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BURNOUT – A MATTER OF IMPAIRED RECOVERY?

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"Success is not final, failure is not fatal: it is the courage to continue that counts."
Winston Churchill

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ABSTRACT

The general aim of this thesis work was to investigate physiological and subjective markers of recovery from stress in order to identify and discuss possible risk factors precipitating burnout, as well as factors related to recovery from burnout and return to work. In particular, sleep and unwinding during leisure time, in relation to burnout, were in focus in the four papers included in this thesis.

The first two papers had cross-sectional designs, in which workday and weekend patterns of sleep, cortisol, sleepiness, mental fatigue, and perceived activation in burnout subjects were investigated. Twenty-four working individuals were selected into two groups on the basis of burnout scores (high or low), 12 subjects in each group matched on age, gender and experience in the company. Physiological sleep data showed a higher frequency of arousals for the high-burnout group. The diurnal pattern of sleepiness, mental fatigue and activation indicated that the high-burnout group did not recover during the weekend, as did the low-burnout group. Other indicators of impaired recovery were seen within the high-burnout group as they reported a higher degree of thoughts of work during leisure time, bringing work home and working on weekends. The burnout group showed higher awakening cortisol during the workday compared to the weekend. The diurnal amplitude of cortisol did not differ between the groups. When objective sleep data was related to cortisol data, it was shown that higher frequency of micro-arousals during the prior sleep was associated with an earlier diurnal peak of cortisol and higher diurnal amplitude of cortisol during the workday.

The third paper was a longitudinal study, conducted over a two-year period. During this time, 15 subjects, out of 388 in the reference sample at one workplace, were identified as 'burnout cases', as they were clinically assessed, found matching the inclusion criteria and referred to treatment for clinical burnout. Baseline data on work stress, sleep, and impaired unwinding, were used as independent variables in a set of logistic regression analyses in order to identify risk factors for subsequent clinical burnout. 'Too little sleep (<6 h)' was identified as the main risk factor for clinical burnout, with adjustment for 'work demands' and 'thoughts of work during leisure time'. The latter two became significant predictors in earlier steps of the multivariate approach.

In the forth paper, 23 patients on long-term sick leave due to clinical burnout and 16 healthy controls were subjected to polysomnographic recordings at baseline and at follow-up (6–12 months later). Decreased sleep fragmentation and decreased anxiety over time predicted recovery from burnout (reduced fatigue). Reduced fatigue was the only significant predictor of return to work.

In short, this thesis has put forward data that support the assumption that, apart from high work demands, impaired or insufficient sleep and unwinding are connected to burnout development. Also, recovery from clinical burnout was shown to be associated with improved sleep quality and alertness. Plausibly, interventions aiming at preventing or treating sleep disturbance, as well as at enhancing the possibilities to unwind during daytime, in groups experiencing high work stress, may be of vital importance in order to decrease the risk for severe exhaustion development.

LIST OF PUBLICATIONS

I. Söderström M, Ekstedt M, Åkerstedt T, Nilsson J, Axelsson J. Sleep and sleepiness in young individuals with high burnout scores. *Sleep*. 2004 Nov;27(7):1369-77.

II. Söderström M, Ekstedt M, Åkerstedt T. Weekday and weekend patterns of diurnal cortisol, activation and fatigue among people scoring high for burnout. *Scandinavian Journal of Work Environment and Health*. 2006; Suppl 2:35–40

III. Söderström M, Jeding K, Ekstedt M, Perski A, Åkerstedt T. Insufficient sleep predicts clinical burnout. *Submitted manuscript*

IV. Ekstedt M, Söderström M, Åkerstedt T. Sleep physiology in recovery from burnout. *Biological Psychology*. 2009 Dec;82(3):267-73. Epub 2009 Aug 21.

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LIST OF ABBREVIATIONS

ACTH	Adrenocorticotropin Hormone
BAI	Beck Anxiety Inventory
BDI	Beck Depression Inventory
BMI	Body Mass Index
CBT	Cognitive Behavioural Therapy
CBT-I	Cognitive Behavioural Therapy for Insomnia
COR	Conservation of Resources
CRP	C-Reactive Protein
CRH	Corticotropin Releasing Hormone
DCS	Demand-Control-Support
DHEAS	Dehydroepiandrosterone Sulfate
DSM-IV-TR	Diagnostic and Statistical Manual for Psychiatric Diagnoses, 4th Edition, Text Revised
EEG	Electroencephalography
EMG	Electromyography
EOG	Electrooculography
ERI	Effort-Reward Imbalance
ESS	Epworth Sleepiness Scale
GAS	General Adaptation Syndrome
HAD-A	Hospital Anxiety and Depression Scale – Anxiety subscale
HAD-D	Hospital Anxiety and Depression Scale – Depression subscale
HADS	Hospital Anxiety and Depression Scale
HPA	Hypothalamic-Pituitary-Adrenocortical
ICD-10	International Classification of Diseases, 10th revision
KSD	Karolinska Sleep Diary
KSS	Karolinska Sleepiness Scale
KSQ	Karolinska Sleep Questionnaire
MBI	Maslach Burnout Inventory
MBI-GS	Maslach Burnout Inventory, General Scale
MSLT	Multiple Sleep Latency Test
MWT	Maintenance of Wakefulness Test
NREM	Non-REM Sleep

OSAS	Obstructive Sleep Apnea Syndrome
PVN	Paraventricular Nucleus
PSG	Polysomnography
REM	Rapid Eye Movement
SAM	Sympathetic-Adrenal-Medullary
SCID	Structured Clinical Interview
SCN	Suprachiasmatic Nuclei
SMBQ	Shirom-Melamed Burnout Questionnaire
STAI	State Trait Anxiety Index
SSS	Stanford Sleepiness Scale
SQI	Sleep Quality Index
SWS	Slow Wave Sleep
WASO	Wake Time After Sleep Onset

INTRODUCTION

The present thesis deals with the relation between burnout and recovery. The background to this research project is the growing numbers of sickness absence in Sweden during the end of the 1990's and the first years of the new millennium. This development has mainly been related to an increase in psychological ill-health and stress-related symptoms, such as persistent fatigue and exhaustion [1-3]. In the absence of a distinct conceptualization of the increasing stress-related exhaustion, *burnout* has become an assembling diagnosis in daily language [4].

The mechanism behind burnout is unknown, but it is assumed to be caused by ineffective coping with long-term stress at work and (or) in daily life [5]. One main hypothesis behind this thesis is that sleep, or rather impaired recovery from stress, may play an important role in burnout development. Sleep complaints have increased in the working population during the same period of time, as have stress related complaints [2]. Increased levels of sleep disturbance have also been shown in burnout subjects [5-7]. This seems logical as prolonged stress activation may disturb sleep and sleep disturbance may cause or aggravate burnout-like symptoms as fatigue, mood changes and decreased cognitive performance. Thus, impaired sleep may mediate burnout development. However, data are scarce regarding the relation between stress, sleep, recovery and burnout.

This thesis brings together four papers focusing on different aspects of the relation between stress, recovery and burnout. Workday and weekend patterns of sleep (physiological and subjective), as well as the diurnal patterns of sleepiness, fatigue, activation and cortisol in burnout groups are covered in two papers. The third paper refers to a prospective study, in which risk factors for subsequent clinical burnout were identified. In the forth paper, the relation between recovery from clinical burnout across time and changes in physiological sleep indicators was in focus.

BACKGROUND

BURNOUT

What are the clinical characteristics of burnout?

The main clinical characteristic of burnout is the excessive and persistent fatigue, including markedly reduced mental and physical energy as well as emotional distress and cognitive weariness [5, 8-13]. To date, there are no generally agreed upon diagnostic criteria for the clinical burnout syndrome [14]. It is not present as a psychiatric diagnosis in the latest edition of the Diagnostic and Statistical Manual for Psychiatric Diagnoses (DSM-IV-TR), and in the 10th revision of the International Classification of Diseases (ICD-10), burnout (Z73.0) is broadly defined as "a state of vital exhaustion" [15, 16].

However, diagnostic criteria for clinical burnout, or stress related exhaustion, have been defined by a group of Swedish researchers and clinicians. In 2005, the Swedish National Board of Health and Welfare added 'exhaustion syndrome' as a supplementary diagnosis (F43.8A) into the Swedish version of the ICD-10 [17]. Exhaustion syndrome refers to a state of physical and psychological exhaustion, due to long-term ($\geq$ 6 months) exposure to one or more identifiable stressors at work and (or) off-work. For the individual, the exhaustion cause significant clinical suffering as well as reduced ability to function at work, socially or in other important aspects of life. The diagnostic criteria include symptoms such as reduced ability to handle demands or time pressure, difficulties with concentration and memory, emotional distress, sleep disturbance and (or) different physical symptoms, such as palpitations, stomach problems and muscle ache. If the individual suffers from any anxiety disorder, depression or dysthymia, exhaustion syndrome will be reported as a secondary diagnosis [13, 17]. Notably, sleep disturbance is a common feature of the condition. Still, the question remains whether disturbed sleep and other aspects of impaired recovery are of importance as precipitating or maintaining factors for burnout development.

When the data collection for the included papers was carried out the diagnostic criteria for exhaustion syndrome were under development, but not yet established, and therefore the term burnout was used in all four papers and within this thesis text.

Research definitions

The most widespread research definition of burnout is the one of Maslach and colleagues. [18, 19]. In this approach burnout has been defined as a syndrome of emotional exhaustion, depersonalisation (cynicism) and reduced personal accomplishment (inefficacy) in relation to work. The Maslach Burnout Inventory (MBI) is the most commonly used burnout scale within the burnout literature. It was first stated that burnout was only occurring among individuals who worked within human services, as within health care or education, or who did other kinds of people-oriented work, for whom certain emotional and social demands were supposed to be high. Accordingly, the first versions of the MBI were developed to fit employees within human service and education. Later this view was revised and the MBI was modified into a General Scale (the MBI-GS) in order to be suitable for employees with all

kinds of work [19]. The MBI-GS scale includes 16 items, such as: “I feel emotionally drained after work”, “I can effectively solve the problems that arise at work”, and “I have become less engaged at work”. The widespread use of the MBI within the burnout research has strongly influenced the conceptualization of burnout [11, 12].

The concept of burnout as defined by Maslach and colleagues postulate a psychological condition solely connected to work [11]. In accordance with this, research on burnout has mostly been conducted on working subjects, and there is a lack of physiological data on burnout groups. Shirom and Melamed and colleagues have argued for a slightly different view. In an extensive review by Shirom (1989), the core feature of the burnout condition was defined as the depletion of the individual’s energetic resources [8]. This energy drain is supposed to arise due to long-term stress exposure at work and (or) off work, resulting in a combination of physical fatigue, emotional exhaustion, and cognitive weariness [20]. In this sense burnout is not exclusively connected to work stress, and not only a psychological phenomenon. Instead it is viewed as a more global condition, which fits with the diagnostic criteria of exhaustion syndrome described above.

Fatigue – the core feature

Persistent fatigue, or exhaustion, is the core feature of burnout. The fatigue experience in burnout has been described as multidimensional – a combination of emotional as well as of physical and cognitive fatigue [8, 20, 21].

Fatigue refers to a state of strain or exhaustion, when energy loss exceeds energy availability due to extended physical, emotional or mental activity, and (or) due to poor restoration [22-24]. Normally, fatigue is relived by rest. Chronic fatigue, however, is often connected to ill-health and may negatively impact work performance, social relationships, daily functioning, and well-being [24-27]. Although fatigue is one of the most common complaints reported to physicians, data are scarce about risk factors predicting fatigue in the working population. A large, prospective, cohort study showed that fatigue, psychological distress, need for recovery (unwinding) and burnout was related [24, 26].

Although the mechanisms behind different kinds of fatigue may vary [26, 28], the fatigue experience is more or less the same, including a feeling of reduced energy, reduced willingness and (or) ability to maintain a certain task [8, 29]. For example, physical fatigue, which is the result of prolonged and (or) intensive physical activity, can develop due to accumulated oxygen debt in the muscle tissue and the muscle’s capacity to maintain activity will be reduced [30]. Several studies have shown that mental fatigue increases with time on task, as does accident risk [31, 32]. Also the type of activity or workload is of importance for the development of mental fatigue; the higher the workload the higher levels of fatigue will develop [33].

Fatigue is also one main effect of disturbed sleep [34]. Sleep deprivation, as well as sleep fragmentation, increases sleepiness and fatigue, which in turn impair cognitive performance [35-38]. Fatigue may also be the result of endocrine and immune reactions and interactions [38]. This fits well with the fact that fatigue is a common complaint among individuals suffering from chronic diseases [24].

Fatigue – a signal of need for recovery

In this thesis, fatigue will be in focus as it is viewed as a signal of need for recovery. Need for recovery after stress has been defined as the time required for returning to baseline after stress. From this perspective, need for recovery has been proposed to serve as a measure of the severity of stress [39]. For example, high work demands [40] and overtime work [41] has been associated with need for recovery, as has stress related disease [39]. Incomplete recovery, plausibly, mediates the relation between exposure to stressful working conditions and the development of health problems [42], such as burnout.

Hence, fatigue can to be associated with both the stress and workload preceding burnout and with the actual recovery process, which – if it is impaired, and which is the assumption behind this thesis – may contribute to burnout development. Thus, fatigue can be the result of high and persistent work demands, sustained activation, impaired or insufficient sleep or other aspects of impaired recovery from stress. The other way around, decreased fatigue in clinical burnout groups would be associated with recovery from burnout, and with lowered stress, enhanced sleep and recovery. All these aspects were, to some extent, examined in the present thesis work.

In order to measure the global fatigue experience characterizing burnout the Shirom-Melamed Burnout Questionnaire (SMBQ) was used in this research project. SMBQ is a multidimensional general measure of burnout, including 22 items such as "My batteries are emptied", "I feel physically exhausted", and "My head is not clear" [9, 10]. In the study focusing on burnout patients on sick leave, the fatigue experience was also measured by a fatigue index. The fatigue index was based on the multidimensional characteristics of fatigue in burnout, comprising cognitive and physical dimensions and a global perception of persistent fatigue. Other aspects of fatigue are the diurnal fluctuations of subjective mental fatigue, which are seen as an important indicator of need for recovery. This was measured by daily ratings, repeatedly throughout the day, within a wake diary.

Burnout – an exhaustion syndrome due to impaired recovery from stress?

Further research is needed to more systematically investigate the role of different kind of stress in burnout, as stress at work and stress related to other areas of life. Moreover, the role of *recovery from stress*, as sleep and unwinding, which perhaps is even more important for burnout development – the latter is the bearing hypothesis behind the present studies – needs to be investigated. In their review, Geurts and Sonnentag (2006) point out recovery, defined as a process of psycho-physiological unwinding after effort expenditure, as a vital explanatory mechanism in the relation between acute stress reactions and health impairments in the long run [42]. This research project builds upon such an assumption.

Also, Almén (2007) puts forward a cognitive behavioural model for burnout development, which is in line with the above assumption [43]. When an individual (at work or in the life situation as a whole) is facing increasing demands and (or) decreasing resources in combination with insufficient flexibility regarding the ability to adjust to the changed situation, the result is often that the individual puts in more effort to handle the demands, which in turn may lead to increased tension and intensified stress reactions. In addition, the individual often decrease the time spent for recovery, such as sleep and unwinding, in order

to meet the increasing demands. The latter can be related to the individual's own high standards for accepted performance, and to learned patterns of how to handle demands, thoughts and feelings. This may become the start of an exhaustion process. Over time, the physiological stress reactions may become chronic and it becomes harder to relax or unwind from stress, even when there are objective possibilities to do so. When the recovery processes get disturbed the exhaustion symptoms become aggravated and eventually the individual cannot handle the work and (or) life situation.

In this thesis I have adopted this view of burnout as a progressively developing exhaustion syndrome, due to a combination of long-term stress and insufficient recovery, and due to both environmental and individual factors. In short, the assumption is that the exposure to chronic stress may negatively impact 'recovery behaviours' as well as the actual physiological recovery processes, which in turn may aggravate the burnout development. To date, however, few studies have investigated these issues, and studies with prospective designs aiming at identifying risk factors for subsequent clinical burnout are lacking.

STRESS

What is stress?

In his pioneering work, Hans Selye introduced the concept of stress (which originally means 'load', 'weight' or 'pressure') to describe the universal physiological responses to different challenges [44]. From experiments on rats, he proposed the General Adaptation Syndrome (GAS) model of stress [45]. The GAS model comprised three phases of stress, the alarm phase, the resistance and the exhaustion phase, which describes the changes of the stress responses during sustained stress. Activation that endures beyond the resistance stage, i. e. into the exhaustion stage, was hypothesized to contribute to disease [45, 46]. More recent stress models view stress as a process, which includes the perception and evaluation of external, or internal, events (stressors), which precipitates the activation of bodily stress responses [47, 48]. What is perceived as stressful and leading to physiological stress responses differs between individuals, depending on as well genetic factors as our personal learning history and the actual stress situation, including type of stressors and available recourses to cope with the situation [49].

In this research project, stress is viewed as such a psycho-socio-physiological process, involving the interaction between the individual (the brain and the body) and the environment. This fits with the Lazarus' and Folkman's (1984) transactional approach, in which stress is defined neither as the stressor nor the stress response, but in the relationship between the two. In their model, stress arises when the demands in a certain, for the individual significant, situation or environment exceed the available recourses to cope with them [50]. Another model with coping in focus is the cognitive approach of Ursin and Eriksen (1994), which emphasizes the individual's appraisal of the stress situation as the mediating link between the stressor and the physiological response. They argued that the level of physiological responses depend on the learned expectancy of being able to cope with the stressful situation. Hence, effective coping might reduce the arousal level, while lack of control over the outcome, or ineffective coping, increases the physiological stress response and is suggested to lead to helplessness, frustration and distress [51].

Work stress and burnout

Regarding stress at work, two of the most influential models are the Karasek and Theorell's demand-control-support (DCS) model [52] and the effort-reward imbalance (ERI) model proposed by Siegrist [53]. According to the DCS model, job strain is the result of combination of high demands and low levels of control and (or) support at work. The ERI model deals with the framework around the job situation, such as the individual's balance between effort and reward (money, esteem, job security). High job strain and (or) effort-reward imbalance at work have in several studies been connected to increased risk for cardiovascular diseases, and other health complaints [53-55].

The above work stress models have influenced theories of burnout development. In Maslach's and colleagues view, burnout arises from chronic mismatches between the individual and the work environment, regarding one or more of six areas of work (workload, control, reward, community, fairness, and values) [11]. Within the burnout literature, the Conservation of Resources (COR) model is another often referred to model for understanding the processes of burnout development [56, 57]. The COR model proposes that lack of vital resources connected to work, or perceived threats to such resources, may lead to a progressive process of energy drain, which over time might lead to a chronic depletion of emotional, cognitive, and physical resources – i. e. burnout. In contrast to the above mentioned work stress models, the COR model also points out off-work resources, such as nurturing relationships within the family, as relevant in the context of burnout as they may be threatened or impaired when work demands are too high [58]. In this sense, aspects of recovery during leisure time are seen a vital resource, and as such of importance in the process of burnout development. As burnout is supposed to be caused by long-term stress and – which is our hypothesis – by *impaired recovery from stress*, the COR, DCS and ERI models, the individual's appraisal and ability to cope with (or adjust to) the situation, and implications for recovery, are highly relevant.

Several cross-sectional studies have indicated that the effect of work stress on burnout seems to involve job strain, high work demands and low recourses at work [11, 56, 59]. Also prospective studies have demonstrated the effect of work stress on emotional exhaustion. In a prospective study, using a representative sample of 3004 workers, significant effects on emotional exhaustion were found for high work demands, low decision authority, lack of support at work, and downsizing [60]. Another longitudinal study, using a sample of nurses, showed that quantitative job demands and professional worries were, over time, associated with emotional exhaustion, as was poor co-worker support associated with depersonalization [61]. A recent meta-analysis identified job demands (including risks, hazards and complexity) as associated with poorer health and with burnout. Further, job resources such as knowledge, autonomy, a supportive environment, and work saftety, were negatively related to burnout [62]. However, as has been mentioned above, data are lacking regarding the role of sleep and recovery in relation to work stress and burnout.

The physiological stress reactions

The brain is the organ that decides what is stressful and determines the responses [63]. Mammals share an innate repertoire of stress reactions governed from brain structures in the limbic system and the hypothalamus, in order to protect the survival of the species [64]. Two

main axes of physiological responding to stress have been distinguished. One is governed by the sympathetic nervous system, the sympathetic-adrenal-medullary (SAM) axis; another by the hormonal system, the hypothalamic-pituitary-adrenocortical (HPA) axis [65].

Four reaction patterns including behavioural aspects in relation to threat can be distinguished; the alarm response (or fight-flight response), the freeze response, the play-dead response, and the defeat response [64]. The most well known of these reactions is the alarm response, or the fight-flight response, which Walter Cannon described already in 1914 [66]. The immediate physiological reactions, governed by the SAM axis – such as elevated heart rate and blood pressure, increased sweat, decreased sensitivity to pain, improved blood coagulation and increased attention – are aiming to prepare the body to *fight* to concur, or *flight* to escape from, a threat [67]. The acute neural stress responses reflected in catecholamine release (e.g. norepinephrine and epinephrine) into the blood is short-lived and difficult to measure, but the cardiovascular changes with a rise in blood pressure and heart rate have been used as markers of the intensity of stress related arousal in several studies [65, 68, 69].

Parallel to the initiation of the above acute stress responses governed by the autonomic nervous system, the hormonal path (the HPA axis) is activated. HPA-axis activity refers to the hormone cascades including the release of corticotropin releasing hormone (CRH) from the hypothalamus. CRH acts on the pituitary, which releases adrenocorticotropin hormone (ACTH), which stimulates the release of cortisol from the adrenal cortex [67]. The effects of the HPA-axis activation are not as immediate as are the ones of the SAM axis. Measured in blood or saliva, cortisol gradually increase within some minutes after stimulation and peaks after 10-30 minutes [70]. HPA activation is thought to reflect more affective, and long-term aspects of stress or strain. [71].

Cortisol is involved in metabolic processes, with the aim to mobilize long-term energy. The hormone also plays an important role in the regulation of the immune activity [72]. Cortisol receptors are found in all major organs and bodily tissues [65]. It can be measured in blood, saliva or in urine, and is one of the most commonly used biomarkers of stress in research. Thus, measures of the physiological stress response (reactivity) often include markers reflecting the activity in the sympathetic nervous system and the HPA axis respectively [49, 70, 73-75].

Prolonged stress and health risks

Through the evolution, it has been of vital importance for survival to immediately react to threats and to be prepared to handle different acute challenges within the environment. Sterling and Eyer (1988) described the physiological aspects of these adaptive processes in the model of *allostasis*. Allostasis refers to the maintaining of homeostasis (balance or stability, which is essential for the function of many bodily systems) through change. The allostasis model states that physiological parameters within an organism must be flexible, or able to vary, in order to appropriately match the environmental demands and to maintain health [76]. After dealing with the acute threat or demand, the stress reactions are terminated and recovery is taken place.

For obvious reasons, what may be stressful in our lives today is not the same as what was threatening for our ancestors some hundred, thousand, or hundred thousand years ago.

However, the biological responses are more or less the same. This means our physiological stress system is not "updated" to the demands in our present environment; i.e. hormones and neuropeptides designed for the handling of acute threats, and for intensive physical activity, may be running around inactive bodies, as what is perceived stressful today, most often, is not physically life-threatening, but more of an ongoing low (or medium) intensive strain. This might, in the long run, have a negative impact on our health [63, 77].

Conditions or situations constituting chronic stress are possibly more harmful with respect to long-term health consequences. McEwen and Stellar (1993) introduced the term *allostatic load* to describe the long-term cost of repeated adaptation [77]. The allostatic load concept refers to the cumulative biological 'wear and tear' upon the body due to repeated (long-term) stress system activation, which can lead to a chronic dysregulation of these systems, and finally cause damage to dependent tissues and organ systems [78]. For example, in response to both acute and prolonged stress, the activation of the autonomic neural system and the subsequent secretion of hormones, as cortisol, contribute to the mobilization of free fatty acids in the circulating blood. In turn, the free fatty acids stimulate the production and release of lipoprotein including triglycerides and cholesterol in order to serve the body with energy [79, 80]. Increased cortisol release inhibit insulin and stimulates glucose mobilization and lipolysis [81]. Long-term increase of circulating cortisol or elevated blood pressure may over time lead to permanent changes of the physiological set points or norms, which in turn may accelerate cardiovascular, metabolic, immunological or neural pathology [63, 75, 77, 82, 83].

Regarding physiological stress markers in burnout, no clear picture has been shown. In a recent meta-analysis, the authors conclude that the comparability between available studies is limited, partly due to diverging methodology and different definitions of burnout [84]. Their analyses included reports of biomarkers in burnout subjects, for which at least three studies were available. This was the case for measures of cortisol, blood pressure, dehydroepiandrosterone sulfate (DHEAS), prolactin, natural killer cells, and C-reactive protein (CRP). The analyses revealed no differences between burnout and control groups, and no potential biomarker for burnout was found. Cortisol is a physiological measure used in one of the studies in this thesis work, as the studies available on cortisol in burnout subjects at the time when our study was carried out had shown inconsistent results. For example, increased morning salivary cortisol, compared to controls, had been found in blue-collar workers scoring high on burnout [5] and in studies of burnout patients [85, 86]. However, the opposite had been shown in a group of teachers scoring high on burnout [87] and in a study on military personnel [88]. Indeed, more controlled and longitudinal research on the physiological aspects of burnout is needed. Data on subjective measures of stress or activation (as the feeling of being 'wound-up') is also scarce regarding burnout groups.

RECOVERY FROM STRESS

The conditions for working life and social communication have radically changed during the last decades. We are facing a 24-hour society, which forces the natural boundaries of night and day, activity and rest. This is one factor which affects today's working life and may contribute to sustained stress or activation, as work and leisure time gets more mixed up. As sustained activation is another side of insufficient or impaired recovery, there is a need for research regarding the role of *recovery form stress* for burnout development.

Recovery has been defined as a process of psycho-physiological unwinding after effort expenditure [42], or as the time required for returning to a normal or pre-stressor level of functioning after the termination of a stressor [71]. Hence, a prolonged stress response can be one aspect of allostatic load as described by McEwen and Stellar (1993) and in the same time a matter of ineffective (insufficient, impaired or inadequate) recovery [71, 77]. The suggestion in theories of the relation between stress and disease is that adequate and quick recovery from stress-induced arousal is of importance for health in the long run [71, 77].

Almén's behavioural model (2007) for burnout development presented above points to how recovery processes might get disturbed when the vicious circle of exhaustion gets started, and – in turn – how disturbed recovery might maintain and aggravate the exhaustion [43]. This fits with Geurts' and Sonnentag's model (2006), in which incomplete recovery is suggested to mediate the relation between the exposure to stressful working conditions and the development of health problems [42]. This thesis work builds upon such an assumption. The recovery processes in focus within the included studies are: recovery from stress through 1) sleep, and 2) aspects of unwinding during leisure time.

We hypothesize further that prolonged exposure to intensive work demands can lead to sustained cognitive activation, such as rumination or anticipation; two conditions that may impede both the above recovery processes, sleep and unwinding [42, 89, 90]. This fits with the allostatic load model, as also psychological states such as worry or rumination, can contribute to the activation of bodily stress reactions [91]. In line with this, the ability to psychologically detach from work during free time has been related to decreased fatigue and increased positive mood [92]. Also, difficulties to psychologically detach from work during leisure time has been shown to predict emotional exhaustion, whereas the opposite has been shown to buffer the relation between job demands and psychosomatic complaints [93]. Further, work related worries predicted emotional exhaustion in a recent longitudinal study of nurses [61]. The ability to cope with work stress, in the sense of not worrying or being able to let go of thoughts of work during leisure time, is likely depending on an interactive process between the individual and the environment. The balance between actual work demands and available resources to handle them, along with the individual's appraisal of and ability to adjust to the situation, is of plausibly vital importance in this process [50, 94].

Hence, persistent thoughts of work during leisure time is one possibly important aspect in relation to burnout, which will be investigated in this thesis work as an indicator of impaired recovery from work stress. Also, the diurnal pattern of perceived activation (the feeling of being 'wound-up', or relaxed), of mental fatigue, as well as other aspects of impaired recovery, such as bringing work home and working on weekends, will be examined.

To sum up, sustained activation (impaired unwinding) might in the long run lead to and allostatic up-regulation and negative health consequences, such as cardiovascular and metabolic diseases. We hypothesize that this could be the case also regarding burnout development, as burnout is viewed as an exhaustion syndrome due to sustained stress activation – or impaired recovery.

SLEEP

Why is sleep important?

Sleep is an essential form of recovery, for both the brain and the body, and as such sleep is one of the main focus of this thesis. This is since inadequate recovery, from stress and from wakefulness itself, plausibly increases the risk for allostatic load and negative health outcomes in the long run [78, 95]. Such a hypothesis seems highly plausible in the cause of exhaustion syndrome or burnout. Evidence of sleep disturbance in burnout subjects are present from subjective ratings in cross-sectional studies [5, 6], but physiological sleep data are lacking. Below, some background regarding the functions and characteristics of normal sleep, and regarding sleep in relation to stress and health.

Several theories of the function of sleep have been proposed. Mainly, sleep is a restorative, anabolic and energy saving process, during which the organism recovers from the 'wear the tear' of wakefulness [96-98]. For example, anabolic hormones as growth hormone and testosterone are released during slow wave sleep (the sleep stage when we sleep most deeply) and, at the same time, catabolic hormones as cortisol are suppressed [99]. Sleep and immune activity seem to be closely linked, as specific parts of the immune system are activated during sleep and some of the cytokines (the intercellular mediators of the immune system) can induce sleep [100]. The body also conserves energy during sleep as the body temperature and metabolism decrease [101]. Furthermore, sleep has been suggested to play an important role in for maintaining synaptic homeostasis (balance) and seems to enhance learning and memory encoding [102, 103].

What is sleep?

Sleep is a condition of decreased consciousness. During sleep perceptual engagement and responsiveness to the environment is substantially lowered. Unlike unconsciousness however, sleep is a reversible behavioural state, as we can be awakened from it if the stimulation is intensive enough. All animals sleep. The nature of sleep, its length and structure, differs however between species, probably as a result of evolutionary demands. The length and quality of sleep also varies between individuals and with age [101, 104]

Sleep can be physiologically measured by polysomnography, which is a combination of measures of brain activity (electroencephalography, EEG), eye movements, (electrooculography, EOG), and muscle tonus (electromyography, EMG). From analyses of polysomnographical recordings five stages of sleep can be distinguished [105]. Stage 1 can be described as the "bridge" from wakefulness to sleep. During this stage the arousal threshold is low and the EEG is characterized by high frequency waves with low amplitudes. Stage 2 usually constitutes around 50 per cent of the total nocturnal sleep. It is characterized by an EEG pattern of moderately low frequencies, featuring so-called K complex (an EEG wave with high amplitude and low frequency) followed by high frequencies waves; a so-called sleep spindle. Stage 3 and 4 are called slow wave sleep (SWS), as the EEG in these stages of sleep is dominated by low frequency waves with high amplitudes. REM sleep, or rapid eye movement sleep, is very much alike stage 1 sleep, with the exceptions that during REM sleep, the EMG shows no muscle tonus, and the EOG shows rapid eye movements. The REM sleep stage is the period when we dream most vividly [104].

The sleep stages 1-4 are called NREM sleep (Non-REM sleep). Progressively during NREM, and mainly during SWS, the cerebral blood flow and metabolism is decreased, as well as the physiological activation overall, such as blood pressure, heart rate, body temperature and respiratory rate. During REM however, the brain metabolism is elevated and similar to that of wakefulness [106]. Sleep is a cyclic process. A normal nocturnal sleep for an adult often contains 4 to 6 sleep cycles, about 90 minutes each. A sleep cycle usually contains all five sleep stages. Normally, the first two or three sleep cycles of a nocturnal sleep contains proportionally more slow wave sleep, and the last cycles more stage 2 and REM sleep [104].

The sleep formula

Why do we sleep as we do? What determines the length and quality of sleep from night to night? Three factors are involved in this process, together constituting what can be called the 'sleep formula'.

The first factor – Homeostasis

The alteration between sleep and wakefulness is a homeostatic process. Homeostasis refers to ' balance' or 'equality'. A need for sleep is built up successively during wakefulness and at a certain point we are ready to fall asleep. This homeostatic process is called Process S in the widely accepted two-factor model of sleep regulation proposed by Borbely [107, 108]. How long and with which quality we sleep is thus influenced by the time awake before sleep and the quality of prior sleep [109]. In particular SWS seems to be related to the time awake preceding sleep. Tononi and Cirelli (2006) suggest that SWS may be regulated by the amount of synaptic potentiation occurred during previous wakefulness [103]. This also seems to be regulated locally, as brain areas that have been highly active during wakefulness show increased power during subsequent SWS [101]. As we sleep, our need for sleep, or the 'sleep drive', is successively lowered.

The second factor – The circadian influence

The second factor involved in sleep regulation is the circadian influence, Process C [107, 110]. Humans and animals show stable diurnal rhythms of many biological, physiological, and behavioural processes and activities. These rhythms run with a period of close to 24 hours [111], and are generated by an internal clock, the suprachiasmatic nuclei (SCN) of the hypothalamus. The circadian rhythms are largely synchronized by light and darkness. Light information is transmitted from the eye to the SCN, from the SCN to the paraventricular nucleus (PVN) of the hypothalamus, and from PVN to the pineal gland. The pineal gland secrets melatonin. Melatonin is a neurohormone, which though its receptors in most organs and cells are involved in the regulation of the circadian rhythms of the body. The endogenous 24-hour patterns of melatonin and of core body temperature are markers of the distinct physiological circadian process, which is involved in sleep regulation. The maximum sleep propensity coincides with the circadian nadir (around 4 AM). Melatonin secretion is suppressed by daylight, and although light is the main external 'zeitgeber', also social activity has been shown to influence the circadian rhythm. Human circadian rhythms promote activity during the day (when it is light) and rest and sleep during the night (when it is dark). For humans and other day-active species this seems to have been the most adaptive path, with respect to evolutionary demands [112, 113].

The third factor – The arousal or activation level

A third factor, which influences the ability to fall asleep and to maintain sleep, is the general arousal or activation level [114]. This third factor disturbs sleep, contradictive to the first and the second sleep promoting factors (from the two-process model). It does not matter if the first and the second factor of the sleep formula are optimal for sleep, if we are too aroused we will not fall asleep anyway, or we will fall asleep, but the amount of slow wave sleep will be reduced or sleep will be fragmented by frequent arousals or awakenings. [115-117] Accordingly, cognitive and bodily hyper arousal are well recognized as mediating and maintaining factors of sleep disturbance [116, 118].

Sleep and stress

Sleep and stress are antithetical. Sleep may be described as the ultimate form of deactivation, or unwinding. Stress, on the other hand, is activation in different forms. In this thesis, different aspects of prolonged stress or activation (cognitive, behavioural and physiological) are in focus as signs of, or risk factors for, impaired recovery and burnout development.

Several studies have shown a relation between subjective stress and impaired sleep [119, 120]. Healy and colleagues (1981) found that individuals suffering from insomnia reported a higher incidence of stressful life events the year preceding the onset of insomnia than controls, and in comparison to other years (before or after the onset of their insomnia) [121]. Also minor daily stressors have been shown to correlate with more complaints of sleep disturbances among insomnia sufferers [122].

As mentioned, hyper arousal is associated with insomnia [116, 123, 124], and is an important aspect in the cognitive-behavioural model of the development and maintenance of insomnia [118, 125-127]. Several cross-sectional studies have shown elevated physiological and cognitive arousal in poor sleepers compared to good sleepers [128-131]. Daytime stress has been associated with increased bedtime arousal and with increased sleep disturbances [120]. Worry, rumination or intrusive thoughts at bedtime is assumed to be one of the important maintaining factors of insomnia [125, 132-134], and it has been associated with increased alpha and beta power (more wakefulness) in the sleep EEG [135]. Similarly, increased cognitive arousal at bedtime has been related to increased sleep latency [132, 136]. Åkerstedt and colleagues (2007) showed that stress or worries at bedtime was associated to increased SWS latency, decreased sleep efficiency and an increased time awake after sleep onset [120]. Experimentally induced stress at bedtime has also been shown to increase arousal and delay sleep onset [136, 137].

Stress at work is one important factor associated with sleep disturbance [138-140]. In a prospective study by Linton (2004), using a Swedish sample, stress in the form of a 'poor' psychosocial work environment was found to double the risk of developing a sleep problem one year later [141]. Other prospective studies, by Jansson and Linton (2006) [142], and by Jansson-Fröjmark and colleagues (2007) [143] have shown that perceived work stressors are associated with the development and maintenance of insomnia. Shift work and irregular working hours are other factors known to be associated with increased sleep disturbances [144-146]. Early morning work has been related to shortened sleep duration [147] and to reduced slow wave sleep [148]. In the latter study by Kecklund and Åkerstedt (1997), the

reduction of slow wave sleep was related to self-rated apprehension of the early awakening, measured at bedtime [148]. This points to the key role of anticipation to sleep disturbance. Further, preoccupation with thoughts of work during leisure time has been identified as a better predictor of sleep disturbances than work demands per se [90]. Accordingly, apart from the impact of work demands or job strain per se, one important factor for burnout development might be increased or persistent cognitive activation (as thoughts, worry or rumination connected to work), which subsequently disturbs sleep.

Sleep and the HPA axis

The contradictive relationship between stress and sleep is evident also regarding the interaction of the HPA axis and sleep. Sleep, and especially SWS, is initiated and enhanced concurrent with low HPA activity. The other way around, SWS in it self has an inhibitatory effect on the HPA axis at the same time as growth hormone is stimulated [149-151]. HPA activity shows a robust circadian rhythm. During the first 2-3 hours of nocturnal sleep, cortisol levels are markedly lowered. Cortisol levels thereafter rise during the second part of sleep and peak in the early morning hours [152]. The diurnal peak of cortisol is also depending of time of awakening [153]. Studies have shown that free cortisol levels peak within the first hour after awakening in the morning [154].

Vgontzas and co-authors examined HPA-axis activation in a group of chronic insomniacs and found increased 24-hour secretions of ATCH and cortisol in plasma compared to healthy controls without sleep disturbances [155]. The most evident elevations were observed in the evening and the first half of the night. Rodenbeck and colleagues also found increased evening and nocturnal cortisol levels in chronic insomnia patients compared to controls [156]. Further, higher evening cortisol has in experimental settings been related to partial sleep deprivation [157]. Regarding the mechanisms of the interaction between sleep and HPA activity, it has been found that especially CRH appears to increase sleep EEG frequency and thereby increase wakefulness and light sleep, as well decrease slow wave sleep [152, 158].

Sleep and health

Sleep constitutes an essential rest period when the organism recovers from the ‘wear and tear’ of wakefulness. Sleep is closely connected to decreased catabolic activity, and increased anabolic and immune activity. For example, pro-inflammatory cytokines (the intercellular mediators of the immune system) appear to be involved in the regulation of sleep and sleepiness in animals and humans [159-161]. Research within the field of psychoneuroimmunolgy has pointed out sleepiness and fatigue as an adaptive ill-health symptom associated with immune activity [162]. In this sense, sleep and rest can be a part of a set of behavioural strategies called ‘sickness behaviour’: when the body needs to conserve energy to fight viruses or diseases, withdrawal from activity, rest and sleep may be the most adaptive behaviours.

Sleep also modulates the metabolic regulation. Insulin resistance as well as higher evening cortisol has been related to partial sleep deprivation in experimental studies [157], and cross-sectional as well as longitudinal epidemiological data have shown associations between short sleep duration and obesity, diabetes and hypertension [163-165], indicating a role of sleep in

the metabolic regulation. In this sense, and according to the allostatic model, sleep plays an important role for the physiological processes of promoting good health [95, 166].

The other way around, disturbed sleep is suggested to be part of the mechanisms involved in the development of different aspects of pathology [95]. For example, in a study among women, higher allostatic load (indicated by higher blood pressure, heart rate, blood lipids, triglycerides, serum DHEAS and prolactin) were associated with higher levels of fatigue and frequent sleeping problems [167]. In general, sleep disturbances have been connected to many different health complaints such as pain [168] depression and anxiety [169-171]. There are also evidence that sleep disturbances are associated with an increased risk for diabetes [172, 173] and cardiovascular disease [174, 175]. Many studies have shown that obstructive sleep apnea syndrome (OSAS) constitutes an increased risk for cardiovascular disease and stroke [176]. In the case of OSAS, i.e. when breathing is frequently blocked during sleep, the body's repetitive "struggle" to reverse the blocked airflow results in increased sympathetic activation, frequent micro-arousals and short awakenings. By looking at OSAS, one can get a picture of the potential role of sleep fragmentation in the process leading to disease. Sleep fragmentation has also been shown to cause impaired performance and decreased mood. In their review, Bonnet & Arand (2003) show that sleep fragmentation, i.e. the frequency of arousals and awakenings from sleep, seems to have similar effects on mood, sleepiness and psychomotor performance as has sleep deprivation [37]. They concluded that it was the degree, rather than the type of sleep disturbance, which varied with the degree of symptoms.

Regarding sleep duration, there is an ongoing debate in the public as well as in the research community regarding how many hours of sleep humans need per night, and at which point sleep duration might constitute a risk for negative health consequences. Of course there is individual differences, night-to-night differences, as well as differences throughout the life span, regarding what is an optimal sleep duration [104]. In their large epidemiological study, Kripke and co-authors (2002) found that participants reporting 8 hours of sleep or more per night experienced significantly increased mortality risk, as did those who habitually slept 6 hours or less, while controlling for demographics, habits, health factors, and use of various medications. The best survival was found among those who slept 7 hours per night [177]. Experimental partial sleep deprivation has been associated with increased evening cortisol, lowered glucose tolerance, decreased leptin levels, increased ghrelin levels, pointing to the potential negative metabolic affects of short habitual sleep [157, 178-180]. In line with this, an increasing number of epidemiological studies have reported an association between short sleep duration and higher risk of developing obesity and type II diabetes [173, 181, 182].

Van Dongen and colleagues (2003) have shown that chronic sleep restriction (4 or 6 hours per night over 14 consecutive days) resulted in significant cumulative, dose-dependent deficits in cognitive performance, equivalent to up to 2 nights of total sleep deprivation [36]. Belenky and co-authors (2003) also showed a marked dose-response effect on performance, when comparing 9, 7, 5 and 3 hours in bed per night over seven consecutive nights [35]. Performance was proportionally poorer in all restricted conditions compared to the 9-hours condition. This points to a relation between sleep duration and cognitive performance; the more you sleep the better you perform, and it appears that even relatively moderate sleep restriction can seriously impair waking neurobehavioral functions in healthy adults.

Sleepiness and fatigue as indicators of impaired recovery

Sleepiness is an evident effect of sleep loss or impaired sleep quality. Experimental studies of total sleep loss, fragmented sleep or partially restricted sleep have all been shown to induce sleepiness [183]. Sleepiness has been defined as a tendency or a drive to fall asleep, which according to the 'sleep formula' presented above is a homeostatic factor increasing with time awake and decreasing with length and quality of sleep [109]. Thus, sleepiness could be seen as a drive towards recovery through sleep – a signal of our need for recovery – stemming from an imbalance between catabolic and anabolic processes [23]. Sleepiness also follows the circadian rhythm with low levels in the morning and during the day, and increasing, higher levels during the evening and night, with some exceptions or individual variation. For example, sleepiness and the sleep tendency show a peak, which coincides with the peak in temperature in the afternoon, the 'post-lunch dip' [184, 185]. Immediately upon awakening sleepiness is usually higher, even after good sleep. One important aspect of sleepiness is the individual's ability to, to some extent, reverse sleepiness with effort or activity [186].

Sleepiness can be physiologically measured by the Multiple Sleep Latency Test (MSLT), the Maintenance of Wakefulness Test (MWT) or polysomnography [187]. However, these procedures might not applicable in all study designs. In such cases subjective measures of sleepiness can be used, such as visual analogue scales [188] (the subject puts a mark on a line with the anchors 0 and 100, indicating the intensity of the perceived sleepiness). The Epworth Sleepiness Scale (ESS) is a commonly used rating scale, in which the subject is to rate his or her expectation of 'dozing' in different situations [189]. Likert type of scales as the Stanford Sleepiness Scale (SSS) [190] or the Karolinska Sleepiness Scale (KSS) [191] are also often used in the research literature. The KSS is closely related to physiological and behavioural sleepiness [191, 192]. In the present thesis, the KSS was used to measure sleepiness.

Sleepiness and fatigue often used interchangeably in daily language, and at times also in clinical practice and research [24]. However, sleepiness and fatigue are two different phenomena, which are important to separate from each other. Sleepiness is, as mentioned, a drive towards falling asleep. As such, sleepiness is a fairly immediate and distinct state, reversed by sleep, whereas fatigue can be a more diffuse, global, ongoing condition, which is not reversed by sleep [13, 24]. One might say that fatigue primarily signals the need of rest or of changing activity, not of sleep.

Both sleepiness and fatigue are connected to impaired performance. The impaired performance concerns vigilance and reaction time tasks as well as more complex tasks such as executive functioning, learning, creativity and planning tasks [35-37, 193, 194]. Further, both sleepiness and fatigue are related to health and well-being [26].

RECOVERY AND BURNOUT – THE SCOPE OF THE THESIS

This thesis work put the aspects of *recovery from stress* in focus in relation to burnout, as, according to the allostatic model, sleep and recovery is crucial in order to prevent negative health outcomes [63, 95]. The included studies build upon the assumption that impaired recovery, such as impaired or insufficient sleep or difficulties unwinding during daytime, mediates the relation between the exposure to stressful work conditions and the development

of health problems such as burnout [42].

Evidence of sleep disturbance in burnout subjects are present from subjective ratings in cross-sectional studies [5, 6]. However, there is a lack of knowledge regarding sleep physiology in burnout groups. Therefore, we found it of great importance to investigate *sleep*, both objectively and subjectively, in working subjects with high burnout scores. In addition, it was of obvious interest to study sleep in patients on sick leave due to a burnout related diagnosis. This had not been done before. Perhaps even more important from an aetiological point of view it would be to study if changes in physiological sleep accompany recovery from burnout.

Sleepiness is closely related to how long we have been without sleep and to the quality of prior sleep, and, as such, an important indicator of impaired recovery [109]. *Mental fatigue* is related to time on task [31], and may reflect a need for recovery due to sustained stress or activation. Neither of these variables had been studied in any detail within burnout groups before, nor had stress reactions, such as perceived *activation (*the notion of being 'wound-up'). In order to investigate the perception of burnout it was of interest to examine the diurnal patterns of all three of these variables (subjective sleepiness, mental fatigue and activation): would they show normal diurnal patterns, and if not, would the patterns change over time connected to recovery from burnout? This had not been studied before.

Further, it is commonly assumed that recovery of freshness or alertness during days off, as during the weekend, is of importance as a buffer to chronic stress. *Weekend recovery* from stress in relation to burnout had not been examined before. Thus, it would be of interest to investigate recovery sleep after the working week, the weekend sleep, compared to sleep within the working week. In line with this, it would also be of interest to investigate the diurnal patterns of sleepiness, mental fatigue and activation during a workday and during the weekend (a day off). Sleepiness, mental fatigue and activation were assumed to be lowered during the weekend, whereas the opposite – sustained (i. e. more or less equal levels workdays and weekends) sleepiness, mental fatigue and (or) activation – were suggested to be indicators of impaired recovery.

The ability to *unwind during leisure time*, for example to detach from thoughts of work, may be a crucial link between stress and sleep disturbance [90, 195], and important for burnout development from the perspective of more or less chronic activation [63]. In this sense, also physiological stress markers, as the diurnal pattern of *cortisol*, would be of interest to compare between burnout subjects and controls. Data on cortisol in burnout subjects had been inconclusive, and no study had investigated whether cortisol varied between workdays and weekends (days off) in burnout groups.

As prospective studies of clinical burnout is lacking, it is of vital importance to *identify risk factors of subsequent clinical burnout* in order to better prevent the syndrome, or to enhance treatment. In this thesis, a prospective approach sought to test whether work stress, unwinding during leisure time, and (or) sleep predicted subsequent clinical burnout. For the same reasons it would be of importance to investigate whether enhanced sleep predicted *recovery from clinical burnout*.

As pointed to above, data are lacking in this field, and, in this sense the present research was a pilot project. The research focus is of importance for several reasons. First, burnout causes severe suffering for the individual, often with negative long-term consequences for daily life functioning, work performance, and health. Secondly, the burnout condition is not well defined, neither the burnout development process. It would be of major importance to identify early risk factors, and factors connected to recovery from burnout, to more fully understand the phenomenon and to be able to prevent it. Thirdly, the high numbers of sickness absence due to burnout, or stress related exhaustion, causes a high cost for the society.

AIMS

The general aim of the present research project was to investigate subjective and physiological markers of stress and recovery in relation to burnout. Also, the purpose was to identify and discuss possible risk factors precipitating burnout, as well as factors related to recovery from burnout and return to work. Especially aspects of recovery – sleep, sleepiness, mental fatigue and unwinding from stress during leisure time – were in focus of this thesis, as it was hypothesized that impaired recovery from stress is of substantial importance for burnout development.

The specific research questions were the following:

- Does sleep quality and sleep duration, measured both objectively and subjectively, differ between working subjects with different burnout scores?

- Does weekend sleep (recovery sleep after the working week) and sleep within the working week differ between working subjects with different burnout scores?

- Do indications of impaired recovery, such as the diurnal pattern of subjective sleepiness, mental fatigue, and activation, vary between 1) working subjects with different burnout scores, and 2) workdays and weekends in working subjects with different burnout scores? Do the diurnal patterns of sleepiness, mental fatigue, and activation change over time when comparing burnout patients and healthy controls?

- Does the diurnal pattern of cortisol vary between workdays and weekends in working subjects with different burnout scores, and are the cortisol data related to objective sleep data?

- Do variables reflecting impaired unwinding from work stress, such as persistent thoughts of work during leisure time, bringing work home, and working on weekends, differ between working subjects with different burnout scores?

- Do aspects of work stress, sleep, and impaired unwinding during leisure time predict subsequent clinical burnout?

- Does sleep physiology predict recovery from clinical burnout, and return to work?

The research field is new and data to support the forming of specific hypothesises for each of the above research questions are scarce. However – building upon the assumption that, in the presence of high work stress, burnout development is aggravated when recovery processes are being disturbed – it was expected that burnout groups (compared to healthy controls) would show more signs of impaired or insufficient sleep and unwinding. It was also expected that signs of impaired or insufficient sleep or unwinding, together with work stress, would predict subsequent clinical burnout. And the other way around, sleep parameters were expected to predict recovery from clinical burnout, and return to work.

The research aims were included in the four papers (**I-IV**) as presented below.

I.
The main purpose of the first paper was to investigate objective and subjective sleep, before a workday and a day off (weekend), in working subjects with different (high and low) burnout scores. The purpose was also to examine the diurnal pattern of sleepiness during a workday and a day off (weekend) in working subjects with different (high and low) burnout scores.

II.
The aim of the second paper was to examine the diurnal pattern of cortisol, perceived activation (being "wound-up") and mental fatigue during a workday and a day off (weekend) in working subjects with different (high and low) burnout scores. The purpose was also to relate the cortisol data to objective sleep data.

III.
The aim of the third paper was to identify possible risk factors for subsequent clinical burnout. In particular, the purpose was to test whether aspects of sleep and unwinding, apart from work stress, contribute to subsequent clinical burnout.

IV.
The forth paper aimed to investigate whether recovery from clinical burnout and return to work was associated with changes in polysomnography data and subjective sleep quality over time. Also, the purpose was to investigate changes over time in the diurnal patterns of sleepiness, mental fatigue and activation in burnout patients compared to healthy controls.

METHODS

DESIGN OF THE STUDIES

An overview of the study designs is presented in table 1 below. Study **I-II** were cross-sectional field studies with both within and between group designs using the same sample of subjects. A group of working subjects scoring high on burnout was compared with a group of matched control subjects scoring low on burnout. Study **III** had a prospective cross-sectional field study design running over a 2-year period. A group of 388 employees constituted the reference group. Data from the baseline questionnaire were analysed for predictors of subsequent clinical burnout. Study **IV** had a repeated measure within and between group design. A group of patients, on long-term sick leave for clinical burnout, were compared to a group of healthy, matched, control subjects at baseline and at follow-up. The study also included a correlative approach, in order to investigate the relationship between changes in sleep physiology and recovery from burnout symptoms from baseline to follow-up.

SUBJECTS

The participants in study **I-II** were selected among 414 respondents to a computerized questionnaire, distributed to all (676) employees at a Swedish IT-company. The questionnaire included questions of work stress, sleep, recovery during leisure time and burnout, etc. The subjects were selected to participation on the basis of their burnout levels, i. e. mean scores on the SMBQ. A modified version of the SMBQ was used as burnout measure, scale range 1-4=almost always (compared to the original scale range 1-7). Inclusion criteria for the high-burnout group was set to $\geq$2,75 (equaling 4,5 on the original scale) based on clinical data from the stress clinic with which we were collaborating in this research project. Mean scores of $\leq$1,5 on the SMBQ was set as inclusion criteria for the low-burnout group (control group). Twelve subjects met the inclusion criteria for the high-burnout group, and all agreed to participate in the study. Thereafter the selection of matched control subjects was conducted among subjects meeting the inclusion criteria for the low-burnout group. The matching criteria were gender, age and experience (time employed) in the company. If more than one individual within the low-burnout group met the matching criteria, the selection between them was made randomly. Two of the selected matched control subjects declined participation in the study, and were replaced by two other subjects, selected as described above.

The subjects in study **III** were selected among the same 414 respondents as described above. 26 subjects were excluded due to missing data in the baseline questionnaire. 388 individuals were included in the pool of subjects, which constituted the reference group. The study had a prospective cross-sectional design and burnout cases were included into the study successively during a 2-year period. Employees were asked to contact the company's health service if experiencing clinically impairing symptoms of exhaustion for assessment and further treatment.

Table 1. Overview of study designs.

Study	Design	Subjects	Measures	Statistical analyses
I	Cross-sectional. Within and between subject design.	24 white-collar workers from the same company were recruited. Two groups were compared: 12 subjects scoring high on burnout, and 12 control subjects scoring low on burnout, matched on gender, age and experience at the company.	* Polysomnography at two times; before a workday and before a day off (weekend), in a balanced order. * Daily ratings of sleepiness, mental fatigue and activation during the workday and the day off after the sleep recordings. * Questionnaire regarding work, stress, sleep, daytime recovery and health	* Two-factor repeated-measures analysis of variance * t-est
II	Cross-sectional. Within and between subject design	24 white-collar workers from the same company were recruited (the same subjects as in study I). 4 subjects were excluded as there were missing data regarding the saliva samples. Two groups were compared: 9 subjects scoring high on burnout, and 11 control subjects scoring low on burnout, matched on gender, age and experience in the company.	* Saliva samples were collected at 10 times throughout a workday and a day off (weekend) * Daily ratings of sleepiness, mental fatigue and activation during a workday and a day off (the same days as which the saliva samples were collected on). * Polysomnography at two times; before the workday and the day off during which the saliva samples were collected.	* Two-factor repeated-measures analysis of variance * Univariate regression analysis.
III	Prospective cross-sectional field study design	Subjects were included successively throughout a period of 48 months. Out of 388 employees who had completed the baseline questionnaire, 32 were assessed by a certified clinical psychologist due to stress related symptoms. Of these, 15 were classified as 'burnout cases' and included in the study.	* Questionnaire (at baseline) regarding work, stress, sleep, daytime recovery and health	* Univariate logistic regression analysis * Multiple hierarchical logistic regression analysis
IV	Repeated measure, within and between subject design. Correlative design.	23 white-collar workers on long-term (> 3 months) sick leave and 16 healthy control subjects, matched on gender, age and occupation, were compared at baseline and follow-up 6-12 months later.	* Polysomnography at two times; at baseline and at follow-up 6-12 months later. * Daily ratings of sleepiness, mental fatigue and activation, at baseline and at follow-up. * Questionnaire regarding burnout, fatigue, anxiety, depression and sleep.	* Two-factor repeated-measures analysis of variance * Three-factor repeated-measures analysis of variance * Correlation analysis * Stepwise regression analysis * Logistic regression analysis

Of 32 individuals who were assessed by a clinical psychologist, 15 were found matching the inclusion criteria of the study. These were as follows: (1) Symptoms of exhaustion (physical, emotional and/or cognitive) during $\geq$2 weeks, (2) The exhaustion symptoms have developed in relation to one or more identifiable stressors, which have been present during $\geq$ 6 months, (3) The symptoms cause a clinically significant suffering or a reduced function at work, socially or in other important aspects, (4) The individual was referred to treatment for clinical

burnout at a stress clinic, (5) The included subjects did not suffer from any ongoing depressive or anxiety disorder as defined by DSM-IV-TR [196]. For inclusion into the study it also was necessary that the subject had responded to the initial baseline questionnaire. When the assessment records were re-evaluated, after the study period, by the psychologist who did the assessments and by a senior clinician with expertise on burnout, all participants were found to fulfill the (at that time established) diagnostic criteria for exhaustion syndrome [17].

The subjects in study **IV** were recruited from the registers of an insurance company. Fifty-eight volunteers were examined. Among these, 23 subjects were included in the study as they fulfilled the inclusion criteria: (1) Clinical symptoms of burnout, i. e. exhaustion and impaired cognitive functioning connected to long-term exposure to work-related stress; (2) No ongoing psychiatric, Axis I or Axis II, disorder based on a Structured Clinical Interview (SCID) for DSM-IV, 4th edition [196-198], and (3) Full-time sick leave, due to the exhaustion symptoms, since at least 3 months. When the assessment records of the included participants were re-evaluated, according to the diagnostic criteria for exhaustion syndrome, all participants were found to fulfill the criteria for that diagnosis. Healthy controls were contacted through internal advertisement at the insurance company. Out of 45 volunteers, 16 full-time white-collar workers, matched on gender, age and occupation, were recruited. The SCID revealed no Axis I or Axis II disorders among the control subjects. None of the controls used hypnotics or antidepressants. There was no significant difference in other types of medical treatment between patients and controls.

ETHICAL ISSUES

Before agreeing to participate in any of the studies, all subjects received written information about the study procedures and the ethical issues regarding participation. All subjects were informed that participation was voluntary and confidential, and that they could terminate participation whenever they wanted without further explanation. Subjects in study **I-II** and **IV** also met with one of the two research assistants responsible for the data collection before entering the study, and got further information about the study protocol. All subjects gave written informed consent to participate. All studies included in this thesis were approved by the ethical committee of Karolinska Institutet.

GENERAL PROCEDURES

The participants in study **I-III** all responded to the initial, baseline, computerized questionnaire regarding work, stress, sleep, recovery and health, etc. The subjects included in study **I** were subjected to a 14-days study protocol including sleep diary ratings upon awakening, daytime ratings of sleepiness (KSS) every second hour from awakenings to bedtime, daily questions about work performance, health and stress symptoms. Two ambulatory polysomnograpic (PSG) recordings were carried out in the subjects' homes, one night before a workday and one night before a day off (weekend) in a balanced design. Repeated saliva samples were collected during the day after the PSG recordings following a schedule as described below. The subjects also underwent blood sampling and 24-hour blood

pressure measurements the day after the PSG recording (workday condition), but these factors were not in focus in the papers included in this thesis.

Study **III** had a prospective cross-sectional design, using data from the initial questionnaire as independent variables in a series of logistic regression analyses in order to investigate possible predictors of subsequent clinical burnout. Clinical burnout was assessed by a certified clinical psychologist according to the following routine: During a period of 2 years from the baseline questionnaire measure, employees who were experiencing pronounced fatigue or stress symptoms, together with impaired work ability, were asked to contact the company's health service department for assessment and further help. During the study period 32 individuals (of the 388 in the reference group) were assessed by a certified clinical psychologist, of which 15 were found matching the inclusion criteria, classified as 'burnout cases' and referred for treatment at a stress clinic. The subjects were included successively in the study, evenly distributed over the two-year period.

In study **IV**, the burnout patients underwent a multi-modal rehabilitation programme at a Stress Clinic in Stockholm. The programme included 15 group therapy sessions based on cognitive behavioural therapeutic (CBT) methods, focusing on handling and reducing stress symptoms. The CBT interventions included psychoeducation regarding stress reactions, and homework assignments regarding relaxation training, planned activity and rest, graded exposure, assertiveness training, etc. Sleep disorder treatment was not an explicit focus of the CBT protocol. The rehabilitation programme also included 15 group sessions of physiotherapy based on Body Awareness Therapy (Roxendal, 1985). Eight of the burnout subjects also underwent 10 sessions of individual psychotherapy. All participants, including the 16 healthy controls, were subjected to PSG recordings in their homes (after one night of habituation) at two times, at baseline (before treatment) and at follow-up (after treatment). Notably though, the purpose of this particular study was not to evaluate the treatment programme. Bedtime and time of rising were in accordance with the participants habitual sleep pattern. Seasonal variation was controlled as the PSG assessments were conducted in spring or in the autumn with as similar light conditions as possible. Subjective sleep quality, work, fatigue, and mood variables were assessed in questionnaires in connection to the PSG measures. Three months after the rehabilitation programme was completed the occupational status was followed-up in a short questionnaire.

PHYSIOLOGICAL MEASURES

Polysomnography

Study **I, II** and **IV** include polysomnographically recorded sleep data. The sleep recordings were conducted using portable EMBLA recorders (Flaga HF®). Ag/AgCl electrodes were used with two EEG derivations C3 –A2 and C4 – A1, one chin EMG derivation and two oblique EOG derivations. The frequency response for the EMBLA is between 0.5 and 100 Hz. The filter settings were 0.5 Hz for high pass filters and 75 Hz for low pass filters. To reduce the impact of low-frequency artefacts in study **I** (relevant for four subjects in each group), a 0.8-Hz high pass filter was applied for one channel during scoring to ensure that the amount of slow wave sleep was not affected. Sleep scorings were compared between the two settings to ensure that the filter settings not had affected the results. No differences were

found for any sleep stage between the two settings. The electrodes for the polysomnographic measurement were attached by a trained research assistant in the subject's homes between 7 and 9 PM in study **I-II**, and in the sleep laboratory between 4 and 6 PM in study **IV**. In the latter study, the subjects where taken home by taxi after the PSG electrodes had been attached in the laboratory.

Sleep stages were scored, blindly, visually in 30-second epochs according to Rechtschaffen and Kales [105]. Arousals were scored using the American Sleep Disorders Association criteria [199]. An arousal was defined as an EEG shift to at least alpha activity from stages 2-4 or REM sleep, preceded by at least 10 seconds of uninterrupted sleep. During REM sleep an increase in EMG activity was also required. For an arousal to be scored it had to last for more than 3 seconds and for less than 15 sec. Sleep onset latency was scored as time from 'eyes closed' to the first occurrence of at least three consecutive sleep epochs.

Cortisol

Cortisol was measured in saliva. Salivary cortisol has shown high correlations with measures from plasma [74]. In study **II**, the participants were instructed to sample saliva at the time of awakening, and at 15, 30, and 60 minutes thereafter in order to identify the postawakening peak [154]. The morning saliva samples were collected before breakfast, between 0530h and 0730h. The participants continued to sample saliva at 1100h, 1500h, 1900h, 2100h, 2300h and/or at bedtime in order to evaluate the diurnal cortisol pattern. The participants were instructed not to eat or to brush their teeth within at least 30 minutes before a saliva sample to avoid contamination of the saliva by food or blood. Salivary cortisol (sampled using Salivette®, Sarstedt; Rommelsdorf, Germany) was determined by radioimmunoassay techniques (Orion Diagnostica, Espoo, Finland). The lower limit of detection was 1 nmol/l in the saliva and the average inter- and intra-assay coefficient of variation never exceeded 10%.

DIARY RATINGS

Sleep

Subjective sleep was measured in study **I** and **IV** using the Karolinska Sleep Diary, KSD [200, 201]. The subjects were instructed to complete the KSD every morning upon awakening. KSD contains questions about bed time, rise time, sleep latency, sleep quality, ease of falling asleep, calm sleep, sleep throughout the allotted time, number of awakenings, ease of awakening, sufficient sleep and the sense of being well rested. A 'Sleep Quality Index' (SQI) was calculated using the following items: 'sleep quality', 'ease of falling asleep', 'calm sleep' and 'sleep throughout the allotted time'. SQI has been shown to correlate with objective parameters, such as sleep efficiency and slow wave sleep [202]. An 'Impaired Awakening Index' was also used, including the items 'feeling refreshed after sleep' and 'ease of awakening'. The response alternatives for both indices ranged from 1 (severe problems/very poor) to 5 (no problems at all/very good).

Diurnal sleepiness, mental fatigue and activation

Daily ratings of sleepiness, mental fatigue and activation (being 'wound-up') were carried out every second hours over a 2-week period in study **I** and **II**, and over a one-week period in study **IV**. In study **I**, the participants rated acute sleepiness every hour during the day after the polysomnographic recordnings, on the Karolinska Sleepiness Scale, KSS (ranging from 1=very alert to 9=extremely sleepy, fighting sleep, an effort to remain awake). KSS has been validated against electrophysiological indices of sleepiness [191]. For purpose of data reduction in study **I**, mean values of sleepiness were computed for the measures at 0900-1000h, 1100-1200h, 1300-1400h, 1500-1600h, 1700-1800h, 1900-2000h. In study **II**, mental fatigue was rated on a 9-point scale ranging from 1=very fresh to 9= totally exhausted. Perceived activation was rated on a 9-point scale ranging from 1=very relaxed to 9=very 'wound-up'. In study **IV,** daily ratings of sleepiness, mental fatigue and activation on the same scales were carried out at awakening (around 0700h), at 1000h, 1400h, 2000h and at bedtime.

Work stress and recovery

Another part of the wake diary, used in study **I**, included items to be answered at the end of the day, concerning 'work load', 'work pace', 'sufficient rest during the day', and 'thoughts about work during leisure time'.

QUESTIONNAIRES AND INDICIES

Burnout and fatigue

Burnout was in all studies measured with the Shirom–Melamed Burnout Questionnaire, SMBQ [8, 10]. The SMBQ consists of a list of 22 symptom sentences that measure different aspects of exhaustion. A modified version of the SMBQ, with a four-point scale ranging from 1=almost never to 4=almost always, was used in the computerized questionnaire (**I-III)**. In study **IV**, the original seven-point scale was used, graded from 1=almost never to 7=almost always. A total index, the mean score over all 22 items, was calculated for each participant with a reliability coefficient (Cronbach's alpha) of 0.90. This index correlates highly with the emotional exhaustion subscale of the Maslach Burnout Inventory, MBI [19] and with Pines Burnout measure [203] in a study of burnout women [6]. Also in study **IV**, a fatigue index was used to measure the multidimensional characteristics of fatigue in burnout, comprising the cognitive and physical dimensions and a global perception of persistent fatigue (Ekstedt and Fagerberg, 2005). The fatigue index contained three items as follows: "During the last 3 months to what extent have you experienced 1) persistent fatigue, 2) physical exhaustion, and 3) mental fatigue?" The response alternatives varied from 6='always/almost every day', 5=4–5 times per week, 4=1–3 times per week, 3=sometimes per month, 2=seldom/a few times per year to 1='never/not at all' (Cronbach's alpha = 0.86).

Work stress

Aspects of work stress were assessed in the baseline questionnaire, addressing psychosocial work factors inspired by the demand-control-support model [204, 205] and the effort-reward imbalance model [53]. The items varied partly between, on the one hand, study **I-III**, and,

one the other hand study **IV,** in order to suit different conditions. The questionnaire was generally shorter in study **IV** since the participants suffered from difficulties to concentrate on paperwork. Psychosocial work factors in study **I** and **III** derives from a factor analysis of the whole sample (n=414) (unpublished), and included four indices: 'Work demands' (10 items, Cronbach's α =0.85), 'Decision latitude' (i.e., 3 items, Cronbach's α =0.88), 'Social support from managers' (4 items, Cronbach's α =0.86), and 'Social support from colleagues' (5 items, Cronbach's α =0.83).

Sustained activation – or impaired unwinding during leisure time

In study **I** and **III** we used three (of six) items from the over-commitment scale presented by Siegrist et al (2004), in order to measure the degree of sustained cognitive activation in the form of preoccupation with thoughts of work, or the ability to psychologically switch off from work, during leisure time. The index were called 'Thoughts of work during leisure time' and included the following items: "As soon as I get up in the morning I start thinking about work problems", "Work rarely lets me go, it is still on my mind when I go to bed", and "When I get home, I can easily relax and 'switch off' work" (Chronbach's alpha: .93). Response alternatives were 1–4 (I do not agree–I fully agree, revised for the latter item). Additionally, in study **I** and **III**, the items 'working on weekends', and 'bringing work home' were used. In study **I**, the item 'work interferes with leisure time' was also used. The response alternatives were; 1=totally disagree to 4=totally agree, except for 'bringing work home', for which the response alternatives ranged from 1= never to 5=always/almost every day. "Working hours per week" was also used in study **I**, for which the subjects were to fill in the average number of working hours per week.

Sleep

Habitual sleep quality was assessed with the Karolinska Sleep Questionnaire (KSQ) [206]. From this was derived the Sleep quality index (SQI), which includes 'sleep quality', 'calmness of sleep', 'ease of falling asleep' and 'sleep throughout the allotted time'. An Impaired awakening index included the items 'not well rested after sleep' and 'difficulties rising'. A Sleepiness index included 'sleepy during work', 'sleepy during leisure time', 'involuntary naps at work', 'involuntary naps during free time' and 'fighting sleep'. Insufficient sleep ($\leq$ 6 hours/night), and 'snoring' were additional items. In study **I** and **III** the response alternatives for all the above items ranged from 1=never to 5=always. In study **IV,** the response alternatives were: 1=never; 2=seldom/a few times per year; 3=sometimes/several times per month; 4=mostly/several days per week; 5=very often/$\geq$ 4 days per week; 6= always/almost every day.

Depression and anxiety

The Hospital Anxiety and Depression scale (HADS) was used in study **I** and **III** [207]. HADS has been tested and evaluated in different groups as a useful instrument because of its brevity, simplicity and lack of effect of somatic conditions [207, 208]. Seven items measure anxiety (HAD-A), and seven items measure depression (HAD-D). Response alternatives are scored from 0 to 3, with higher values indicating more severe symptoms. A sum of 11 or more on each scale indicates symptoms on a clinical level. HADS shows strong correlations with the Beck Depression Inventory (BDI) and Spielberger's State Trait Anxiety Inventory

(STAI) in a Swedish sample [209]. In study **IV**, BDI [210], and the Beck Anxiety Inventory (BAI) [211] were used to assess depression and anxiety. Higher total scores indicate more severe depressive and anxiety symptoms.

Return to work

In study **IV** 'return to work' were assessed with questions about to which extent the individual had returned to work, or to what degree he or she still was on sick leave or had received early retirement pension.

CLINICAL ASSESSMENTS

In study **III**, employees at the specific workplace who were experiencing clinically impairing symptoms of exhaustion were assessed by a certified clinical psychologist. Subjects with clinical burnout symptoms were referred to a stress clinic for further treatment, and if the subjects fulfilled the inclusion criteria of the study subjects were included successively. The inclusion criteria were based on a preliminary approach regarding diagnostic criteria for 'exhaustion syndrome' developed by the Swedish National Board of Health and Wellfare (described in the 'Subjects' section above). The clinical records were re-evaluated (blind) after the study period, by the psychologist who did the initial assessments and a senior clinican with expertise on burnout. All subjects were, in the re-evaluation procedure, found to fulfill the later established diagnostic criteria for exhaustion syndrome. In study **IV**, the participants were assessed regarding psychiatric aspects by an experienced clinician (psychiatrist), using the Structured Clinical Interview (SCID) for DSM-IV-TR, 4th edition [196-198].

RESULTS

PAPER I – SLEEP AND SLEEPINESS IN YOUNG INDIVIDUALS WITH HIGH BURNOUT SCORES

This study aimed to investigate physiological and subjective sleep in working subjects scoring high on burnout, compared to a matched control group scoring low on burnout. The purpose was also to identify the diurnal pattern of sleepiness during a workday and a day off (weekend), as well as other indicators of impaired recovery from work stress in groups with different burnout scores.

Twenty-four working individuals (14 women and 10 men) between the ages of 24 and 43 years participated. The subjects were selected out of a 414 respondents to a questionnaire on the basis of burnout scores into two groups (high or low on burnout), 12 subjects in each group. Sleep was recorded in the subjects' homes during two nights; one night before a workday and one night before a day off, in a balanced order. Subjective sleep quality was measured by a sleep diary. The diurnal pattern of sleepiness was analyzed for the workday and the day off after the sleep recordings.

The results of the polysomnographical recordings showed a higher frequency of arousals for the high-burnout group (see table 2), significant for both conditions. Total sleep time was longer during the weekend for both groups, as was stage 2 and REM sleep.

Table 2. EEG-parameters (mean±se) for sleep before a workday and before a day off in groups with high vs. low burnout (BO) scores. Results from repeated measures ANOVAs.

	High BO		Low BO		p		
Sleep variables	Workday	Day off	Workday	Day off	BO	D	BO*D
Bedtime (h:min)	22:54±:14	23:42±:18	23:28±:11	23:50±:18	n.s.	.0193	n.s.
Time of rising (h)	06:42 ±:14	08:13±:16	06:36 ±:07	08:11±:20	n.s.	<.0001	n.s.
TST (min)	401±14	455±21	377±8	449±21	n.s.	.0002	n.s.
Sleep efficiency (%)	87±2	89±1	90±1	92±1	.0581	n.s.	n.s.
Sleep onset latency (min)	19±7	13±4	16±2	13±3	n.s.	n.s.	n.s.
SWS latency (min)	29±5	40±10	27±5	34±8	n.s.	n.s.	n.s.
REM latency (min)	87±12	85±9	75±7	76±8	n.s.	n.s.	n.s.
Waso (min)	43±10	35±5	36±9	34±6	n.s.	n.s.	n.s.
Stage 1 (min)	16±4	20±4	17±3	14±3	n.s.	n.s.	n.s.
Stage 2 (min)	236±13	266±12	234±11	272±16	.n.s.	.0019	n.s.
Stage 3+4 (min)	36±8	31±6	33±10	32±8	n.s.	n.s.	n.s.
REM (min)	113±7	138±11	93±8	132±9	n.s.	.0004	n.s.
Tot # awakenings	7±1	8±1	6±1	7±1	n.s.	n.s.	n.s.
Tot # arousals	80±9	84±7	51±6	59±8	.0143	n.s.	n.s.
# arousals/h	12±1	12±2	8±1	8±1	.0299	n.s.	n.s.

BO=Burnout, D=Workday/Day off, n.s.=non significant effect, TST=Total sleep time, SWS=Slow wave sleep, REM=Rapid eye movement, Waso= Wake time after sleep onset. Degrees of freedom: 1/22/1.

The diurnal pattern of sleepiness indicated that the high-burnout group did not recover in the same way, as did the low-burnout group during the weekend (see figure 1). There were no significant differences between the groups regarding sleepiness during the workday. However, during the weekend the high-burnout group remained on the same sleepiness levels as during the workday, whereas the sleepiness levels decreased during the weekend for the low-burnout group. Another indicator of impaired weekend recovery was the result from the sleep diary ratings, which showed a significant interaction effect indicating that the high-burnout group experienced the same level of awakening problems during the weekend as they did during the working week, whereas the low-burnout group felt more refreshed upon awakening during the weekend.

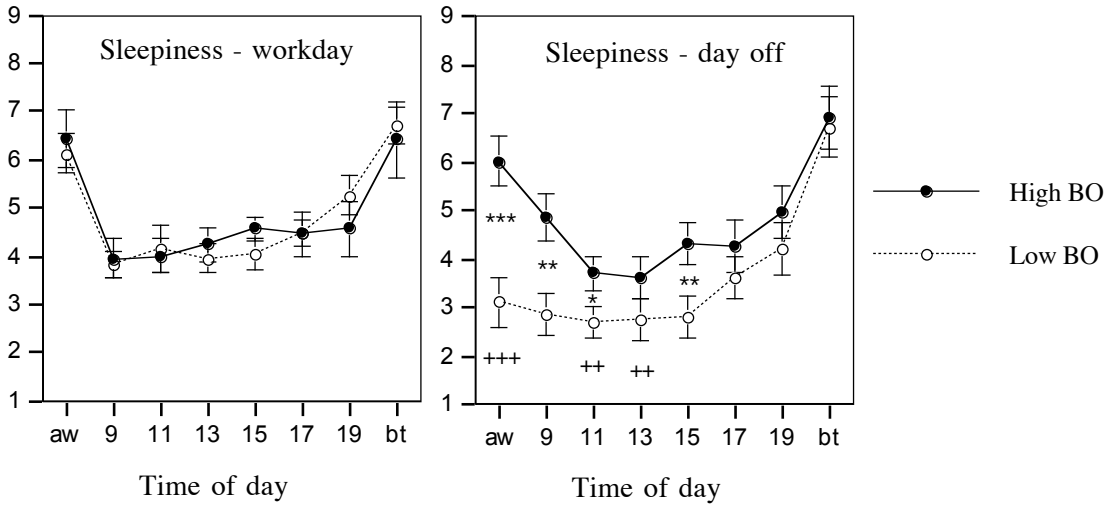

Figure 1. Diurnal pattern of sleepiness (KSS) on a workday and on a day off in groups with high vs. low burnout scores (aw=awakening; bt=bedtime). Differences between the groups on the day off were tested with t-tests; ***=p<.001; **=p<.01; *=p<.05. Paired t-tests *within* groups compared sleepiness levels for each point in time on the different days; +++=p<.001; ++=p<.01; +=p<.05.

From the questionnaire data, it was demonstrated that the high-burnout group experienced significantly higher work demands than the low-burnout group, whereas decision latitude or support at work did not differ between the groups. Indicators of impaired recovery, or sustained activation, were also seen within the high-burnout group as they reported a higher degree of thoughts of work during leisure time, bringing work home and working on weekends, as well as more complaints of work interfering with leisure time.

PAPER II – WEEKDAY AND WEEKEND PATTERNS OF DIURNAL CORTISOL, ACTIVATION AND FATIGUE AMONG PEOPLE SCORING HIGH FOR BURNOUT

This study attempted to investigate weekday and weekend patterns of diurnal cortisol, mental fatigue and activation (the notion of being 'wound-up') among workers with different burnout scores. The purpose was also to relate the cortisol data to objective sleep data.

Nine working subjects scoring high on burnout, and 11 working subjects scoring low on burnout (all from the same workplace), matched on gender, age and experience in the

company, were compared. Diurnal cortisol was sampled in saliva throughout a workday and a day off in order to measure free cortisol concentrations. Ratings of mental fatigue and of being 'wound-up' were carried out every second hours from awakening to bedtime during the same day. Ambulatory sleep recordings were carried out in the subjects' homes the night prior to the saliva sampling.

The high-burnout group showed higher awakening cortisol during the workday than during the weekend. There were no significant differences between the groups regarding the diurnal amplitude of cortisol (calculated as the difference between the peak value and the bedtime value) during either day. Nor were there any differences regarding the absolute peak level between the groups during either day. When objective sleep data were used in univariate regression analyses against cortisol data, it was shown that higher frequency of micro-arousals during the prior sleep was associated with an earlier diurnal peak of cortisol and higher diurnal amplitude of cortisol during the workday.

The diurnal pattern of mental fatigue and of being 'wound-up' (activation) indicated that the high-burnout group did not recover in the same way, as did the low-burnout group, during the day off (see figure 2). There were no significant differences between the groups regarding activation or fatigue during the workday. However, during the weekend the high-burnout group reported the same levels of mental fatigue and of 'being wound-up' as during the workday, whereas the low-burnout group felt more relaxed and fresh during the weekend. Hence, the high-burnout group showed a pattern of sustained activation also during the day off.

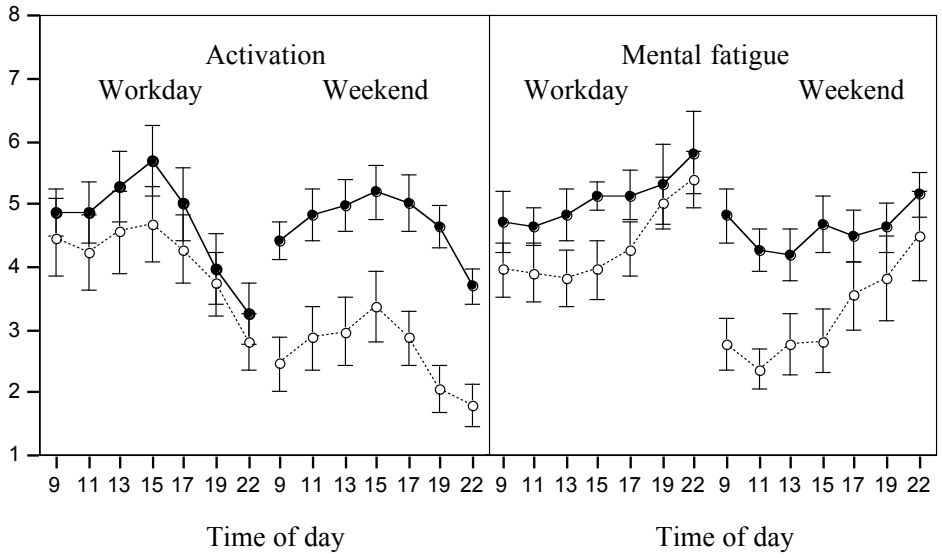

Figure 2. Diurnal ratings of activation and of mental fatigue during a workday and a day off in groups with high (filled circles) or low (open circles) burnout scores.

PAPER III – INSUFFICIENT SLEEP PREDICTS CLINICAL BURNOUT

This study had a longitudinal design with the aim to identify risk factors for subsequent clinical burnout. The study was conducted at a specific work organization during a two-year period. During this time, fifteen subjects (8 men and 7 women), out of 388 in the reference sample, were identified as 'burnout cases', as they were clinically assessed, found matching the inclusion criteria of the study and referred to treatment for clinical burnout. In this way, subjects were successively included to the study. Baseline questionnaire data on work stress, sleep, and aspects of sustained activation, were used as independent variables in a set of univariate logistic regression analyses, as well as in a multiple logistic regression approach in order to predict subsequent clinical burnout.

The results from the univariate logistic regression analyses showed that work demands, thoughts of work during leisure time, sleep quality, insufficient sleep and burnout scores, respectively, predicted subsequent clinical burnout. Work demands, thoughts of work during leisure time and insufficient sleep were then tested in a multiple hierarchical logistic regression analysis, and the results yielded 'too little sleep (<6 h)' as the main risk factor for subsequent clinical burnout, with adjustment for 'work demands' and 'thoughts of work during leisure time' (see table 3). The latter two independent variables were significant predictors in earlier steps of the multivariate approach. The model explained 15,9% of the variance. When entered in a forth step, as a control variable, burnout scores did not became a significant predictor, and the results of the complete model did not change. Adding, respectively, the control variables gender, age, anxiety or depression scores, did not change the results.

Table 3. Multiple hierarchical logistic regression with burnout case as dependent variable and the independent variables entered stepwise.

Variables in the equation		B	Wald	p	Exp(B)	CI Lower	CI Upper	sig. Step	sig. Block	sig. Model	Nagel-kerke R2
Step 1	Work demands	1.28	5.56	.018	3.59	1.24	10.39	.015	.015	.015	.057
	Constant	-6.47	19.37	.000	0.00	,=	,=		,=	,=	,=
Step 2	Work demands	0.79	1.85	.174	2.21	0.70	6.97	.038	.038	.006	.097
	Thoughts of work	0.89	3.95	.047	2.44	1.01	5.89		,=	,=	,=
	Constant	-7.65	21.66	.000	0.00	,=	,=		,=	,=	,=
Step 3	Work demands	0.58	1.04	.307	1.79	0.59	5.45	.037	.037	.002	.159
	Thoughts of work	0.88	3.16	.075	2.40	0.91	6.31		,=	,=	,=
	Too little sleep	1.05	6.39	.011	2.86	1.27	6.47		,=	,=	,=
	Sleep quality	-0.08	0.04	.847	0.92	0.40	2.14				
	Constant	-9.72	24.26	.000	.000	,=	,=		,=	,=	,=

ExpB=Exponent beta; CI=Confidence Interval

PAPER IV – SLEEP PHYSIOLOGY IN RECOVERY FROM BURNOUT

The main purpose of this study was to investigate whether sleep physiology was related to recovery from clinical burnout over time. As the diagnosis of burnout mainly is based on the presence of high levels of fatigue, the fatigue experience was used as a criterion of the degree of recovery from burnout. Depression and anxiety may be overlapping symptoms with burnout and therefore it was necessary to adjust for their role in any relation between fatigue and sleep physiology. Also, the study aimed to investigate the relation between recovery from burnout and return to work. A third purpose was to investigate changes over time in daily ratings of sleepiness, fatigue and the feeling of being 'wound-up'.

Twenty-three white-collar workers on long-term sick leave (>90 days) due to clinical burnout and 16 healthy controls were subjected to polysomnographic recordings at baseline and at follow-up after 6–12 months, a period during which the burnout group were undergoing rehabilitation.

The results showed that sleep physiology improved after treatment within the burnout group, with respect to number of arousals, sleep fragmentation, sleep efficiency, wake time after sleep onset (WASO), and sleep onset latency, whereas sleep in the reference group remained essentially the same. No significant improvement over time was, however, seen in the burnout group regarding the relative amount slow wave sleep.

Moreover, significant correlations were found between recovery from fatigue over time and sleep physiology with respect to decreased number of arousals, increased sleep efficiency, and decreased WASO. Decreased fatigue was also correlated with decreased anxiety over time, and with use of antidepressants (SSRI) at baseline. Notably, neither anxiety nor depression at baseline, change in depression or change of use of SSRI, nor gender or age correlated with recovery from fatigue over time. When the significant factors from the above correlation analyses were tested in a stepwise regression analysis against change in the fatigue index, only change in the number of arousals became a significant predictor in the first step. After adding possible confounders in the second step, the results showed that recovery from fatigue was predicted by two factors: 1) decreased number of arousals during sleep and 2) decreased anxiety over time. The model explained 34% of the change in the fatigue index. Finally, recovery from fatigue over time was the only significant predictor of return to work.

Regarding the diurnal patterns of sleepiness, mental fatigue and of being 'wound-up', the patients showed significantly higher levels at baseline, compared to the healthy controls. A significant improvement was, however, shown over time for the burnout group regarding all these variables, although the follow-up levels did not reach the levels of the controls (see figure 3).

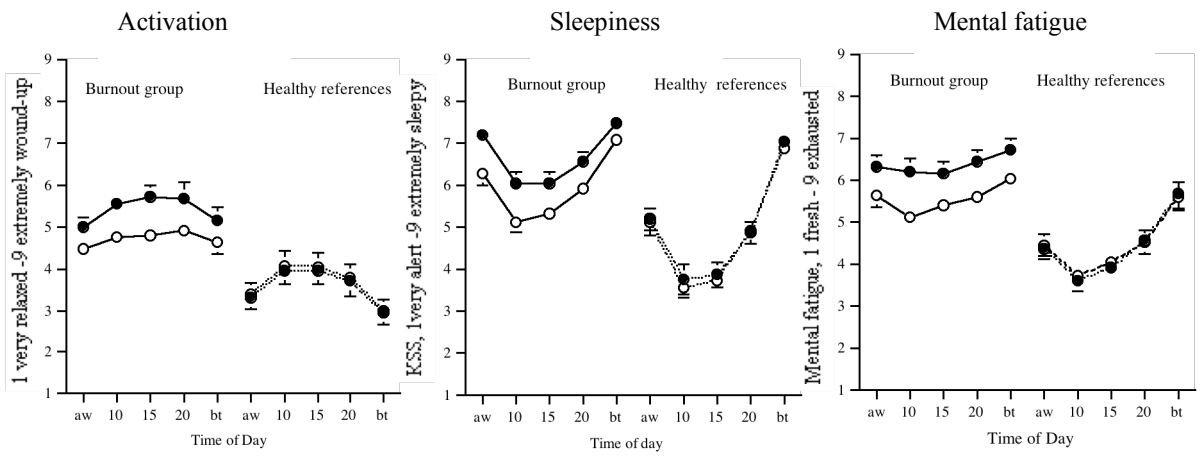

Figure 3. Diurnal ratings of activation, sleepiness and mental fatigue at baseline (filled circles) and follow-up (open circles) in burnout patients and healthy controls.

The patient group also showed significant improvement after treatment regarding the ratings of fatigue, burnout, depression and anxiety, although the follow-up levels did not reach the levels of the control group. Taken together, the results indicate a clear improvement in the key characteristics of burnout across a one-year (maximum) period, also supported by the return to work for the majority of participants.

DISCUSSION

The scope of this thesis was burnout in relation to sleep and other aspects of impaired recovery from stress. There are methodological problems with this attempt. All the mentioned areas are complex enough to be a topic for extensive research, and all include intricate interactions between physiology and psychology, medicine and behaviour. Although, as data are lacking within this field, the present thesis is important as one of the first focusing on recovery aspects more than on stress factors in relation to burnout, and dealing with both objective and subjective measures.

In short, this thesis has put forward data that are in line with the assumptions that 1) sleep and aspects of recovery during leisure time are impaired or insufficient in burnout subjects compared to controls; 2) insufficient sleep, difficulties detaching from thoughts of work during leisure time, and high work demands, predict clinical burnout; and 3) recovery from clinical burnout is associated with improved sleep and alertness. The results from the included studies are discussed below.

SLEEP

The main hypothesis behind this thesis was that impaired recovery from stress – not stress per se – is of substantial importance for burnout development. Sleep is our most important source of recovery. Besides that sleep disturbance is a common symptom of burnout [5-7], disturbed sleep may also be an important risk factor contributing to burnout development, and in this sense sleep is in focus of this thesis. Below, the results taken together regarding impaired sleep quality or insufficient sleep as possible risk factors for burnout, and the other way around, enhanced sleep as a factor predicting recovery from burnout, are discussed.

One strength with this thesis work is that it examined objective as well as subjective aspects of sleep in working subjects with different burnout scores as well as in subjects on sick leave due to burnout symptoms. This is of evident value especially as objective sleep data in burnout subjects are lacking. The polysomnographical measurements in study **I** investigated sleep during one night within the working week (mid-week condition) and one night before a day off (weekend condition). The latter was chosen as it could be regarded as a form of recovery sleep after the working week and with presumably no or low anticipatory stress involved. The mid-week sleep condition was also considered a measure of recovery from the past working day (or days), but with presumably more anticipatory stress as it was before another working day. It has been demonstrated in previous research that anticipatory stress, as persistent thoughts of work at bedtime [195] or the knowing of a very early morning shift coming up the next day [115], is related to disturbed sleep. In study **IV,** the polysomnographical measures on the burnout patients and the healthy controls were carried out twice, at baseline (before treatment) and at follow-up 6-12 months later (after treatment). The main aim with that particular study was to relate changes in burnout severity with changes in sleep over time.

Sleep quality

The results of the polysomnographical measurements of working subjects showed a higher frequency of arousals within the high-burnout group **(I)**. This was significant for both recordings, which indicate a relatively robust result. However, the mean frequency of arousals per hour in the high-burnout group was only moderately increased, or more or less equal to what has been found in other studies of healthy adults [212, 213]. A higher frequency of arousals during sleep may be related to sleep apnea. Although sleep apnea was not investigated in this study, it seems not to be a plausible explanation for the results in our study, as there was no significant difference between the groups regarding self-reported snoring or body mass index (BMI), which are factors highly correlated to sleep apnea [214]. Increased frequency of arousals was shown also for the burnout patients in study **IV**, and in this study the results were controlled for disturbance due to sleep apnea as saturation was monitored during the sleep recording for all subjects.

Micro-arousals can be seen as a form of sleep fragmentation. A more evident measure of sleep fragmentation is sleep efficiency, which refers to total sleep time relative to time in bed. Sleep efficiency below .85-.90 (when the total sleep time is less than 85-90% – depending on age – of the time in bed) is regarded as an indication of clinically disturbed sleep [213, 215]. The results from the PSG measurements of the working subjects showed no significant effect, but there was a trend towards lower sleep efficiency for the high-burnout group, for both conditions **(I)**. Power analysis showed that the result regarding sleep efficiency would have been significant with an increase by only three subjects per group. Notably, data for the high-burnout group during the working week showed an average sleep efficiency at .87, which is touching clinical levels, when taken into account that the subjects in study **I** were quite young.

Frequent arousals from sleep have been related to excessive daytime sleepiness [212]. Further, sleep fragmentation in general seems to have similar effects on mood, sleepiness and psychomotor performance as has sleep deprivation [216]. Although sleep continuity seems to be important for daytime functioning, the specific role of sleep fragmentation for the recuperative value of sleep is not clear. In animal studies, sleep fragmentation has been connected to reduction of hippocampal neurogenesis [217] and impaired spatial learning in rats [218]. In a study of individuals with obstructive sleep apnea syndrome, the number of micro-arousals during sleep was the best predictor of memory deficit [219]. The sleep fragmentation, together with the other abnormalities seen in individuals with OSAS (such as vascular endothelial dysfunction, increased oxidative stress, inflammation, metabolic dysregulation), is plausibly involved in the mechanism behind the increased incidence of cardiac and vascular diseases in this group [176].

Although the sleep-physiology data for the working subjects with high burnout scores did not demonstrate any marked sleep disturbance (**I**), our results suggest that aspects of sleep fragmentation may play a role in the early stages of burnout, as risk factors for further development of sleep disturbance, fatigue and (or) exhaustion. This is supported by the results from the sleep physiology measurements of the burnout patients on sick leave (**IV**), which showed evident sleep fragmentation within the patient group compared to controls at baseline. As mentioned, in this study the effects were controlled for disturbance due to sleep

apnea. This points to sleep fragmentation as one of the main characteristics of occupational burnout.

From our results it is a plausible hypothesis that work stress and sustained cognitive activation may lead to tension and higher physiological arousal or activation, and that this in turn may negatively affect sleep, for example, increase sleep fragmentation. This topic was in focus in another study from our lab by Ekstedt and co-authours (2004), using the same sample of subjects as in study **I**. The results from that study showed that the frequency of arousals was associated with a higher degree of subjective tension, as well as with elevated lipids, systolic and diastolic blood pressure, cortisol at awakening and heart rate [220]. This is in line with the results of Carrington and colleagues (2008), who in a group of healthy adults demonstrated that repetitive arousals during sleep independently contribute to elevations in blood pressure at night [221]. Further, the results from study **II** pointed to that higher frequency of arousals during prior sleep was associated with higher diurnal amplitude of cortisol and an earlier diurnal peak of cortisol during the subsequent workday. The direction of the relationship is, however, not possible to decide from this cross-sectional study.

Our data showed that improvement in sleep quality followed improvement in the core feature of burnout, the global perception of fatigue. Decreased number of arousals during sleep, together with decreased anxiety, became the only significant predictors of recovery from burnout (reduced fatigue) over time (**IV**). Further, return to work was predicted only by the reduction in fatigue over time (**IV**). This is somewhat in line with Sonnenschein and colleagues' results, which showed that daily ratings of fatigue were related to reports of impaired sleep, and that sleep played an important role in both symptom improvement and return to work in clinical burnout subjects [222, 223]. However, Sonnenschein and colleagues' results were based on self-reported sleep. One important strenght with our studies is that sleep was measured physiologically.

Apart from sleep fragmentation, other aspects of impaired sleep quality were also shown within the patient group from the PSG measurements (**IV**). This may suggest that the sleep impairment increases as the burnout syndrome progresses. The burnout patients showed increased sleep onset latency at baseline, and decreased relative amount of slow wave sleep for both conditions, compared to controls (**IV**). Increased sleep onset latency and decreased amounts of slow wave sleep may both be signs of a decreased 'sleep drive' according to the homeostatic first factor of the 'sleep formula' described in the introduction, or it may be effects of an increased arousal (i.e. tension, worry or being wound-up, bodily activation) according to the third factor of the 'sleep formula', or, it could be due to a combination of the two. In our data, the group of healthy control subjects showed an earlier time of rising than the burnout patients, whereas the bedtime did not differ between the groups (**IV**). This is logical as the control group were working and the patient group were on sick leave. However, the longer time in bed could indicate a somewhat weaker homeostatic drive for sleep in the patient group. Although, it seems perhaps even more plausible that the increased sleep onset latency and the decreased slow wave sleep for the burnout group was related to increased arousal. For example, the burnout patients reported significantly higher levels of perceived activation, or 'being wound-up', at bedtime compared to the control group (**IV**). Also, both depression and anxiety scores were markedly higher, and above clinical cut-off levels, for the patient group (**IV**). The fact that change in anxiety followed change in arousals from sleep, and that both these measures became significant predictors of reduced fatigue over time in the

stepwise regression analysis, indicate that hyperarousal (or sustained cognitive or bodily activation), could contribute to impaired sleep quality in clinical burnout.

Regarding slow wave sleep, in the paper by Ekstedt and colleagues (2006), sleep physiology was investigated in the same sample of burnout patients as in study **IV**. The results of that study showed less delta power density in NREM sleep in the burnout patients compared to the controls [224]. Such a finding together with the results described above suggests a severe sleep disturbance being a part of the clinical burnout syndrome. Early signs of sleep disturbance in working subjects with emerging burnout symptoms are therefore of importance to take in to account when estimating risks for further burnout development.

Worth noticing, in our study focusing on sleep physiology in the working sample, the relative amount of slow wave sleep did not significantly differ between subjects with high and low burnout scores **(I)**. Instead, the relative amount of slow wave sleep was relatively low in both groups of working subjects, compared to normative data [104, 213]. How to interpret this is unclear. A suggestion is that both groups experienced a stressful work situation, which could contribute to increased activation or anticipation, which in turn could be connected to lower amounts of slow wave sleep.

Regarding subjective sleep quality, our results showed significant differences between the working burnout groups with respect to self-reported habitual 'sleep quality' and 'impaired awakening'. In both cases the high-burnout group reported more impairments (**I**), which is in line with previous research [6] and which is indicating a less refreshing sleep compared to the low-burnout group. 'Sleep quality' was also a significant predictor of subsequent clinical burnout in the univariate regression analysis (**III**). In the study of burnout patients, subjective sleep quality was markedly impaired at baseline within the patient group, but a significant improvement was shown over time (**IV**). A couple of predictive studies based on questionnaire data have demonstrated that insomnia predicts burnout [225], or that burnout and insomnia are mutually interrelated and predict each other [226]. Taken together, it is possibly important to prevent and treat sleep disturbance in the working population in order to prevent more severe burnout development.

Sleep duration

The results of our study **I** showed that the objective sleep duration did not significantly differ between the working subjects with different burnout scores. Mean sleep duration, if counted over both conditions (mid-week and weekend), were, for the high-burnout group 7 hours and 8 minutes, and for the low-burnout group 6 hours and 53 minutes. This is, for both groups, close to 7 hours, which in the study of Kripke and co-authors (2002) was associated with the best survival [177]. Looking at differences between sleep duration within the working week (mid-week sleep) and after the working week (weekend sleep), both groups slept significantly longer during the weekend compared to the mid-week condition, which can be interpreted as a sign of recovery from the working week (**I**). Notably, both working groups slept relatively short during the working week, on average 6 hours and 41 minutes for the high-burnout group, and 6 hours and 17 minutes for the low-burnout group. Regarding the burnout patients, their total sleep time was 6 hours and 27 minutes at baseline and 6 hours and 39 minutes at follow-up. No significant differences were found between the patients and the healthy controls regarding sleep duration (**IV**).

Notably, although the our PSG measurements within the working subjects (**I**) yielded no differences between the groups regarding sleep duration, it is a striking result that the subjective report of getting 'too little sleep (less than 6 hours per night)', became the strongest predictor of subsequent clinical burnout (**III**). This points to the relative importance of the actual length of sleep on a habitual basis, as an early risk factor for burnout. A possible path is that in an early phase of burnout development individuals are shortening their habitual sleep, perhaps in order to free more time to handle every-day demands (work or social). This fits with Almén's (2007) model of burnout development [43] and with Geurts' and Sonnentag's (2006) recovery model [42]. If, over a period of time, sleep quality in addition gets impaired, the process of burnout development is plausibly entering a new, more severe, phase. This is in line with the findings of Ekstedt and Fagerberg (2004) in their qualitative study of the burnout process [21]. Our data fits well with such a hypothesis. Plausibly, the interaction of impaired sleep quality and sleep duration is an important aspect for eventual burnout development and for negative health outcomes in general.

IMPAIRED RECOVERY DURING LEISURE TIME

Stress and strain are supposed not to be harmful if proper recovery is taken place in-between stressful events or activation tops [42, 77, 78]. The term recovery refers to sleep, but also the ability to regularly unwind after stress, or detach, mentally and physically, during our time awake [71]. If this ability is impaired, the activation, or stress state, will be prolonged, which might be harmful for our health, well-being and performance capacity. Evidence of this has been shown, for example, regarding rest breaks at work [227] and long work hours [228]. Indicators of impaired recovery during leisure time were investigated in our studies, in order to identify possible risk factors for burnout development, as well as aspects important for treatment and recovery from burnout.

Diurnal sleepiness, mental fatigue and activation – workday and weekend patterns

From our studies, indications of impaired recovery (or sustained activation) were seen in the results of the daily ratings of sleepiness, mental fatigue, and activation. Data from the working sample showed that the high-burnout group did not recover, as did the low-burnout group during the weekends. The results showed that the diurnal levels of sleepiness (**I**) and mental fatigue (**II**) did not differ between the groups during the working week. However, a significant difference was shown for the weekend, as sleepiness and fatigue levels then decreased for the low-burnout group, but not for the high-burnout group, which remained on the same levels also during the weekend (**I, II**). This indicates a less effective weekend recovery for the high-burnout group, which may be related to a less recuperative sleep for the high-burnout group. It is worth noticing that both groups slept significantly longer during the weekend condition, compared to the working week, but still the sleepiness ratings the day after the PSG recordings differed between the groups. In another study from our lab, by Ekstedt and colleagues (2006), weekday-weekend patterns of sleepiness and mental fatigue were investigated in the same sample of burnout patients as in study **IV**. The results showed increased levels of sleepiness and fatigue, for the patient group, throughout the days for both the weekday and the weekend condition; that is, no reduction in sleepiness or mental fatigue was seen for the patient group during the weekend [224].

Diurnal ratings of sleepiness and mental fatigue were also carried out in study **IV** in order to assess daytime recovery and eventual changes in these measures over time among the burnout patients on sick leave compared to healthy controls. As was shown in the study by Ekstedt and co-authors (2006) [224], the patient group showed significantly higher levels of sleepiness and mental fatigue throughout the day compared to the control group (**IV**). In fact, the sleepiness levels of the burnout patients at baseline reached similar levels as what has been shown for shift workers during a night shift or during a morning shift with early rising [148, 229]. Sonnenschein and colleagues (2007) have shown a similar pattern. The results of their study, in which 60 clinically burned-out individuals repeatedly rated fatigue in an electronic diary for 14 days, showed that the burnout subjects suffer from a severe fatigue throughout the day [230].

Further, subjective ratings of activation, or the notion of being 'wound-up', showed the same diurnal workday-weekend patterns as was shown for sleepiness and mental fatigue (**II**). During the workday the groups did not differ, but during the weekend the low-burnout group were significantly more relaxed (compared to the workday), whereas the high-burnout group reported being as 'wound-up' as during the workday (**II**). Thus, the activation pattern from the workday was sustained over the weekend, indicating a less effective weekend recovery (or a sustained stress) for the burnout group. Also the clinical burnout group reported to be more 'wound-up' throughout the day compared to healthy controls (**IV**). Further, the burnout patients showed a shallower pattern for all three variables – sleepiness, mental fatigue and activation – across the day (**IV**). Significant interaction effects indicated that the burnout group improved on all these variables from the baseline measures to follow-up (after treatment), although the follow-up levels did not reach the levels of the healthy controls (**IV**).

Comparable data from other studies are lacking. However, the above results indicate an impaired recovery, during weekends in working subjects with high burnout scores, and in general in burnout patients on sick leave. Taken together, one main conclusion from this thesis work is that a lack of variation over time regarding perceived activation, sleepiness and mental fatigue, may constitute an increased risk for burnout development. This supports the hypothesis that it is not stress per se that is the problem, but the lack of proper recovery or deactivation in-between.

Diurnal cortisol – workday and weekend patterns

Cortisol release has a profound diurnal variation, with markedly lowered levels during the evening and the first hours of sleep, a nocturnal rise during the last hours of sleep and studies have shown that free cortisol levels peak within the first hour after awakening in the morning [154]. The nocturnal onset of the cortisol rise and a morning peak is driven by endogenous circadian oscillators, but metabolic aspects also play a part in this, as the HPA axis is important for energy mobilization when the energy demands of the brain is increasing towards the end of the night. Further, the final awakening per se is augmenting the morning peak of cortisol, as it ends the inhibiting effects of sleep on the HPA-activity [152, 154]. Besides the above factors influencing the diurnal cortisol pattern is the influence of stress and mental activation.

The results of our study **II**, which due to the small sample size should be interpreted with caution, showed no significant differences between the groups regarding the diurnal cortisol patterns, but within-group comparisons showed that the high-burnout group showed higher awakening cortisol during the workday than during the weekend. This is somewhat in line with the study of Rystedt and colleagues (2008). In the latter, the authors investigated morning and evening salivary cortisol during 7 days, and compared workday with weekend cortisol levels in groups with high or low long-term job strain [231]. Both groups showed a significant reduction of morning salivary cortisol levels from the working week to the weekend. In our data, such a reduction during the weekend was shown only for the high-burnout group. This plausibly reflects a higher stress and mental activation at awakening during workdays than weekends within the high-burnout group. As mentioned, the high-burnout group experienced a higher degree of work demands and thoughts of work during leisure time than did the low-burnout group (**I**). One of the items constituting the 'thoughts of work index' was: "As soon as I get up in the morning I start thinking about work problems", pointing to an elevated mental stress starting already at awakening.

Further, higher morning cortisol could be associated with an impaired recovery. This is in line with the findings in the study of Gustafsson and colleagues (2008), in which poor rest and recovery was associated with high levels of morning cortisol. Among the strongest relationships were found for "rested in the morning", "tired during the working day", "sufficient sleep" and "worry about something" [232]. Anticipation stress of the coming workday may also be involved. In the study by Kunz-Ebrecht and colleagues (2004) using a sample of 196 working subjects from the Whitehall-II study, a greater cortisol awakening response (defined by the difference between waking and 30 minutes later) was found during the workday compared to the weekend [233]. The authors argue that this indicate that anticipation of the working day is associated with an enhanced response. Born [234] have shown anticipation effects on the HPA-axis during sleep.

Study **II** showed that a higher frequency of arousals during the prior sleep was associated with an earlier diurnal peak of cortisol and higher diurnal amplitude of cortisol during the following workday. This is in line with the results of a recent study by Stamatakis and colleagues (2010), which showed increased morning cortisol levels following two nights of experimental sleep fragmentation across all sleep stages. Sleep fragmentation was also associated with a shift in the sympathovagal balance, estimated from heart rate variability analyses, towards an increase of sympathetic nervous system activity. Further, a decrease in insulin sensitivity was shown after the sleep fragmentation [235]. Such findings, again, indicate the important relation between stress, sleep and metabolism, and eventual negative health consequences of disturbed recovery from stress. Results from the Whitehall II-study, using a cohort of more than 2700 middle-aged men and women, showed that short self-reported sleep duration was associated with an increased cortisol awakening response, and that both short sleep duration and disturbed sleep were independently associated with a slower rate of decline of cortisol levels across the day and thus with increased evening levels [236].

The interaction between sleep and the HPA axis is complex and bidirectional. HPA hyperactivity and decreased sleep duration or impaired sleep quality seem to be tightly linked in a vicious circle, which could play an important causative role in the pathogenesis of metabolic and mood disorders, and possibly also in burnout development. A model has been

proposed to explain the perpetuation of chronic insomnia, and the role of cortisol for insomnia. In fact, evening cortisol levels have been shown to correlate with the number of awakenings during the subsequent night in insomnia subjects as well as in controls [237]. Thus, elevated HPA activity before sleep seems to promote sleep fragmentation, and sleep fragmentation and sleep loss have in turn been shown to increase evening cortisol levels [157], as discussed before. Taken together, this suggest the occurrence of a vicious circle that could be responsible for the chronicity of stress-insomnia relation, and which may be relevant also for burnout development, over time.

Impaired unwinding from work stress – sustained activation

Indications of impaired unwinding from work stress were seen among the working subjects with high burnout scores as they reported a higher degree of bringing work home, working on weekends, and work interfering with leisure time. They also complained more of persistent thoughts of work during leisure time (**I**). The latter index was one of the strongest predictors of subsequent clinical burnout in the longitudinal study (**III**). When it was entered into the hierarchical logistic regression analysis, at the second step, controlling for work demands, it became the only significant predictor and the explained variance of the model increased from 5,7% to 9,7%. The high-burnout group also showed a more sustained activation level, regarding the weekday and weekend patterns of being 'wound-up' (**II**). The patients suffering from clinical burnout, although they were on sick leave and not in a present work context, also showed generally increased levels of being 'wound-up' compared to controls (**IV**), indicating chronic stress activation.

Taken together, our data points to a somewhat persistent stress, which may contribute to sustained cognitive and bodily activation and undermine the prerequisites for appropriate recovery. As fatigue and performance impairment from other studies is known to increase as a function of time on task [31, 238], such a persistent work-attention pattern (as for the working subjects with high burnout scores) may over time hamper a good work performance and increase fatigue and physiological stress activation, which in the long run may affect health negatively. Sustained activation and aspects of impaired recovery were also reported as precursors of burnout in the qualitative study of burnout development by Ekstedt and Fagerberg [21].

This pattern of sustained ("limit-less") activation may probably be a result of the interaction between the individual and the work environment (for the working subjects). Our data showed that the high-burnout group reported significantly higher psychological work demands than did the low-burnout group (**I**). High work demands predicted subsequent clinical burnout (**III**). However, decision latitude, which refers to the degree of control of *what* job to do and *how* to do the job, did not differ between the groups (**I**), and did not predict subsequent burnout (**IV**). Nor did social support at work (**I, III**). This is in line with some of the previous literature, as data have not been consistent. Some studies have demonstrated the relation between job strain and burnout [239, 240]. Other studies have pointed out high work demands to be more strongly related to burnout than control or social support, which is in line with our results [60, 241, 242]. Further, the study by Schnorpfeil and colleagues (2003) showed that work demands was the only psychosocial factor predicting allostatic load [243]. Also, high work demands have been shown to predict sleep disturbance [90, 138] and increased sickness absence [244].

The fact that work demands, but not decision latitude, predicted clinical burnout in our study (**III**) could possibly be due to that "the essence" of 'demands' and 'control' at work have changed during the last decade. Perhaps are increased work demands related to an increased degree of individual control at work in today's working life. For example, factors as high meaning of work, but low possibilities for development, low predictability, and low role clarity have been found to be prospectively associated with increased risk of burnout [245]. The working subjects in our studies experienced a high degree of control of what job to do and how to do the job, but perhaps this freedom also may reflect a somewhat unclear organizational structure or leadership, perhaps resulting in uncertainties regarding work goals, how to prioritize among conflicting goals, how to evaluate ones work performance, etc., which may cause stress (higher psychological demands, increased worry and higher effort) for the individual. Such kind of work stress may on the one hand increase the individuals' need for recovery, but on the other hand it may contribute to sustained cognitive and bodily stress reactions, which can impede recovery processes. This is in line with Guerts' and Sonnentags' recovery model, and with the cognitive-behavioural model of burnout presented by Almén [42, 43]. Individual differences regarding recovery habits, coping behaviour and prior stress experiences are plausibly involved, although we did not investigated this in the present studies. Most probably, longitudinal approaches which take into account combinations of job stress models (as the DCS model, the COR model, the ERI model), the recovery aspects, as well as the cognitive-behavioural model for burnout development may improve our understanding of the relationship between the psychosocial work environment and burnout [246].

Impaired recovery impairs sleep – the vicious circle

Sustained cognitive or bodily activation, impaired sleep quality, daytime symptoms such as sleepiness, fatigue, worry, mood changes and less effective daytime functioning, are all important aspects of what may become a vicious circle connected to sleep [125, 126, 247]. Data from our studies (**I-III**) indicate that working subjects at risk of developing clinical burnout show a pattern of high work demands, difficulties detaching from thoughts of work during leisure time, impaired weekend recovery, insufficient sleep (<6 hours per night) and impaired sleep quality. Sleep disturbance often cause negative daytime consequences, such as sleepiness, mental fatigue, irritability, tension, difficulties concentrating, etc. (which also are core symptoms of burnout). As a result of these symptoms, the individual often puts in more effort to meet the demands at work or in other aspects of life, which may maintain or increase fatigue, tension and stress reactions. Also, in order to minimize the aversive consequences of impaired or insufficient sleep, it often becomes very important for the individual to sleep well. As a result, worry and anxiety connected to sleep may increase, and the individual may "try harder" to sleep better [125, 126, 247]. However, sleep is something we cannot deliberately control. On the contrary, worry, anxiety, and trying to control sleep, disturbs sleep [248]. Hence, the vicious circle of stress or worry – sleep disturbance – fatigue – effort becomes manifest and maintains a long-term negative development, of which, in combination with high work stress, burnout might be one end point. This might have been the case for the burnout subjects on long-term sick leave, who were in focus in study **IV**. Important to notice though, the included studies in this thesis had cross-sectional designs, and therefore no conclusion regarding the directions of the relationship between sleep and burnout can be drawn. However, this is an important issue for future research.

BURNOUT IN RELATION TO INSOMNIA, DEPRESSION AND ANXIETY

Clinical burnout, or exhaustion syndrome, shares in part symptom characteristics with other psychiatric disorders as insomnia, depression and anxiety. However, important differences between burnout and insomnia concern the fact that insomnia refers to difficulties falling asleep or maintaining sleep, un-refreshing sleep and psychological distress regarding sleep with consequences for daytime functioning [16]. In the case of burnout, the focus is on the daytime exhaustion or fatigue symptoms, built-up by long-term stress. In table 4 below the diagnostic criteria for exhaustion syndrome are presented, which was added in 2005 by the Swedish National Board of Health and Welfare as a supplementary diagnosis (F43.8A) into the Swedish version of the ICD-10 [17]. Notably, sleep disturbance is included in the diagnostic criteria for exhaustion syndrome, and disturbed sleep has in many cross-sectional studies been reported as one of the core symptoms of the burnout condition [6, 224]. This makes it difficult to draw any conclusions regarding cause and effect with respect to the relation between burnout and sleep. The prospective study by Armon (2008) showed a mutal relationship between insomnia and burnout; the both conditions predicted each other over time [226]. However, the design of Armon's study does not allow any conclusions of cause and effect. Neither do the studies included in the present thesis. The study of Jansson-Fröjmark and Lindblom (2010) showed evidence for insomnia predicting burnout, but not the other way around, which points to sleep disturbance as a predisposing factor in relation to burnout and that insomnia and burnout not are the same condition [225]. Burnout also seems to be a more severe and global clinical condition than insomnia.

Table 4. The diagnostic criteria for Exhaustion syndrome (F43.8.A). Criteria referring to all capital letters must be fulfilled for the diagnosis.

A	Physical and psychological exhaustion for at least two weeks. The symptoms should be developed as a consequence of one or several stressors during at least six months.
B	Marked lack of mental energy in the form of reduced initiative, reduced endurance, or an extended time for recovery after mental stress.
C	At least four of the following symptoms almost every day during a two week period: 1 Difficulties with concentration or memory 2 Reduced ability to handle demands or time pressure 3 Emotionally unstable 4 Disturbed sleep 5 Physical weariness 6 Physical symptoms as pain, chest pain, palpitations, digestive complaints, dizziness or hypersensitivity to sounds
D	Symptoms should cause clinical suffering or reduced capacity at work, in social life or in other important respects.
E	The condition is not caused by substances or somatic disease.
F	If diagnositic criteria are fulfilled for any of the psychiatric diagnoses depressive episode, dysthymia or anxiety disorder, the exhaustion syndrome will be reported as secondary diagnosis.

Regarding the insomnia-burnout relation, it is our tentative conclusion that insomnia in combination with chronic stress and impaired ability to unwind during leisure time, can develop to burnout, or exhaustion syndrome, over time. Notably, however, the opposite (that burnout may lead to insomnia) is also possible. The direction of the relationship remains to be tested in future, more controlled, longitudinal designs.

According to the above criteria for exhaustion syndrome, it is also worth noticing that exhaustion syndrome will be set as a secondary diagnosis if the criteria for depression, dysthymia or any anxiety disorder are met. In study **III**, the clinical assessment records were re-examined, at the end of the study period, by the clinical psychologist who did the assessment and by a senior clinician. All included subjects were then found to fulfil the diagnostic criteria for exhaustion syndrome presented above. Hence, none of the included subjects in study **III** met the diagnostic criteria for depression or for any anxiety disorder. In study **IV**, the group mean for depression and anxiety (scores from BDI and BAI) showed clinical levels within the burnout patient group. Although, all subjects had been screened by an experienced psychiatrist using Structured Clinical Interview (SCID) for DSM-IV-TR [197, 198], and patients with an ongoing major depression was excluded from participation in the study. Among the working subjects in study **I**, mean anxiety scores, but not depression scores, were above clinical levels in the high-burnout-group. In that study, there was less control over co-morbibity, as no clinical interview or assessment for other psychiatric or somatic disorders were made.

Notably, change in depression from baseline to follow-up within the burnout patient group did not show any significant correlation with change in fatigue index over time (**IV**). Nor did depression scores at follow-up predict return to work (**IV**). Reduced fatigue over time became the only significant predictor of return to work (**IV**). The latter indicates that fatigue is the core symptom of burnout, which mainly counts for the effects of reduced work capacity seen in clinical burnout. These results point to that burnout and depression are different conditions and that depression symptoms may accompany exhaustion symptoms, but recovery paths may be separate. Also, sleep problems seem to affect burned-out individuals independent of co-morbid major depression, suggesting that sleep impairments are independent concomitant symptoms of burnout, despite their strong relationship with depression [249]. In line with this are the results from the study by Sonnenschein and colleagues (2007), which showed that impaired recovery from sleep was related to severity of exhaustion, but not to severity of depressive mood [223].

Changes in anxiety from baseline to follow-up, however, significantly correlated with changes in the fatigue index (**IV**). Anxiety scores at follow-up also significantly correlated with return to work (**IV**). From the data presented in this thesis, anxiety seems to be closer connected to clinical burnout than depression. This seems logical, as anxiety is constituted by an increased physiological stress reaction, and burnout is emerging over time due to chronic stress activation. Also, anxiety can start a vicious circle, as negative emotions can become associated with certain settings or situations, and lead to avoidance behaviour, which will make the anxiety grow and endure over time [43, 126, 134]. On the other hand, to some extent it may seem surprising that anxiety, in this set of data, was more closely linked to burnout than depression, as the symptoms of depression, such as markedly reduced activity, as well as (often) sleep disturbance, and an affective component which could resemble the fatigue experience. Although, important differences between depression and exhaustion are

probably the aspects of willingness and engagement. Burnout patients often express an engaged interest to be more active, or a will to return to work, but are hampered by reduced cognitive, emotional and physical energy. In the case of depression, the affective component, the reduced sense of meaning, or lack of joy or interest in engaging in different activities, is plausibly the core behind the behaviour changes seen in depression.

Finally, our data showed that the burnout patient group improved over time on all the key symptoms variables, as burnout, fatigue, anxiety, depression and sleep (**IV**). The improvement may or may not be attributed to the specific treatment or to spontaneous recovery. The design of the study does not allow a conclusion of causuality.

BURNOUT – A MATTER OF IMPAIRED RECOVERY?

To sum up, this thesis has put forward data, which support the assumptions that 1) impaired or insufficient sleep and recovery during leisure time are related to burnout development; 2) insufficient sleep, and impaired unwinding during leisure time, predict clinical burnout and; 3) recovery from clinical burnout is associated with improved sleep and alertness.

This thesis has focused on the recovery aspects, and the results from the predictive study showed that insufficient sleep (less than 6 hours per night), as well as difficulties unwinding from thoughts of work during leisure time were the strongest predictors of subsequent clinical burnout, controlling for the stress of high work demands. This indicates that impaired recovery is more harmful than the stress per se. Our results also demonstrated a severe sleep disturbance as a part of the clinical burnout syndrome, and that recovery from fatigue in burnout patients was related to reduction of arousals from sleep, along with decreased anxiety. Decreased fatigue became the only significant predictor of return to work.

The integrative tentative conclusion from this thesis may be: As long as sleep, and the ability to disengage from thoughts of work during leisure time, is sufficient and undisturbed, the risk for burnout in relation to high work demands (or a high stress level) is not as high. Another conclusion from this thesis work, which needs to be investigated and confirmed in future research, is that sleep fragmentation may contribute to an essential part to the development of burnout, and to the recovery process. To this background, treatment of sleep disturbances seems to be very important both in the prevention of burnout development, but also when clinical burnout is established in order to enhance recovery from burnout and return to work.

To summarize, signs of impaired recovery as risk factors for burnout were seen in the following results:

Impaired or insufficient sleep

- Objective sleep data showed a higher frequency of arousals within working subjects scoring high on burnout compared to controls (**I**).
- Working subjects scoring high on burnout reported less good sleep quality and more awakening problems compared to controls (**I**), which indicate a less refreshing sleep.
- ‘Too little sleep (less than 6 hours per night)’ became the strongest predictor of subsequent clinical burnout, controlling for ‘work demands’ and ‘persistent thought of work during leisure time’, in the multivariate logistic regression approach (**III**).

- Self-reported impaired sleep quality was a significant predictor of subsequent clinical burnout in the univariate logistic regression analysis (**III**).
- Objective sleep data in burnout patients showed, compared to healthy controls, disturbed sleep before treatment with respect to increased sleep latency, increased sleep fragmentation, increased micro-arousals and decreased relative amount of slow wave sleep. The patient group improved on all these variables over time, except regarding the amount of slow wave sleep (**IV**).
- Reduction of micro-arousals over time predicted recovery from clinical burnout (decreased fatigue) (**IV**).

Impaired weekend recovery

- Diurnal sleepiness (**I**), mental fatigue (**II**) and activation (**II**) did not decrease during the weekend for the working subjects with high burnout scores, as was evident for the control group.
- Working subjects with high burnout scores reported a higher degree of working on weekends (**I**).

Other aspects of impaired recovery

- Working subjects with high burnout scores showed increased difficulties letting go of thoughts of work during leisure time, as well as a higher degree of bringing work home, and of work interfering with leisure time (**I**).
- Difficulties detaching from thoughts of work during leisure time was one of the strongest predictors of subsequent clinical burnout (**III**).
- Diurnal sleepiness, fatigue and perceived activation were markedly increased in clinical burnout patients at baseline, and did significantly decrease over time (after treatment), but did not reach the level of controls (**IV**).
- Decreased fatigue was the only predictor of return to work, which indicates that fatigue is the core symptom of burnout, mainly counting for the effects of reduced work capacity seen in clinical burnout (**IV**).

LIMITATIONS

Some general limitations and weaknesses regarding the included studies, concerning design, power, selection bias, and other biases, are mentioned below.

Regarding the design of the studies, it is important to underline that the cross-sectional and descriptive nature of the studies does not permit any conclusions regarding cause and effects, or of the direction of the relations, in the case of burnout development. Also the longitudinal study (**III**) suffers from the cross-sectional limitations, as the level of clinical burnout at baseline was not controlled. The subjects in study **IV** underwent a cognitive-behavioural treatment protocol for burnout between baseline and follow-up. Although it was not the primary aim with the study to evaluate the treatment protocol, the study design does not allow any conclusions regarding treatments effects.

Regarding statistical power, one of the most obvious limitations is the relatively small number of participants in the studies. Small sample sizes increase the risk for type II error, which means that significant effects may not have been detected. Further, there is a risk that

the results loose in precision and reliability. A weakness with the present studies is that no power analyses were computed before the study designs were decided and participants were selected. This can be understood as the research field is new and data, to build power analyses on, were lacking when the studies were planned and conducted.

Regarding selection biases, in three of the studies (**I-III**), the subjects were sampled from the same workplace, a specific Swedish company within the IT sector. This may negatively affect the possibility to generalize the results to other populations (decrease the external validity). There was also a fairly high proportion of the original sample, which did not complete the baseline questionnaire. This is a weakness, as we lack information regarding whether the non-replying subjects significantly differed in any vital aspects from the included subjects.

A weakness concerning the selection of subjects in study **III** is that there was no test-retest procedure regarding the clinical assessments, at the time of inclusion. The clinical records were, however, re-examined after the study period had ended by the psychologist who did the assessments and a senior clinician. All subjects were by both clinicians found adequate for inclusion into the study, and all subjects were found fulfilling the diagnostic criteria for exhaustion syndrome. Despite these control procedures, there is always a possibility that potential cases may have been missed, or that an unknown number of individuals within the reference group may have suffered from clinical or sub-clinical burnout, without reporting it to the health service department of the organization. If so, this may have affected the predictive power of the independent variables.

In our studies the SMBQ was used to measure burnout and to select participants. However, the most commonly used burnout measure in the literature is the MBI. This hamper the possibility to compare and generalize the results from this thesis with studies of burnout using the MBI or other burnout measures. Also, modifications of the DSC and ERI scales were used in the present studies, which in the same way limits the possibilities to generalize and compare the results from this thesis with other studies within the literature.

IMPLICATIONS FOR FUTURE RESEARCH

Further research on burnout in relation to recovery from stress is of importance for several reasons. As burnout causes severe suffering for the individual and is often associated with negative long-term consequences such as reduced work capacity or sick-leave, which causes high costs for the society, it would be of major importance to identify early risk factors or indicators for burnout to more fully understand the phenomenon and to be able to prevent it.

In general, studies using larger sample sizes, and prospective, theoretically based designs, focusing on both subjective and physiological measures, are preferable in future research in order to more fully understand the burnout development processes, and likewise the processes of recovery from burnout. In particular, the possibly mediating role of sleep and daytime recovery on the relation between stress and burnout development, needs to be further investigated. Further, longitudinal research on the effect of treatment of sleep disturbance for future burnout would be of great value.

The definition of the burnout condition needs to be clarified. The most commonly used burnout questionnaires in the research literature, the MBI and the SMBQ, are highly related, but there are also differences between the scales. This is of importance to explicitly investigate and discuss more in detail in further research. This is especially important when it comes to comparison between studies and when self-reported measures of burnout are related to physiological measures or to clinical assessments. Systematic comparisons between self-reported and clinically assessed burnout is also needed. Data on this is now lacking, probably due to the fact that generally agreed upon clinical criteria for burnout are lacking. Hence, there is also a need to establish diagnostic criteria for clinical burnout. In Sweden, diagnostic criteria for 'exhaustion syndrome' have been established [17] and are used in the clinical practice for diagnosing the stress related condition of exhaustion, which in this thesis has been called burnout. Until generally agreed upon diagnostic criteria are established, the Swedish criteria for 'exhaustion syndrome' may be of help in future research focusing on clinical burnout.

There is a lack of knowledge regarding what constitute (behaviourally and physiologically, etc.) the actual recovery during leisure time (evenings and weekends). What activities or factors enhance or hampers recovery? How are physiological parameters connected to sustained cognitive activation, or to unwinding from mental stress? Can unwinding from cognitive stress be trained and optimized, for the prevention and treatment of clinical burnout? When investigating the recovery aspect in future research, indications of impaired recovery as sleepiness and fatigue are of interest, how they relate to burnout development and to recovery from burnout. Further, there is a need of more knowledge regarding non-occupational stressors (stressors during off-work time), as burnout likely is built up by multi-factorial stress.

From the results of this thesis work, a preliminary 'screening tool package', for identifying individuals at risk for clinical burnout, could include the following:

- Shirom-Melamed Burnout Questionnaire (SMBQ)
- Ratings of work stress (or work demands)
- Karolinska Sleep Questionnaire (KSQ)
- Diurnal ratings of sleepiness (KSS), mental fatigue and activation during workdays and weekends
- Ratings of the ability to unwind from thoughts of work (or other stressful thoughts) during the evenings.

To test the predictive value of such a screening tool, a longitudinal research approach would be of value with regard to the prevention and treatment of burnout.

IMPLICATIONS FOR CLINICAL PRACTICE – SOME THOUGHTS ON PREVENTION AND TREATMENT

The results from the studies in this thesis have to be confirmed in future studies before any conclusion with implications for prevention or clinical practice can be drawn. Below, however, are some of my thoughts on the issue of burnout prevention and treatment, based on our pilot data and results from previous studies.

Plausibly, core points in the prevention and treatment of work related exhaustion or burnout are to analyze what stress the individual is perceiving, how this is connected to fatigue, and how this could be handled, as by:

- changing the actual work situation (organizational approach)
- changing the individual's way of handling the stress (individual approach)
- increasing and improving recovery, during work as well as during leisure time (organizational and individual approach).

A meta-analysis by Richardson and Rothstein (2008) investigated the effectiveness of different stress management interventions in occupational settings [250]. Interventions were coded as cognitive–behavioral, relaxation, organizational, multimodal, or alternative. The results showed that cognitive–behavioral programs consistently produced larger effects than other types of interventions, and if additional treatment components were added the effect was reduced. Within the sample of studies, relaxation interventions were most frequently used, and organizational interventions were scarce. Effects were based mainly on psychological outcome variables, as opposed to physiological or organizational measures. This meta-analysis was not focusing on burnout, but as burnout is a connected to long-term work stress, it is of plausible relevance for burnout prevention.

Another possibly important aspect, which can affect both the stress at work and the recovery aspects, is the fact that we are facing a 24-hour society, in which almost everything can be done almost any hour of the day. This can increase work stress and impair our daily recuperation, as we with, for example, lap tops, smart phones and internet connection can be working or engaging in different activities wherever we are, and around the clock. In order to prevent sustained activation, sleep disturbance, and over time, allostatic up-regulation or negative health consequences as burnout, it is probably of importance to, more or less, stick to daily routines (as regular eating, taking regular breaks from work, unwinding during the evenings, keeping regular sleep-wake times etc.), which are in "synch" with our inner circadian clock. As daylight is the main external cue for setting our inner circadian clock, daylight exposure every day, preferably in the mornings, is of importance for synchronising or circadian rhythm and to increase alertness during daytime. Also, in order to strengthen our circadian rhythm and to promote good recuperative sleep, restricting lights in the evening hours, keeping regular bedtimes, and sleeping in a dark, cool bedroom is preferable.

Burnout is a multidimensional, progressively developing condition. As such it may be related to different stressors for different individuals, and show different features during different phases. This will have impact on the prevention and treatment of burnout. For example, within the early phases of the burnout development, the individual may show more active behaviours (such as putting in more effort, showing more competitive behaviours towards others), and, eventually, more passive behaviour (such as increased avoidance, reduced activity, submissive or dejected behaviours) within the exhaustion phase [21, 43, 48]. In the latter phase, new stressors may be developing. For example, the individual may, due to the exhaustion symptoms, fail to match his or her high standards for acceptable performances at work or in other important aspects of life. According to cognitive-behavioural models, this in turn may lead to avoidance, increased worry, anxiety, and depression, which all contribute to keep the exhaustion going [43]. In this sense it becomes important to build treatment on a detailed analysis of the actual situation, and to discriminate between factors or behaviours

that may be *starting* the negative development, and factors that may be *maintaining* or *aggravating* the exhaustion.

Data from this thesis are in line with the hypothesis that insufficient or impaired sleep could be of importance both as precipitating and maintaining factors for burnout. If so, treatment interventions focusing on enhancing sleep would be of vital importance in the prevention and treatment of burnout. As the sleep disturbance in burnout is supposed to be associated with long-term stress, behavioural and lifestyle aspects, the most adequate treatment seems to be non-pharmacological. Behavioural interventions for insomnia have been proven as effective as pharmacological treatment in short-term follow-up studies and more effective in long-term follow-up studies [251]. Stimulus control and sleep restriction are two effective behavioural techniques, which are used in most cognitive behavioural treatment protocols for insomnia (CBT-I) [215, 252]. Cognitive techniques, as well as mindfulness and acceptance strategies are often included in effective multi-component CBT-I protocols. There is a lack of data, however, regarding the unique contribution of these components to overall treatment efficacy [248, 253, 254] However, the strong evidence for the efficacy of CBT-I leads me to suggest that CBT-I interventions could be of value in the prevention and treatment of clinical burnout.

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