term computer work. Apart from effects that may accumulate over time, physiological processes
may change during prolonged exposure to repetitive computer work. The computer task involved constrained and repetitive wrist movements, and may therefore be useful in studying the effects of such risk factors on potential mechanisms behind computer-related musculoskeletal disorders. However, other factors may be important in the development of musculoskeletal disorders as well. One such factor may be the recovery after work, which was not assessed in these studies.

In study III and IV, subjects with stress-related illnesses were selected on the basis of what was specified in their illness certificate, issued by their primary care physician. Due to the high proportion of females among the subjects, no gender differences were investigated. It is possible that the results would be different if both genders were represented equally in the study samples. In the assessment of autonomic activity, no hormonal measurements were performed, thereby limiting the findings to some of the stress effector systems. Nevertheless, the findings in study III of increased autonomic reactivity to laboratory stressors in the cases compared to the healthy controls might suggest an involvement of autonomic regulation in the development of their symptoms. However, since the study was cross-sectional, it cannot be excluded that it might be a consequence of a personality trait that was already manifested prior to the development of their symptoms. Longitudinal studies will be needed to clarify this issue.

The fact that all subjects agreed to participate in the studies might have implications for the results, particularly in study IV where the study sample is likely biased with a greater number of subjects that actively seek treatment in order to return to work. This adds to the difficulty in evaluating the interventions for the population of interest, and it might explain the improvement seen in all intervention groups. It is also possible that larger differences between the treatment groups and the control group would have been found if the subjects were not randomly allocated to the treatment groups, but rather allocated according to their rated expectations of the treatments.

In study IV, the effects of a cognitive-behavioral training program and a physical activity program, respectively, were evaluated. It may be that a combination of the two programs would have yielded better results, although it would have required more time and effort from the participants. By involving the subjects’ workplaces to a greater extent in the rehabilitation, the probability of the subjects returning to
work might also increase. One may argue that the 12-month follow-up period was short, when considering the subjects’ history of sick leave from work. However, the inclusion of a control group of subjects that were not offered any treatment during the study limited the follow-up assessment period due to ethical considerations.
CONCLUSIONS

A repetitive computer-mouse task associated with perceived fatigue in the upper extremity lead to reproducible negative effects on some, but not all, measures of positions sense accuracy, illustrating the complexity of proprioceptive functions. Increased autonomic activity and perceived tenseness and fatigue, and decreased muscle oxygenation, during elevated performance had no exaggerated effect on position sense accuracy. Rather, position sense was less affected when additional demands were imposed than when they were not imposed on the task.

Symptoms of musculoskeletal pain and signs of increased autonomic reactivity to laboratory stressors were found in subjects with non-specific diagnoses of stress-related illnesses, compared to healthy control subjects. This might suggest an involvement of autonomic regulation in the development of their symptoms.

When evaluating the effects of a cognitive-behavioral training program and a physical activity program for subjects with stress-related illnesses, a relative decrease in autonomic reactivity to laboratory stressors and improvement of health ratings were found during the 12-month follow-up period, irrespective of intervention. For pressure-pain thresholds and ratings of pain, however, no such improvement was seen. Subjects’ ratings of expectations of health appeared to be informative of their return to work after the intervention period. It is possible that long-term follow-up assessments may reveal gradual improvements in subjects’ health that are not evident shortly after the intervention.
ACKNOWLEDGEMENTS

A lot of thoughts are going through my mind as I am writing this. It does not seem that long ago since I started my PhD work. During this time, I have had the privilege to work with a number of people whom I wish to thank specifically.

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away from work-related issues and demands.

Finally, I would like to thank my good friend Charlotte Jalmelid. We go way back and we have been through a lot together. You have a great sense of humour, and I enjoy spending time with you and your family, talking about anything and everything that has nothing to do with work.

Umeå, August 2006

Marina Heiden
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