Sick and tired: psychological and physiological aspects of work-related stress

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1 Introduction

Work-related stress is a state of distress resulting from exposure to work-related stressors (Schaufeli & Buunk, 2003). Work-related stress is common (Paoli & Merllié, 2001; Netherlands Central Bureau of Statistics, 2005a,b) and it is associated with health problems, such as fatigue or hypertension, and often leads to sickness absence or even work-disability (Netherlands Central Bureau of Statistics, 2005a,b; European Communities, 2004; Houtman, Smulders & Hesselink, 2004; Jones, Huxtable, Hodgson & Price, 2003; Molenaar-Cox & Deursen, 2001; Paoli & Merllié, 2001; Spreeuwers, Pal & van der Laan, 2005). The health-related costs associated with work-related stress are considerable (Blatter, Houtman, van den Bossche, Kraan & van den Heuvel, 2005). While work-related stress is studied broadly and extensively, questions remain about the presence physiological dysregulation, psychological characteristics, and treatment of work-related stress. The aim of this thesis was twofold: a) to enhance the insight in fundamental physiological and psychological characteristics of work-related stress, and b) to assess whether cognitive behavioural treatment (CBT) is an effective treatment for work-related stress. We expected a) to find support for a dysregulated physiological stress-response system, b) to identify dysregulation in emotion processing as a risk factor for work-related stress, and c) to confirm that CBT is effective as a treatment for work-related stress, also in clinical samples.

Before presenting the individual studies, this introduction provides background information on the definition and prevalence of work-related stress. Furthermore, in order to understand how dysregulation of the physiological stress-response system can develop and why CBT may be effective for treating work-related stress, developmental models of (work-related) stress are summarised and the physiological stress-response is described. In addition, the research questions central to this thesis are introduced. Finally, a brief outline of the thesis is presented.

General background

Work-related stress definitions

Work-related stress is a state of temporary adaptation, which occurs when job demands do not match a person's adaptive abilities (Schaufeli & Buunk, 2003). The end-stage of this process, when a breakdown in the adaptation occurs after prolonged work-related stress, is called burnout (Schaufeli & Buunk, 2003). Burnout is frequently described as a three-dimensional construct consisting of *emotional exhaustion*, *depersonalisation*, and *professional incompetence* (Maslach, Schaufeli & Leiter, 2001). Emotional exhaustion refers to excessive fatigue due to work, depersonalisation to a distant, cynical attitude towards work and colleagues, and professional incompetence

to the feeling of being unable to perform well at work. Originally, burnout was considered exclusively applicable to the social professions, but nowadays, burnout is commonly accepted as a general work-related stress state (Maslach et al., 2001).

No specific diagnosis for a clinically elevated level of work-related stress is included in the main classification systems for mental disorders, that is, the Diagnostic and Statistical Manual of mental disorders (DSM-IV; American Psychiatric Association [APA], 1994) or the International Classification of Diseases (ICD-10; World Health Organisation [WHO], 1992). However, a clinically elevated level of work-related stress can be captured with other diagnoses that more generally refer to physical complaints and/or significant distress associated with impairment in social, occupational, or other important areas of functioning. These diagnoses are a) adjustment disorder (DSM-IV, ICD-10); b) undifferentiated somatoform disorder (DSM-IV); and c) neurasthenia (ICD-10). The essential characteristics that determine which diagnosis should be applied are: a) presence/absence of a specific, aetiologically related, non-traumatic stressful event, and b) duration of complaints. Regarding the former characteristic, for adjustment disorder, a specific stressful event (e.g., a reorganisation in the company) should be present and is deemed causally linked to the complaints, while for undifferentiated somatoform disorder or neurasthenia, no specific stressful event can be identified. Regarding the latter characteristic, for adjustment disorder the duration of complaints is less than six months, for undifferentiated somatoform disorder the duration of complaints is longer than six months, and for neurasthenia persistence of the situation is emphasised, without specifying an exact duration. Some clinicians have suggested to use work-related neurasthenia as a clinical description specific for the burnout syndrome (Hoogduin, Schaap & Methorst, 1996).

The Netherlands Society of Occupational Medicine (2000) applies a concise categorisation of work-related stress disorders, inspired by the available diagnoses in the DSM-IV and ICD-10, and based on severity. This categorisation is: work-related stress complaints (sub-clinical level of complaints), work-related adjustment disorder (similar to adjustment disorder in the DSM-IV and ICD-10), and burnout (similar to undifferentiated somatoform disorder in the DSM-IV and work-related neurasthenia in the ICD-10). In addition to the criteria presence/absence of a specific aetiologically related stressful event and duration of complaints used in the DMS-IV and ICD-10, a third criterion considering the development of complaints is applied in this categorisation. Work-related adjustment disorder is considered to develop progressively within three months after the occurrence of the stressful event, while burnout is considered to develop gradually, e.g., after years of working in a stressful working environment.

For the present thesis, a clinical level of work-related stress was defined as work-related adjustment disorder or burnout as described by the Netherlands Society of Occupational Medicine (2000). The exact criteria that we applied are listed in Box 1.

Box 1: Definition of a clinical level of work-related stress used in the present thesis.

- Persistent bodily and/or mental fatigue, or increased fatigability after mental of physical efforts.
- At least two of the following cognitive, emotional, physical, or behavioural complaints:

muscle pain	dizziness
tension headache	sleeping problems
irritability	dyspepsia
concentrations problems	emotional instability
anhedonia	inability to relax

- Work is aetiologically related to the complaints
- Disturbed daily functioning manifested as sickness absence

Prevalence of work-related stress

Work-related stress is common in the working population as indicated by a) the prevalence of complaints due to the work-situation or working; b) the prevalence of sickness absence due to high workload; or c) the prevalence of mental disorders comprising work-related stress. First, regarding the prevalence of complaints, 60% of the European working population reported in 2000 that work negatively affected their health (Paoli & Merllié, 2001). Of the workers reporting work-related health problems, 28% reported occupational stress, 23% fatigue, 8% sleeping problems, and 11% reported irritability. Second, concerning the prevalence of sickness absence, high workload (working under time-pressure or working in a high pace) is a frequently reported reason (23-36%) to call oneself sick at work in the Netherlands (Bakhuys Roozeboom, Gouw, Hooftman, Houtman & Klein Hesselink, 2008; Netherlands Central Bureau of Statistics, 2005a). Third, with respect to the prevalence of mental disorders, prevalence rates vary between 18 and 30% in Europe (Spreeuwers, et al., 2005; European Communities, 2004; Jones et al., 2003; Molenaar-Cox & Deursen, 2001). Among these mental disorders, adjustment disorder is among the most common disorders. For example, in the Netherlands, about 80% of the mental disorders causing absenteeism consist of adjustment disorder or burnout (van der Molen et al., 2008; Spreeuwers et al., 2005). Prevalence estimates of burnout alone in the Netherlands vary from 8% to 20% (van der Molen et al., 2008; Netherlands Central Bureau of Statistics, 2005b; Houtman et al., 2004; Kant, Janssen, van Amelsvoort, Mohren & Swaen., 2004).

Health consequences, functional impairment, and associated costs

Enduring exposure to chronic, none life-threatening stressors such as work-related stressors has been linked to various serious and less serious bodily health problems, such as hypertension (Landsbergis, Schnall, Pickering, Warren & Schwartz, 2003; Manuck, Kasprowick, & Muldoon, 1990; Schwartz et al., 2003; Selye, 1975), cardiovascular disease (Chandola et al., 2008; Manuck, 1994; Melamed, Shirom, Toker, Berliner & Shapira, 2006), stomach ulcers (Levenstein, Ackerman,

Kiecolt-Glaser & Dubois, 1999; Selye, 1975), and common infections (Mohren et al., 2003; Cohen & Herbert, 1996; Kiecolt-Glaser & Glaser, 1995). Work-related stress is also associated with chronic functional impairment. For example, 4.0-6.5% of the work-disabled people in The Netherlands have a diagnosis of burnout or adjustment disorder (Blatter et al., 2005; Landelijk Instituut Sociale Verzekeringen, 2001). Health-related costs associated with work-related mental disorders are substantial. Estimated yearly costs in the Netherlands associated with psychosocial workload, that is, costs of medical consumption, sickness absence, and work-disability due to work-related mental disorders, are three billion euro (Blatter et al., 2005).

Development of work-related stress

Below, psychological, physiological, and hybrid models that account for the development of (work-related) stress are summarised. These models serve as the theoretical background for the research questions that are introduced in the next section.

Psychological models

In the field of stress research, many models are transactional, which means that they consider stress to occur in a situation of imbalance between demands (e.g., workload) and resources (e.g., skills). One of the most influential transactional stress models is the Transactional Model formulated by Lazarus and Folkman (e.g., Lazarus & Folkman, 1987). This model states that an individual's reaction to the environment is mediated by the subjective evaluation or *appraisal* of the environment and by the process of *coping* with the as stressful appraised event. Within the cognitive appraisal process, two phases are distinguished: 1) primary appraisal, during which an event or demand is evaluated for instant harm, the threat of harm in the future, and challenge; and 2) secondary appraisal, during which the availability of coping resources is evaluated. This cognitive appraisal influences the way an individual will cope with a stressor. The actual way of coping that follows the appraisal is labelled problem-focused when coping is aimed at solving the problem, or emotion-focused when coping is aimed at regulating distress (Lazarus & Folkman, 1987). The Transactional Model distinguishes affective, cognitive, physiological, and behavioural outcomes of dealing with a stressor. When the stressful experience persists for a considerable period, exaggerated psychological and physiological responses occur and complaints and impaired functioning develop (Lazarus & Folkman, 1987). According to the model, personal characteristics, such as personality, beliefs, social and problem-solving skills, previous experiences, and emotional states affect the stress-response by their influence on appraisals of situations and coping resources.

Within the field of work-related stress, the best-known transactional models are the Job-Demands Control Support (JDCS) model (Karasek, 1979; Karasek & Theorell, 1990; Karasek, Triantis, & Chaudry, 1982) and the Effort-Reward Imbalance (ERI) model (e.g., Siegrist, 1995). These models describe in different ways under what circumstances workload results in health problems. In the JDCS-model, significant job characteristics that influence job performance and health are job-demands, job-control, decision authority, and support. The model states that job-control, deci-

sion authority, and support compensate for the job-demands. An imbalance between these factors, e.g., a state of high job-demands and low control and/or low support, is considered a risk factor for developing health complaints, cardiovascular diseases, and impaired daily functioning. Alternatively, the ERI model focuses on rewards at work as a compensation for conducted efforts. Health complaints and impaired daily functioning are hypothesised to develop when effort is high and material and immaterial rewards (e.g., salary, acknowledgement) are low.

Physiological models

Cannon developed a sympathetic stress model, in which he described the immediate bodily reactions associated with a fight-flight response to threat (Cannon, 1914). During the fight-flight response, sympathetic stimulation of the adrenal medulla results in a release of catecholamines in the blood, such as adrenaline. Cannon showed that the response of the adrenal medulla to produce adrenaline was contingent upon physical and emotional threat (Canon, 1934; Cannon & de la Paz, 1911). The connection between the sympathetic nerve that originates in the hypothalamus and ends in the adrenal medulla is nowadays known as the Sympathetic-Adrenal Medullary (SAM) axis. In addition to sympathetic effects on the body via catecholamines released by the adrenal medulla, a sympathetic stress response affects the body through direct neural innervation of muscles and organs (Kaltsas & Chrousos, 2007).

The General Adaptation Syndrome is a neuroendocrine stress model developed by Selye (1975). This model describes three phases in the reaction to stressors: a) the alarm phase, b) the resistance phase, and c) the phase of exhaustion. Selye stated that prolonged exposure to a stressor could lead to a variety of 'maladaptations', such as ulceration of the stomach, hypertension, and insomnia. An important bodily agent in this process of developing adverse health consequences is cortisol that is released by the adrenal cortex (Selye, 1975). The connection via the blood stream between the paraventricular nucleus of the hypothalamus, the pituitary gland, and the adrenal cortex is nowadays referred to as the Hypothalamic-Pituitary-Adrenocortical (HPA) axis.

McEwen and Wingfield (2003) have formulated a process theory of stress and disease that refines and integrates the models of Cannon and Selye. The refinement consists of their distinction between homeostasis and allostasis. Originally, Cannon (1929) introduced the term homeostasis to describe the physiological processes that maintain steady states in an organism. McEwen and Wingfield use a more narrow definition; they describe homeostasis as the control of *vital* physiological systems. Vital conditions that can only vary within a rather limited range are for example temperature, oxygen tension in the tissues, and glucose in the blood. Allostasis, a term originally introduced by Sterling and Eyer (1988), means maintaining 'stability [in vital conditions] through change'. According to McEwen and Wingfield, allostasis refers to the active process in which physiological systems, including the SAM axis, the HPA axis, and the immune system, through continuous adaptation to the environmental demands, regulate the stability of vital conditions. The integration of McEwen and Wingfield's model is reflected in their focus on a broad spectrum of so-called mediators of allostatic processes, such as catecholamines of the SAM axis, glucocorticoids of the HPA axis, and cytokines

from the immune system. Furthermore, they describe different phases in the stress-adaptation process and their related changes in physiological functioning and health. McEwen and Wingfield state that allostatic mediators have protective effects in the short run, but can have damaging effects over longer time intervals. According to their model, an allostatic state occurs, when an altered and sustained activity level of the allostatic systems is required to adapt to environmental changes. An allostatic state is characterised by imbalances of allostatic mediators, e.g., enhanced or reduced levels of catecholamines or cortisol. Cumulative bodily consequences of an allostatic state are called allostatic load. When an allostatic state is sustained for a prolonged time and/or additional adaptations are needed, allostatic load can turn into overload. McEwen (1998) has distinguished different patterns of physiological responses that can result in allostatic load, that is, repeated exposure to multiple stressors, lack of physiological adaptation, prolonged response due to delayed turn-off of the physiological response, and an inadequate response that results in overcompensation of other physiological systems. McEwen and Wingfield (2003) pose that allostatic overload causes illness or physical damage and physiological changes that may be irreversible. Examples of these consequences are psychopathology, stomach ulcers, and cardiovascular disease.

Hybrid Models

Various models have been developed that integrate the psychological and physiological aspects of stress, e.g. the Cognitive-Affective Stress response model (Wofford & Daly, 1997), the Cognitive Activation Theory of Stress (e.g., Ursin & Eriksen, 2004), and the psychobiological model of traumatic stress-coping (Olff, 1999; Olff, Langeland & Gersons, 2005). These models can be seen as expansions or refinements of the Transactional Model of Lazarus and Folkman (1987) with a more prominent role of cognition and physiology. The model of Olff et al. (2005) for example, states that appraisal influences emotional and physiological reactions, which are both moderated by coping strategies. Adverse health outcomes can be expected when a) situations are appraised as threatening (in contrast to for example challenging), and b) the coping strategy is inadequate to reduce affective and physiological responses.

Research Questions

Below, five interrelated research questions that were formulated to meet our aims to enhance the insight in fundamental physiological and psychological characteristics of work-related stress and to evaluate the effectiveness of CBT for the treatment of work-related stress are introduced.

I: Is work-related stress characterised by dysregulation of the physiological stress-response system?

Dysregulation of the physiological stress-response system in association with work-related stress can be expected for three reasons. First, various models describe an effect of prolonged or repeated

exposure to stressors on physiological stress-response systems due the body's adaptation to increased environmental demands (e.g., Lazarus & Folkman, 1987; McEwen & Wingfield, 2003; Selye, 1975). Second, associations between physiological changes and chronic stress have been established (e.g., Lepore, Miles & Levy, 1997; Miller, Chen & Zhou, 2007; Nicolson & van Diest, 2000; Pike et al., 1997; Segerström & Miller, 2004; Wüst, Federenko, Hellhammer & Kirschbaum, 2000). Third, work-related stress demonstrates symptomatic and aetiological overlap with major depression, anxiety disorders, post-traumatic stress syndrome, and chronic fatigue syndrome; disorders that are characterised by physiological changes (Chrousos & Gold, 1992; Cleare, 2003; Heim, Ehlert, & Hellhammer, 2000; McEwen, 2003; Meewisse, Reitsma, de Vries, Gersons & Olff, 2007; Olff, Güzelcan, de Vries, Assies & Gersons, 2006).

To assess physiological dysregulation, we studied the following stress-response subsystems: a) the sympathetic system, including the SAM axis, b) the parasympathetic system, c) the HPA axis, and d) the immune system. The sympathetic system prepares the body for action, for example to fight or to flight in cases of threat. The parasympathetic system serves to bring the body in a state of rest in order to promote maintenance processes and digestion. The HPA axis is a neuroendocrine system that is involved in stress-regulation and other bodily processes, including the immune function, emotions, and energy storage and expenditure. The immune system is involved in the protection of the body against pathogens. Since the autonomic nervous system, the HPA axis, and the immune system broadly affect bodily functions, including the cardiovascular function, memory, emotion, and energy balance, studying these systems may also enhance the insight in the health complaints and the elevated risk for cardiovascular disease associated with work-related stress. The role of the stress-response subsystems in the acute stress-response is described in Box 2.

Box 2: The acute stress response.

An acute physiological stress response consists of an increase in activation of the sympathetic system (including the SAM axis), the HPA axis, and the immune system (Brownley, Hurwitz & Schneiderman, 2000; Lovallo & Thomas, 2000). The parasympathetic system can assist sympathetic functions by withdrawing its activity (Berntson et al., 2007). Via sympathetic innervation of the adrenal medulla, SAM axis activation results in release of catecholamines, such as adrenaline and noradrenaline, in the blood stream (Berntson et al., 2007; Cannon & de la Paz, 1911; Figure 1). These hormones are responsible for immediate rises in heart rate and blood pressure, extra blood supply to skeletal muscles, increased glucose levels in the blood (Lovallo & Thomas, 2000; Cannon, 1934), and increases of cardiac output and total peripheral resistance (Berntson et al., 2007). Cardiac output and total peripheral resistance are also directly regulated by sympathetic and parasympathetic innervation of the heart, arteries, and veins (Brownley et al., 2000).

The acute stress response of the HPA axis involves release of corticotropin releasing hor-

Box 2: continued.

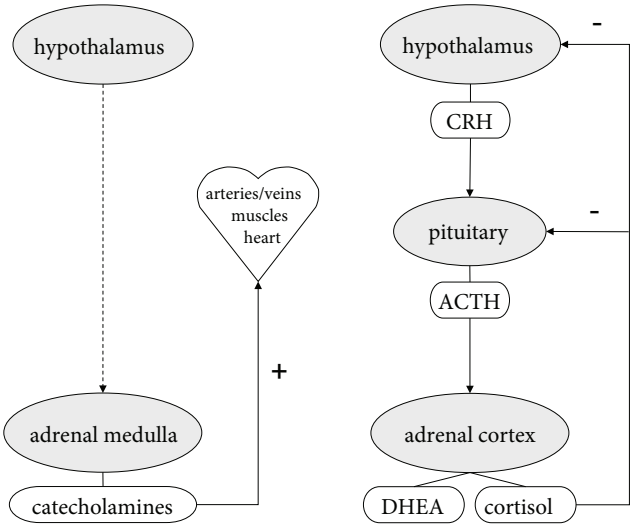

Figure 1: *Schematic overview of the Sympathetic Adrenal Medullary (SAM) axis (left) and the Hypothalamic Pituitary Adrenocortical (HPA) axis (right).*

Note: CRH: corticotropin releasing hormone; ACTH: adrenocorticotropic hormone; DHEA: dehydroepiandrosterone.

mone (CRH) from the hypothalamus, which activates the pituitary gland to release adrenocorticotropic hormone (ACTH) (Lovallo & Thomas, 2000; Figure 1). ACTH, in its turn, stimulates the adrenal cortex to release glucocorticoids (e.g., cortisol; Lovallo & Thomas, 2000) and steroids (e.g., DHEA; Kroboth et al., 1999). Increases of glucocorticoids and steroids occur within minutes after the onset of an acute stressor (Eriksen, Olff, Murrison & Ursin, 1999). Glucocorticoids enhance and prolong already enhanced blood glucose levels in tissues that need glucose, and suppress blood glucose utilisation and transport in peripheral tissues (Sapolsky, Romero & Munck, 2000). Further, cortisol enhances focused attention to the stressor and memory of the stressful event by its effects on brain structures such as the amygdala and the hippocampus (Erickson, Drevets & Schulkin, 2003; Sapolsky et al., 2000).

Cortisol production by the adrenals is regulated by a feedback system, in which cortisol in the brain indirectly inhibits its own production in the adrenals (Sapolsky et al., 2000; de Kloet, Vreugdenhil, Oitzl & Joels, 1998). De Kloet et al. (1998) describe this feedback mechanism in the brain in their Corticosteroid Receptor Balance model. The model states that the balance in actions mediated by two receptor types in the brain is critical for HPA axis activity. These two receptor types are the minerocorticoid receptors (MRs) and the gluco-

Box 2: continued.

corticoids receptors (GRs). MRs have a tenfold higher affinity for cortisol than GRs. Hence, when cortisol levels are within the normal range, cortisol binds considerably more to MRs than to GRs. MRs are the medium through which cortisol maintains the basal state of the HPA axis and controls the systems sensitivity to generate a stress response. In a situation of elevated cortisol levels, for example due to a stress response, all MRs become occupied by cortisol and cortisol starts to bind also to GRs. MRs and GRs together are considered to be essential to the inhibition of HPA axis activation in stressful situations.

In comparison to glucocorticoids, the effects and mechanisms involved in the release of steroids by the adrenal cortex in response to an acute stressor is less clear. DHEA rises in reaction to an acute stressor (Izawa et al., 2008). The exact target tissues and role of DHEA inthe stress response have not been clarified yet (Kroboth et al., 1999). There are indications, though, that DHEA affects activation in the anterior cingulated cortex, a part of the brain that is among others associated with memory processing (Alhaj et al., 2006).

An immune response to a stressor consists of a redistribution of immune cells and proteins into the body parts where they will be most effective, for example in locations such as oral tissue or skin-tissue where invaders or damage can be expected (Segerström & Miller, 2004; Sapolsky et al., 2000). When challenged, the natural immune reaction develops within minutes to hours. The generalised response by the natural immune reaction is inflammation (Segerström & Miller, 2004). In addition to damaging invaders and damaged tissue, the natural immune reaction also releases communication molecules, that is, cytokines (Segerström & Miller, 2004). Cytokines signal the specific immune system; they can be pro- or anti-inflammatory.

The SAM axis, the HPA axis, and the immune system have mutual influences. One of the most well known effects of the HPA axis is the anti-inflammatory effect by cortisol (Elenkov, Wilder, Chrousos & Vizi, 2000; Sapolsky et al., 2000). However, it has become clear that the SAM axis and HPA axis exert both stimulatory and inhibitory effects on different aspects of the immune system and vice versa (Dhabhar, 2007; Elenkov et al., 2000; Sapolsky et al., 2000).

Physiological dysregulation: basal activity, reactivity, and recovery

Changes in physiological activity can appear as changes in the *basal state* and as changes in *reactivity* to and/or *recovery* from an acute stressor. Changes in basal states may be expected when work-related stress is associated with ongoing physiological arousal due to cognitive processes such as worrying. Ongoing physiological arousal presumably results in an enhanced sympathetic tone, a more active HPA axis, and a suppressed inflammatory response. Alternatively, changes in basal states may develop as a physiological adaptation to ongoing or repeated arousal. Physiological stress adap-

tation of the sympathetic system is considered to lead to an enhanced sympathetic tone (e.g., Julius, 1993). Physiological stress adaptation with regard to the HPA axis is suggested to be associated with either a hyperactive HPA axis or a hypoactive HPA axis (Fries, Hesse, Helhammer & Hellhammer, 2005; Raison & Miller, 2003). Likewise, physiological stress adaptation may result in predominance of certain parts of the immune system (Segerström & Miller, 2004). Hence, we hypothesised that work-related stress would be associated with an enhanced sympathetic tone, with either a hyperactive, or a hypoactive HPA axis, and with a shift in the balance between parts of the immune system.

We predicted that work-related stress would be associated with enhanced cardiovascular and glucocorticoid responses to an acute stressor. The extent of cardiovascular reactivity to stressors is considered to be a trait-like response to stressors (Manuck, 1994; Kamarck & Lovallo, 2003). According to the 'reactivity hypothesis', enhanced sympathetic reactivity to stressors is a risk factor for hypertension and cardiovascular disease (e.g., Manuck, 1994). In other words, enhanced sympathetic reactivity may be a mechanism through which changes in basal activity develop. Evidence that enhanced reactivity is related to developing adverse cardiovascular profiles and hypertension has indeed been found (Gasperin, Netuveli, Dias-da-Costa & Patussi, 2009; Treiber et al., 2003). Since (work-related) stress has been linked to an increased risk for developing hypertension and cardiovascular disease (Chandola et al., 2008; Landsbergis et al., 2003; Manuck, 1994; Manuck et al., 1990; Melamed et al., 2006; Selye, 1975), enhanced reactivity may be the mechanism through which the adverse consequences develop. Accumulating evidence suggests that reactivity of the HPA axis to stressors is also a trait-like response (e.g., Gotlib, Joorman, Minor & Hallmayer, 2008; Kirschbaum et al., 1995a). Following similar reasoning as for sympathetic reactivity, enhanced HPA axis reactivity may be a mechanism through which changes in basal HPA axis activity develop. However, based on models of stress-adaptation of the HPA axis (e.g., Fries et al., 2005; Raison & Miller, 2003), reduced reactivity of the HPA axis may also be expected.

Delayed cardiovascular recovery is also hypothesised to be a risk factor for cardiovascular disease (e.g., Schwartz et al., 2003). Although the process of physiological recovery has been less extensively investigated, changes in recovery in association with prolonged exposure to stressors and with increased risk for cardiovascular disease have been reported (e.g., Schuler & O'Brien, 1997; Matthews, Gump & Owens, 2001; Moseley & Linden, 2006; Lepore et al., 1997). We also expected to find support for delayed sympathetic and HPA axis recovery in association with work-related stress.

To assess the patterns of reactivity and recovery, we applied an acute stress induction procedure, which is described below. Subsequently, the selected indicators of the sympathetic system, parasympathetic system, HPA axis, and immune system that were used to study dysregulation of the physiological stress-response system are introduced.

Acute stress induction

To investigate the acute physiological stress response, we chose a psychosocial stressor to induce stress. The psychosocial stressor consisted of a procedure highly similar to the Trier Social Stress Test (Kirschbaum, Pirke & Hellhammer, 1993). Psychosocial stressors have been proven to result

in subjective, cardiovascular, and neuroendocrine responses (e.g., Childs & de Wit, 2009; Nicholson & van Diest, 2000; Olff, Mulder, The, de Leij & Emmelkamp, 1999; Roy, Kirschbaum & Steptoe, 2001). In our opinion, to study acute physiological stress responses in work-related stress, a psychosocial stressor is more ecologically valid, than for example a physical stressor, such as the cold pressure test (Saab et al., 1993). Although separate central neurendocrine circuits have been suggested for different stressors (e.g., Pacák & Palkovits, 2001), the most important distinctions in stress-responses are considered to occur between physical and psychological stressors (Ostrander, Ulrich-Lai, Choi, Richtand & Herman, 2006; Sapolsky et al., 2000; Singh, Petrides, Gold, Chrousos & Deuster, 1999), supporting the external validity of our manipulation.

The sympathetic and parasympathetic system

The following indicators of the sympathetic and parasympathetic system were studied in rest and during a psychosocial stressor: heart rate, systolic blood pressure, diastolic blood pressure, cardiac output, peripheral resistance, alpha-amylase, and short-term heart rate variability. Cardiac output is the amount of blood that is pumped by the heart per minute (Berntson, Quigley & Lozano, 2007). Total peripheral resistance is a measure of the cumulative resistance of the peripheral arteries and veins (Berntson et al., 2007). Resistance is dependent upon the extent of vasoconstriction and blood viscosity; stronger vasoconstriction and lower oxygen levels in the blood increase resistance (Brownley et al., 2000). Heart rate, blood pressure, cardiac output, and total peripheral resistance all reflect the joint effect of sympathetic and parasympathetic activity (Berntson et al., 2007). Cardiac output and total peripheral resistance reflect haemodynamic properties of the cardiovascular system. Similar blood pressure levels may be a result of different balances between cardiac output and vascular resistance (e.g., Ring, Burns & Carroll, 2002). Hence, studying these measures in addition to heart rate and blood pressure results in a more refined view of the cardiovascular function. Alpha-amylase is a neuroendocrine indicator of sympathetic and parasympathetic activity. Alpha-amylase is an enzyme that is secreted by the salivary glands into the saliva. It is involved in initial carbohydrate digestion (Humphrey & Williamsion, 2001). Initially, an increase in alpha-amylase in reaction to an acute stressor was suggested to be a relatively pure measure of sympathetic reactivity (e.g., Chatterton, Vogelsong, Lu, Ellman, & Hudgens, 1996; Rohleder, Nater, Wolf, Ehlert & Kirschbaum, 2004). Recent evidence, however, supports the notion that an alpha-amylase increase in reaction to a *psychosocial* stressor reflects the sympathetic tone, which is determined by both sympathetic and parasympathetic activity (Nater et al., 2006). Rapid, or short-term, heart rate variability is a relatively pure measure of parasympathetic activity (Penttilä et al., 2001; Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996). We predicted that work-related stress would be associated with elevated basal levels and enhanced reactivity and delayed recovery of blood pressure, heart rate, cardiac output, vascular resistance, and alpha-amylase. We also predicted that work-related stress would be associated with a reduced basal level, stronger reductions during exposure to a psychosocial stressor, and delayed recovery of short-term heart rate variability.

The HPA axis

We chose to measure cortisol and dehydroepiandrosterone (DHEA), the main agents secreted by the adrenal cortex, as indicators of the HPA axis. Cortisol influences glucose levels in the blood and has anti-inflammatory effects (Sapolsky et al., 2000). DHEA is a precursor of androgens in men and estrogens in women and is further known to be related to glucose sensitivity, insulin activity (Kroboth, Salek, Pittenger, Fabia & Frye, 1999), mood (Alhaj, Massey & McAllister-Williams, 2006; Izawa et al., 2008), and memory (Alhaj et al., 2006). Higher DHEA levels are generally associated with better health conditions (e.g., Barrett-Connor, Khaw & Yen, 1986). DHEA has been proposed as a functional cortisol antagonist (e.g., Hechter, Grossman & Chatterton, 1997), and support for this notion has been obtained (e.g., Alhaj et al., 2006).

Salivary cortisol and DHEA fluctuate over the day (Hucklebridge, Hussein, Evans & Clow, 2005; Zhao et al., 2003). In the morning, during the first hour after awakening, cortisol demonstrates a steep rise, reaching levels in the range of a stress response. This rise is called the cortisol awakening response (CAR; Wilhelm, Born, Kudielka, Schlotz & Wüst, 2007). Studying the CAR may provide information about the HPA axis in a state of stress (Schmidt-Reinwald et al., 1999). Cortisol and DHEA levels were measured in saliva in the first hour after awakening and during the day. Cortisol levels were also measured upon exposure to the psychosocial stressor. We expected that work-related stress would be associated with either elevated basal levels, an elevated CAR, elevated reactivity, and delayed recovery during the psychosocial stressor of cortisol, or reduced basal levels, a reduced CAR, and reduced reactivity. We expected further that work-related stress would be associated with reduced basal levels of DHEA, as measured in its sulphated condition, that is, DHEAS.

The immune system

Within the immune system, two main components are commonly distinguished, namely natural (or innate) and specific immunity (Segerström & Miller, 2004). Cells involved in natural immunity are non-specific; they attack different pathogens. A specific immune response is slower than the natural immune response (Segerström & Miller, 2004). Specific immunity is composed of cellular and humoral responses (Segerström & Miller, 2004). Cellular immune responses are raised against intracellular pathogens, like viruses and intracellular bacteria (Dhabhar, 2007). These responses are coordinated by a particular type of T-helper lymphocytes called Th1 cells. Humoral immune responses are mounted against extracellular pathogens, such as parasites and extracellular bacteria (Sanders, Kin & Pongratz, 2007). They are coordinated by another type of T-helper lymphocytes called Th2 cells (Dhabhar, 2007). Th1 and Th2 responses are mutually inhibitory (Elenkov, Iezzoni, Daly, Harry & Chrousos, 2005). To assess the immune function, we selected C-reactive protein (CRP) and Immunoglobulin G (IgG) against Epstein Barr virus (EBV). These measures can be adequately determined in saliva. CRP is a marker of the inflammatory response of the complement system (Koenig, 2001), which is a subsystem of the natural immune response. IgG against EBV is an indicator of cellular immunity, that is, a higher level of IgG against EBV is a sign of poorer cellular immunity (Sarid, Anson, Yaari & Margalith, 2001). We expected that the changes in CRP

and IgG against EBV would be contingent upon the direction of change of cortisol. Hence, we predicted that upon finding enhanced cortisol levels we would observe reduced CRP and enhanced IgG against EBV, or, upon finding reduced cortisol levels we would detect enhanced CRP and reduced IgG against EBV.

II: Can different phases be distinguished in the physiological stress-adaptation process?

Physiological process theories introduced earlier (e.g., McEwen & Wingfield, 2003; Selye, 1975) describe that the nature of physiological dysregulation is contingent upon the duration of exposure to a stressor. More specifically, physiological changes during the initial resistance phase or in an allostatic state are hypothesised to differ from changes during the subsequent exhaustion phase or in a state of allostatic overload. Exposure duration is a well-controlled factor in experimental animal stress research, but this factor is commonly neglected in human research about chronic stress. Nevertheless, human research also provides many indications for differences between short-term and long-term physiological adaptations to stressors. The short-term dysregulation developing within weeks to months of stressor exposure can be considered as characteristic of the resistance phase or an allostatic state. The long-term dysregulation that develops within months to years can be viewed as characteristic of exhaustion or allostatic overload. The details of the development of these physiological processes and associated mechanisms of change remain far from clear. The contrasts between short-term and long-term sympathetic and parasympathetic adaptation to stress that guided our hypothesis are documented below.

Short-term and long-term adaptations of the sympathetic and parasympathetic systems

In the short term, the balance between sympathetic and parasympathetic activity appears to shift to a more dominant sympathetic system, resulting in enhanced indicators of sympathetic activity in rest and in reaction to stressors. To illustrate, animal research has demonstrated that repeated exposure to stressors initially results in elevated basal levels of catecholamines and elevated systolic blood pressure within a month (Henry, Meehan & Stephens, 1967; McCarthy, Horwatt & Konarska, 1988). Furthermore, increased reactivity is observed to repeated exposure to novel stressors (McCarthy et al., 1988). In humans, elevated basal cardiovascular activity in stressed individuals has been frequently confirmed (e.g., Cacioppo et al., 2000; Vrijkotte, van Doornen & de Geus, 2000). In addition, indications were found for an association between persistent exposure to stressors and increased cardiovascular reactivity and delayed recovery to an acute stressor (Lepore et al., 1997; Pike et al., 1997).

Concerning the longer-term effects of stressor exposure, human and animal research suggest that the balance between cardiac and vascular activity changes and that this changed balance persists and represents a new physiological equilibrium. A study with monkeys, for instance, revealed that during eight months of exposure to a stressor, basal blood pressure started to increase between four and eight months, while heart rate decreased in this period (Forsyth, 1969). Similarly, in humans, the process of developing hypertension is considered to start with tachycardia and el-

evated cardiac output (Grassi, Quarti-Trevano, Dell'Oro & Mancia, 2008; Palatini & Julius, 2009), which gradually changes towards increased vascular resistance, and normalisation of heart rate and cardiac output (Palatini & Julius, 2009). Regarding persistence of a changed cardiovascular balance, animal studies provide indications that irreversibility of physiological adaptations can occur after stressor exposure of six to twelve months duration (Forsyth, 1969; Henry et al., 1967). In these studies, hypertension sustained for at least several months after cessation of the stressor. In humans, findings suggest that established hypertension develops after the transition from an enhanced sympathetic tone to a state of enhanced vascular resistance (Palatini & Julius, 2009). A new cardiovascular equilibrium has been proposed to result from reduced sensitivity of β–adrenergic receptors in the heart and reduced stroke volume and vascular hypertrophy and hypersensitivity to vasoconstrictive agents (Palatini & Julius, 2009). In sum, we predicted that short-term cardiovascular stress adaptation would be associated with elevated levels of heart rate and cardiac output, while long-term cardiovascular adaptation would be associated with elevated vascular resistance.

III: Is cognitive behavioural treatment effective as a treatment for work-related stress?

Effectiveness of cognitive behavioural treatment for work-related stress and associated physiological changes may be expected for three reasons. First, effectiveness can be deferred from the presumed central role that cognitive and behavioural processes play in the development and perpetuation of stress and associated physiological changes, as for example described in the stress-model of Lazarus and Folkman (1987). Second, cognitive behavioural interventions are effective for a variety of psychiatric disorders (Butler, Chapman, Forman & Beck, 2006; Price & Couper, 2000). These disorders include mood and anxiety disorders, disorders that demonstrate symptomatic and aetiological similarities to work-related stress. Third, evidence for effectiveness of cognitive behavioural interventions as preventive interventions in relatively healthy samples with work-related stress is present (van der Klink, Blonk, Schene & van Dijk, 2001; de Jong & Emmelkamp, 2000; Rowe, 2000; van Dierendonck, Schaufeli & Buunk, 1998). In these studies, improvements of complaints and coping were achieved. In addition, influences of cognitive behavioural interventions on physiological functioning have been demonstrated in healthy or physically ill individuals (e.g., Antoni et al., 2005; Cruess et al., 2000; Gaab et al., 2003; Kiecolt-Glaser et al., 1985; McCraty, Barrios-Choplin, Rozman, Atkinson & Watkins, 1998; Miller & Cohen, 2001) and in individuals with a diagnosis of generalised anxiety disorder (Tafet, Feder, Abulafia & Roffman, 2005). Hence, we hypothesised that CBT would result in stronger reductions of complaints, more work-resumption, and larger physiological changes than care as usual. Basic treatment characteristics of our CBT are documented below.

Cognitive Behavioural Treatment: content, dosing, and format

CBT consisted of cognitive behavioural elements and relaxation techniques. We chose to include relaxation techniques because they have yielded positive effects on cardiovascular and neuroendocrine functions in healthy individuals (e.g., McCraty et al., 1998).

The CBT comprised twelve treatment-sessions. The number of sessions is similar to other regular cognitive-behavioural treatments in primary psychological care. Our choice was supported by the conclusions drawn in the meta-analyses of van der Klink et al. (2001). They reported optimal effectiveness of cognitive behavioural interventions (excluding relaxation techniques) of 6-8 sessions in relatively healthy samples.

Effectiveness of cognitive behavioural treatment in a group format and in the more common individual format was investigated. Based on potent treatment factors specific to group interventions, such as disconfirmation of the uniqueness of problems, interpersonal learning, and social support (Yalom, 1985), effectiveness of treatment in a group format was expected. As preventive interventions, effectiveness of cognitive behavioural interventions for work-related stress in a group format is indeed well established (van Dierendonck et al., 1998; de Jong & Emmelkamp, 2000; van der Klink et al., 2001; Reynolds & Briner, 1994; Rowe, 2000). Social support is also associated with cortisol (e.g., Evolahti, Hultcrantz & Collins, 2006; Kirschbaum Klauer, Filipp & Hellhammer, 1995b; Turner-Cobb, Sephton, Koopman, Blake-Mortimer & Spiegel, 2000; Wadhwa, Dunkel-Schetter, Chicz-DeMet, Porto & Sandman, 1996) and with immune functioning (e.g., Gallangher, Phillips, Ferraro, Drayson & Carrol, 2008; Glaser et al., 1992; Lutgendorf et al., 2005; Miller, Chen & Cole, 2009). Hence, an effect of social support as a treatment component may also be expected on physiological variables.

IV: What are predictors of recovery of work-related stress?

While the development of work-related stress has been extensively studied and has resulted in potent models including the JDCS-model of Karasek (Karasek & Theorell, 1990), the process of recovery has been studied less comprehensively. In order to enhance insight in the recovery process, determinants of complaints improvement and work-resumption were investigated. Furthermore, the association between complaints reduction and work-resumption was assessed and a mediation model was tested.

Selected predictors were work-related characteristics, personal characteristics, and illness-related features. The predictors age, gender, and education were chosen because of demonstrated relations with recovery from work-related stress or similar conditions by other researchers (Nieuwenhuijsen, Verbeek, de Boer, Blonk & van Dijk, 2006; Huibers et al., 2004; Eshøj, Jepsen & Nielsen, 2001). Selection of other predictors was based on their hypothesised role in the development and/or maintenance of work-related stress or similar conditions as described in the JDCS-model of Karasek et al. (1982), the Transactional Model of Lazarus and Folkman (1987), or the Cognitive Theory of Beck (1976). Becks Cognitive Theory states that certain schemas and cognitive biases are associated with different forms of psychopathology.

There are two arguments supporting the expectation that predictors of development of work-related stress also predict recovery. First, higher levels of predictor variables are likely to be associated with more severe complaints, which may take longer to normalise. Second, higher levels of predictor variables are probable indicators of less favourable conditions for recovery. For exam-

ple, work characterised by high workload and low supervisor support may reduce motivation to resume work. Alternatively, conflict at work may function as a persistent stressor during sickness absence preventing recovery. Otherwise, a stronger tendency for avoidant coping and/or dysfunctional cognitions suggests presence of dispositional features of negative affect, which may hinder complete recovery. Selection of the illness-related variables complaint duration and absence duration was based on similar reasoning. It was assumed that duration can be seen an indicator of severity of complaints and/or an indirect indicator of adverse conditions for recovery (e.g., presence of a persistent stressor).

V: Is alexithymia a vulnerability factor or a consequence of work-related stress?

Alexithymia is a deficit characterised by impaired emotional processing (Sifneos, 1996; Taylor, Bagby & Parker, 1997). A clinically elevated level of alexithymia is characterised by difficulties in experiencing and expressing emotions, a diminished inclination to think about emotions, a reduction or incapacity to fantasise, and a more externally oriented cognitive style (Sifneos, 1996; Taylor et al., 1997).

Two types of alexithymia are distinguished, primary alexithymia and secondary alexithymia (Taylor et al., 1997). Primary alexithymia is described as a personality characteristic that increases the risk of developing psychopathology (Sifneos, 1996; Taylor et al., 1997). Secondary alexithymia is defined as an inadequate coping reaction, a defensive state, or a state of failure of defences in reaction to a stressful, painful, or traumatic situation (Freyberger, 1977; Hendryx, Haviland & Shaw, 1991; Taylor et al., 1997). An association between both primary and secondary alexithymia and work-related stress was expected for the following reasons. First, based on the view that emotions are essential for an adequate interaction with the external world, primary alexithymia is hypothesised to be a vulnerability factor for, among others, work-related stress. Alexithymia is indeed related to a large variety of psychopathology, including anxiety and depressive disorders, disorders that bear resemblance to work-related stress in symptoms and aetiology (e.g., Söndergaard & Theorell, 2004; Duddu, Isaac & Chaturvedi, 2003; Bankier, Aigner & Bach, 2001). Second, secondary alexityhmia may develop parallel to work-related stress in reaction to a stressful work-situation. In the field of organisational psychology, depersonalisation is described as a cynical, distant attitude towards work that develops in reaction to work-overload (Maslach et al., 2001). This depersonalisation suggests presence of emotional disturbances related to emotional numbing that are to some extend similar to characteristics of alexithymia.

Brief outline of the thesis

In this thesis, psychological and physiological characteristics of work-related stress were investigated and the efficacy of a CBT protocol for work-related stress was tested. First, it was assessed whether work-related stress was characterised by changes in the sympathetic, parasympathetic, neuroendocrine, and/or immune functions (Chapters 2-4). For these studies, patient samples were

compared with healthy reference groups. Second, it was investigated whether different phases could be distinguished in the physiological stress-adaptation process (Chapter 5). Therefore, subgroups of patients with shorter and longer duration of complaints were followed longitudinally and compared on cardiovascular variables. Third, differential effectiveness of cognitive behavioural treatment as compared to care as usual was studied. Outcome variables were complaints, work-resumption, subjective effectiveness (Chapter 6), and physiological functioning (Chapters 7-8). For these studies, a patient sample was followed for a period of 10 months. Fourth, the process of recovery was assessed. Predictors of two indicators of recovery, that is, complaints levels and work-resumption, were investigated and potential mediation of improvement of complaints in the association between predictors and work-resumption was examined (Chapter 9). Selected predictors were work-related, person-related, and illness-related characteristics. Predictors, complaint reduction, and work-resumption were investigated over a period of about one year in a patient sample. Fifth, the association between alexithymia and work-related stress was studied (Chapter 10). It was assessed whether alexithymia was a risk factors or a consequence of work-related stress. Therefore, longitudinal stability and change of alexithymia in association with work-related stress were studied in a patient sample and a healthy reference group. Finally, the general discussion integrates research findings, discusses limitations, presents clinical implications, and provides suggestions for further research (Chapter 11).

The data used in the individual chapters come from subsamples of a larger patient sample and three independent healthy samples. In Figure 2, a representation of the (sub)samples studied per chapter is provided. Since the chapters are presented as autonomous parts, they demonstrate textual overlap, specifically in method sections.

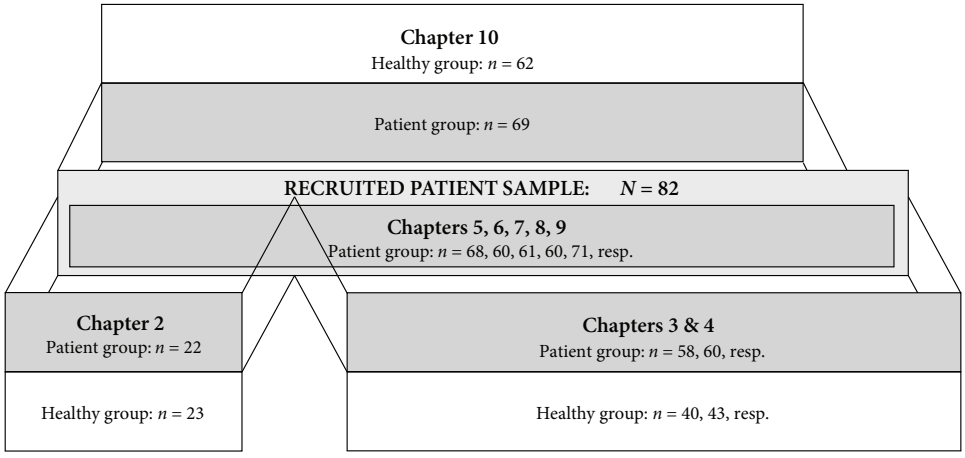

Figure 2: *Overview of the (sub)samples studied per chapter*

References

Alhaj, H.A., Massey, A.E. & McAllister-Williams, R.H. (2006). Effects of DHEA administration on episodic memory, cortisol and mood in healthy young men: a double-blind, placebo-controlled study. *Psychopharmacology*, *188*, 541-551.

Antoni, M.H., Cruess, D.G., Klimas, N., Carrico, A.W., Maher, K., Crues, S., Lechner, S.C., Kumar, M., Lutgendorf, S., Ironson, G., Fletcher, M.A. & Schneiderman, N. (2005). Increases in a marker of immune system reconstitution are predated by decreases in 24-h urinary cortisol output and depressed mood during a 10-week stress management intervention in symptomatic HIV-infected men. *Journal of Psychosomatic Research*, *58*, 3-13.

American Psychiatric Association (1994). *Diagnostic and statistical manual of mental disorders: 4th ed. (DSM-IV).* Washington DC: American Psychiatric Association.

Bakhuys Roozeboom, M., Gouw, P., Hooftman, W., Houtman, I. & Klein Hesselink, J. (2008). *Arbobalans* 2007/2008. *Kwaliteit van arbeid, effecten en maatregelen* [Occupational balance 2007/2008. Quality of labour, effects and interventions]. TNO Kwaliteit van Leven, Hoofddorp, The Netherlands.

Bankier, B., Aigner, M. & Bach, M. (2001). Alexithymia in DSM-IV disorders. Comparative evaluation of somatoform disorder, panic disorder, obsessive-compulsive disorder, and depression. *Psychosomatics*, *42*, 235-240

Barrett-Connor, E., Khaw, K.T. & Yen, S.S. (1986). A prospective study of dehydroepiandrosterone sulphate, mortality and cardiovascular disease. *New England Journal of Medicine*, *315*, 1519–1524.

Beck, A.T. (1976). *Cognitive therapy and the emotional disorders.* New York: International Universities Press, United States of America.

Berntson, G.G., Quigley, K.S. & Lozano, D. (2007). Cardiovascular physiology. In: J.T. Cacioppo, L.G. Tassinary, G.G. Berntson (Eds.), *Handbook of psychophysiology* (3rd ed., pp. 182-210). Cambridge University Press, New York, United States of America.

Blatter, B., Houtman, I., van den Bossche, S., Kraan, K. & van den Heuvel, S. (2005). *Gezondheidsschade en kosten als gevolg van RSI en psychosociale arbeidsbelasting in Nederland* [Health impairment and costs as a consequence of repetitive strain injury and psychosocial workload in the Netherlands]. TNO, Kwaliteit van Leven, Hoofddorp, The Netherlands.

Brownley, K.A., Hurwitz, B.E. & Schneiderman, N. (2000). Cardiovascular psychophysiology. In: J.T. Cacioppo, L.G. Tassinary, G.G. Berntson (Eds.), *Handbook of psychophysiology* (2nd ed., pp. 224-264). Cambridge University Press, New York.

Butler, A.C., Chapman, J.E., Forman, E.M. & Beck, A.T. (2006). The empirical status of cognitive behavioural therapy: A review of meta-analyses. *Clinical Psychology Review*, *26*, 17-31.

Cacioppo, J.T., Burleson, M.H., Poehlman, K.M., Malarky, W.B., Kiecolt-Glaser, J.K., Berntson, G.G., Uchino, B.N. & Glaser, R. (2000). Autonomic and neuroendocrine responses to mild psychological stressors: effects of chronic stress on older women. *Annals of Behavioral Medicine*, *22*, 140-148.

Cannon, W.B. (1934). The significance of the emotional level. *The Scientific Monthly*, *38*, 101-110.

Cannon, W.B. (1929). The sympathetic division of the autonomic system in relation to homeostasis. *Archives of Neurology & Psychiatry*, *22*, 282-294.

Cannon, W.B. (1914). The emergency function of the adrenal medulla in pain and the major emotions. *American Journal of Physiology*, *33*, 356-372.

Cannon, W.B. & de la Paz, D. (1911). Emotional stimulation of adrenal secretion. *American Journal of Physiology*, *28*, 64-70.

Chandola, T., Britton, A., Brunner, E., Hemingway, H., Malik, M., Kumari, M., Badrick, E., Kivimaki, M. & Marmot, M. (2008). Work stress and coronary heart disease: what are the mechanisms? *European Heart Journal*, *29*, 640-648.

Chatterton, R.T., Vogelsong, K.M., Lu, Y., Ellman, A.B., Hudgens, G.A. (1996). Salivary α-amylase as a measure of endogenous adrenergic activity. *Clinical Physiology*, *16*, 433-448.

Childs, E. & de Wit, H. (2009). Hormonal, cardiovascular, and subjective responses to acute stress in smokers. *Psychopharmacology*, *203*, 1-12.

Chrousos, G.P. & Gold, P.W. (1992). The concepts of stress and stress system disorders. Overview of physical and behavioural homeostasis. *Journal of the American Medical Association*, *267*, 1244-1252.

Cleare, A.J. (2003). The neuroendocrinology of chronic fatigue syndrome. *Endocrine Review*, *24*, 236-252.

Cohen, S. & Herbert, T.B. (1996). Health psychology: Psychological factors and physical disease from the perspective of human psychoneuroendocrinology. *Annual Review of Psychology*, *47*, 113-142.

Cruess, D.G., Antoni, M.H., McGregor, B.A. Kilbourn, K.M., Boyers, A.E., Alferi, S.M., Carver, C.S. & Kumar, M. (2000). Cognitive-behavioral stress management reduces serum cortisol by enhancing benefit finding among women being treated for early stage breast cancer. *Psychosomatic Medicine*, *62*, 304-308.

de Jong, M. & Emmelkamp, P.M.G. (2000). Comparative trainer effectiveness. *Journal of Occupational Health Psychology*, *5*, 309-320.

de Kloet, E.R., Vreugdenhil, E., Oitzl, M.S. & Joels, M. (1998). Brain corticosteroid receptor balance in health and disease. *Endocrine Reviews*, *19*, 269-301.

Dhabhar, F.S. (2007). Innate and cell-mediated immunity: Basic principles and psychophysiological influences. In: J.T. Cacioppo, L.G. Tassinary, G.G. Berntson (Eds.), *Handbook of psychophysiology* (3rd ed, pp. 347-366). Cambridge University Press, New York, United States of America.

Duddu, V., Isaac, M.K. & Chaturvedi, S.K. (2003). Alexithymia in somatoform and depressive disorders. *Journal of Psychosomatic Research*, *54*, 435-438.

Elenkov, I.J., Wilder, R.L., Chrousos, G.P. & Vizi, E.S. (2000). The sympathetic nerve – An integrative interface between two supersystems: The brain and the immune system. *Pharmacological Reviews*, *52*, 595-638.

Elenkov, I.J., Iezzoni, D.G., Daly, A., Harris, A.G. & Chrousos, G.P. (2005). Cytokine dysregulation, inflammation and well-being. *Neuroimmunomodulation*, *12*, 255-259.

Eriksen, H.R., Olff, M., Murrison, R. & Ursin, H. (1999). The time dimension in stress responses: relevance for survival and health. *Psychiatry Research*, *85*, 39-50.

Erickson, K., Drevets, W. & Schulkin, J. (2003). Glucocorticoid regulation of diverse cognitive functions in normal and pathological emotional states. *Neuroscience and Biobehavioral Reviews*, *27*, 233-246.

Eshøj, P., Jepsen, J.R. & Nielsen, C.V. (2001). Long-term sickness absence – risk indicators among occupationally active residents of a Danish county. *Occupational Medicine*, *51*, 347-353.

European Communities (2004). *Work and Health in the EU: A statistical portrait. Data:* 1994-2002. Luxem-

bourg: Office for Official Publications of the European Communities. Retrieved August 16, 2005, http://epp.eurostat.cec.eu.int/cache/ITY_OFFPUB/KS-57-04-807/EN/KS-57-04-807-EN.PDF.

Evolahti, A., Hultcrantz, M. & Collins, A. (2006). Women's work-stress and cortisol levels: A longitudinal study of the association between the psychosocial work environment and serum cortisol. *Journal of Psychosomatic Research*, *61*, 645-652.

Forsyth, R.P. (1969). Blood pressure responses to long-term avoidance schedules in the restrained rhesus monkey. *Psychosomatic Medicine, XXXI*, 300-309.

Freyberger, H. (1997). Supportive psychotherapeutic techniques in primary and secondary alexithymia. *Psychotherapy and Psychosomatics*, *28*, 337-342.

Fries, E., Hesse, J., Helhammer, J. & Hellhammer, D.H. (2005). A new view on hypocortisolism. *Psychoneuroendocrinology*, *30*, 1010-1016.

Gaab, J., Blättler, N., Menzi, T., Pabst, B., Stoyer, S. & Ehlert, U. (2003). Randomized controlled evaluation of the effects of cognitive-behavioral stress-management on cortisol responses to acute stress in healthy subjects. *Psychoneuroendocrinology*, *28*, 767-779.

Gallangher, S., Phillips, A.C., Ferraro, A.J., Drayson, M.T. & Carrol, D. (2008). Psychosocial factors are associated with the antibody response to both thymus-dependent and thymus-independent vaccines. *Brain, Behavior, and Immunity*, *22*, 456-460.

Gasperin, D., Netuveli, G., Dias-da-Costa, J.S. & Patussi, M.P. (2009). Effect of psychological stress on blood pressure increase: a meta-analysis of cohort studies. *Cadernos de Saúde Pública*, *25*, 715-726.

Glaser, R., Kiecolt-Glaser, J.K., Bonneau, R.H., Malarky, W., Kennedy, S. & Hughes, J. (1992). Stress-induced modulation of the immune response to recombinant hepatitis B vaccine. *Psychosomatic Medicine*, *54*, 22-29.

Gotlib, I.H., Joorman, J., Minor, K.L. & Hallmayer, J. (2008). HPA axis reactivity: A mechanism underlying the associations among 5-HTTLPR, stress and depression. *Biological Psychiatry*, *63*, 847-851.

Grassi, G., Quarti-Trevano, F., Dell'Oro, R. & Mancia, G. (2008). Essential hypertension and the sympathetic nervous system. *Neurological Sciences*, *29*, S33-S36.

Hechter, O., Grossman, A. & Chatterton, R.T. Jr. (1997). Relationship of dehydroepiandrosterone and cortisol in disease. *Medical Hypotheses*, *49*, 85-91.

Heim, C., Ehlert, U. & Hellhammer, D.H. (2000). The potential role of hypocortisolism in the pathophysiology of stress-related bodily disorders. *Psychoneuroendocrinology*, *25*, 1-35.

Hendryx, M.S., Haviland, M.G. & Shaw, D.G. (1991). Dimensions of alexithymia and their relationships to anxiety and depression. *Journal of Personality Assessment*, *56*, 227-237.

Henry, J.P., Meehan, J.P. & Stephens, P.M. (1967). The use of psychosocial stimuli to induce prolonged systolic hypertension in mice. *Psychosomatic Medicine, XXIX*, 408-432.

Hoogduin, C.A.L., Schaap, C.P.D. & Methorst, G.J. (1996*). Burnout: Klinisch beeld en diagnostiek* [Burnout: clinical description and diagnostics]. In: C.A.L. Hoogduin, C.P.D., Schaap, A.J. Kladler & W.A. Hoogduin (Eds.), *Behandelingsstrategieën bij burnout* [Treatment strategies for burnout]. Bohn Stafleu van Loghum, Houten/Diegem.

Houtman, I.L.D., Smulders, P.G.W., & Hesselink, D.J. (Eds.) (2004). *Trends in arbeid* [Trends in labour]. Nederlandse Organisatie voor Toegepast Natuurwetenschappelijk Onderzoek, Hoofddorp, The Netherlands.

Hucklebridge, F., Hussain, T., Evans P. & Clow, A. (2005). The diurnal patterns of the adrenal steroids cortisol and dehydroepiandrosterone (DHEA) in relation to awakening. *Psychoneuroendocrinology*, *30*, 51-57.

Huibers, M.J.H., Beurskens, A.J.H., van Schayck, C.P., Bazelmans, E., Metsemakers, J.F.M. & Knottnerus, J.A. (2004). Efficacy of cognitive-behavioural therapy by general practitioners for unexplained fatigue among employees: A randomised controlled trial. *British Journal of Psychiatry*, *184*, 240-246.

Humphrey, S.P. & Williamsion, R.T. (2001). A review of saliva: normal composition, flow, and function. *The Journal of Prosthetic Dentistry*, *85*, 162-169.

Izawa, S., Sugaya, N., Shirotsuki, K., Yamada, K.C., Ogawa, N., Ouchi, Y., Nagano, Y., Suzuki, K. & Nomura, S. (2008). Salivary Dehydroepiandrosterone secretion in response to acute psychosocial stress and its correlations with biological and psychological changes. *Biological Psychology*, *25*, 294-298.

Jones, J.R., Huxtable, C.S., Hodgson, J.T. & Price M.J. (2003). *Self-reported work-related illness in* 2001/02*: results from a household survey*. Health and Safety Executive. Retrieved May 11, 2005, http://www.hse.gov.uk/statistics/causdis/swio102.pdf.

Julius, S. (1993). Sympathetic hyperactivity and coronary risk in hypertension. *Hypertension*, *21*, 886-893.

Kaltsas, G.A. & Chrousos, G.P. (2007). The neuroendocrinology of stress. In: J.T. Cacioppo, L.G. Tassinary, G.G. Berntson (Eds.), *Handbook of psychophysiology* (3rd ed., pp. 303-318). Cambridge University Press, New York, United States of America.

Kamarck, T.W. & Lovallo, W.R. (2003). Cardiovascular reactivity to psychological challenge: Conceptual and measurement considerations. *Psychosomatic Medicine*, *65*, 9-21.

Kant, IJ., Janssen, N.W.H., van Amelsvoort, L.G.R., Mohren, D.C.L. & Swaen, G.M.H. (2004). Burnout in de werkende bevolking. Resultaten van de Maastrichtse Cohort Studie [Burnout in the working population. Results of the Maastricht Cohort Study]. *Gedrag en Organisatie: tijdschrift voor sociale, economische en arbeids- en organisatiepsychologie*, *17*, 15-17.

Karasek, R.A. (1979). Job demands, job decision latitude and mental strain: implication for job redesign. *Administrative Science Quarterly*, *24*, 285-306.

Karasek, R.A. & Theorell, T. (1990). Healthy work. New York, Basic Books, United States of America.

Karasek, R.A., Triantis, K.P. & Chaudry, S.S. (1982). Coworker and supervisor support as moderators of associations between task characteristics and mental strain. *Journal of Occupational Behaviour*, *3*, 181-200.

Kiecolt-Glaser, J.K., Glaser, R., Willinger, D., Stout, J., Messink, G., Sheppard, S., Ricker, D., Romisher, S.C., Briner, W., Bonnell, G. & Donnerberg, R. (1985). Psychosocial enhancement of immunocompetence in a geriatric population. *Health Psychology*, *4*, 25-41.

Kiecolt-Glaser, J.K. & Glaser, R. (1995). Psychoneuroimmunology and health consequences: Data and shared mechanisms. *Psychosomatic Medicine*, *57*, 269-274.

Kirschbaum, C., Klauer, T., Filipp, S. & Hellhammer, D.H. (1995b). Sex-specific effects of social support on cortisol and subjective responses to acute psychological stress. *Psychosomatic Medicine*, *57*, 23-31.

Kirschbaum, C., Pruessner, J.C., Stone, A.A., Federenko, I., Gaab, J., Lintz, D., Schommer, N. & Hellhammer, D.H. (1995a). Persistent high cortisol responses to repeated psychological stress in a subpopulation of healthy men. *Psychosomatic Medicine*, *57*, 468-474.

Kirschbaum, C., Pirke, K.M. & Hellhammer, D.H. (1993). The 'Trier Social Stress Test' – a tool for investigating

psychobiological stress responses in a laboratory setting. *Neuropsychobiology*, *28*, 76-81.

Koenig, W. (2001). C-reactive protein: risk assessment in the primary prevention of atherosclerotic disease. Has the time come for including it in the risk profile? *Italian Heart Journal*, *2*, 157-163.

Kroboth, P.D., Salek, F.S., Pittenger, A.L., Fabia, T.J. & Frye, R.F. (1999). DHEA and DHEA-S: A review. *Journal of Clinical Pharmacology*, *39*, 327-348.

Landelijk Instituut Sociale Verzekeringen (2001). *Ziektendiagnoses bij uitkeringen voor arbeidsongeschiktheid* [Diagnoses of disability benefit recipients]. LISV, Amsterdam, The Netherlands.

Landsbergis, P.A., Schnall, P.L., Pickering, T.G., Warren, K. & Schwartz, J.E. (2003). Life course exposure to job strain and ambulatory blood pressure in men. *American Journal of Epidemiology*, *157*, 988-1006.

Lazarus, R.S. & Folkman, S. (1987). Transactional Theory and research on emotions and coping. *European Journal of Personality*, *1*, 141-169.

Lepore, S.J., Miles, H.J. & Levy, J.S. (1997). Relation of chronic and episodic stressors to psychological distress, reactivity, and health problems. *International Journal of Behavioral Medicine*, *4*, 39-59.

Levenstein, S., Ackerman, S., Kiecolt-Glaser, J.K. & Dubois, A. (1999). Stress and peptic ulcer disease. *Journal of the American Medical Association*, *281*, 10-11.

Lovallo, W.R. & Thomas, T.L. (2000). Stress hormones in psychophysiological research. Emotional, behavioural, and cognitive implications. In: J.T. Cacioppo, L.G. Tassinary, G.G. Berntson (Eds.), *Handbook of psychophysiology* (2nd ed., pp. 342-367). Cambridge University Press, New York, United States of America.

Lutgendorf, S.K., Sood, A.K., Anderson, B., McGinn, S., Maiseri, H., Dao, M., Sorosky, J.I., De Geest, K., Ritchie, J. & Lubaroff, D.M. (2005). Social support, psychological distress, and natural killer cell activity in ovarian cancer. *Journal of Clinical Oncology*, *23*, 7105-7113.

Manuck, S.B. (1994). Cardiovascular reactivity in cardiovascular disease: "Once more unto the breach". *International Journal of Behavioural Medicine*, *1*, 4-31.

Manuck, S.B., Kasprowicz, A.L. & Muldoon, M.F. (1990). Behaviorally-evoked cardiovascular reactivity and hypertension: conceptual issues and potential associations. *Annals of Behavioral Medicine*, *12*, 17-29.

Maslach, C., Schaufeli, W.B. & Leiter, M.P. (2001). Job Burnout. *Annual Review of Psychology*, *52*, 397-422.

Matthews, K.A., Gump, B.B. & Owens, J.F. (2001). Chronic stress influences cardiovascular and neuroendocrine responses during acute stress and recovery, especially in men. *Health Psychology*, *20*, 403-410.

McCarthy, R., Horwatt, K. & Konarska, M. (1988). Chronic stress and sympathetic-adrenal medullary responsiveness. *Social Science and Medicine*, *26*, 333-341.

McCraty, R., Barrios-Choplin, B., Rozman, D., Atkinson, M. & Watkins, A.D. (1998). The impact of new emotional self-management program on stress, emotions, heart rate variability, DHEA and cortisol. *Integrative Physiological and Behavioral Science*, *33*, 151-170.

McEwen, B.S. (2003). Mood disorders and medical illness; Mood disorders and allostatic load. *Biological Psychiatry*, *54*, 200-207.

McEwen, B.S. (1998). Protective and damaging effects of stress mediators. *Seminars in Medicine of the Beth Israel Deaconess Medical Center*, *338*, 171-179.

McEwen, B.S. & Wingfield, J.C. (2003). The concept of allostasis in biology and biomedicine. *Hormones and Behavior*, *43*, 2-15.

Meewisse, M.L., Reitsma, J.B., de Vries, G.J., Gersons, B.P.R. & Olff, M. (2007). Cortisol and posttraumatic stress disorder in adults: a systematic review and meta-analysis. *British Journal of Psychiatry*, *191*, 387-392.

Melamed, S., Shirom, A., Toker, S., Berliner, S. & Shapira, I. (2006). Burnout and risk of cardiovascular disease: Evidence, possible causal paths, and promising research directions. *Psychological Bulletin*, *132*, 327-353.

Miller, G., Chen, E. & Cole, S.W. (2009). Health psychology: Developing biologically plausible models linking the social world and physical health. *Annual Review of Psychology*, *60*, 501-524.

Miller, G.E., Chen, E. & Zhou, E.S. (2007). If it goes up, must it come down? Chronic stress and the hypothalamic-pituitary-adrenocortical axis in humans. *Psychological Bulletin*, *133*, 25-45.

Miller, G.E. & Cohen, S. (2001). Psychological interventions and the immune system: A meta-analytic review and critique. *Health Psychology*, *20*, 47-63.

Mohren, D.C., Swaen, G., Kant, IJ, van Amelsvoort, L.G., Borm, P.G. & Galama, J.M. (2003). Common infections and the role of burnout in a Dutch working population. *Journal of Psychosomatic Research*, *55*, 201-208.

Molenaar-Cox, P.G.M. & Deursen, P.C.L. (2002). *Aan de poort van de WAO in* 2001*: achtergronden en trends* [Work disability in 2001: background and trends]. Uitvoering Werknemersverzekeringen, Amsterdam, The Netherlands.

Moseley, J.V. & Linden, W. (2006). Predicting blood pressure and heart rate change with cardiovascular reactivity and recovery: Results from 3-year and 10-year follow-up. *Psychosomatic Medicine*, *68*, 833-843.

Nater, U.M., La Marca, R., Florin, L., Moses, A., Langhans, W., Koller, M.M. & Ehlert, U. (2006). Stress-induced changes in salivary alpha-amylase: associations with adrenergic activity. *Psychoneuroendocrinology*, *31*, 49-58.

Netherlands Central Bureau of Statistics (2005a). *Arbeidsomstandigheden: controle over werk, werkdruk en beloningen* [Working conditions: job control, workload and rewards]. http://statline.cbs.nl/StatWeb/publication/?DM=SLNL&PA=03710&D1=35&D2=0&D3=(l-11)-l&STB=G1,G2,T&VW=G, 16th July 2008.

Netherlands Central Bureau of Statistics (2005b). *Arbeidsomstandigheden: werk en gezondheidsaspecten* [Working conditions: work and health aspects]. http://statline.cbs.nl/StatWeb/publication/?DM=SLNL&PA=37633&D1=5&D2=0&D3=(l-11)-l&VW=T, 16th July 2008.

Netherlands Society of Occupational Medicine (2000). *Handelen van de bedrijfsarts bij werknemers met psychische klachten, richtlijn voor bedrijfsartsen* [Employees with mental health disorders, guideline for occupational physicians]. J.J.L. van der Klink (Ed.). NVAB, Utrecht, The Netherlands.

Nicolson, N.A. & van Diest, R. (2000). Salivary cortisol patterns in vital exhaustion. *Journal of Psychosomatic Research*, *49*, 335-342.

Nieuwenhuijsen, K., Verbeek, J.H.A., de Boer, A.G.E., Blonk, R.W.B. & van Dijk, F.J.H. (2006). Predicting the duration of sickness absence for patients with common mental disorders in occupational health care. *Scandinavian Journal of Work, Environment & Health*, *32*, 67-74.

Olff, M. (1999). Stress, depression and immunity: the role of defense and coping styles. *Psychiatry Research*, *85*, 7-15.

Olff, M., Güzelcan, Y., de Vries, G.J., Assies, J. & Gersons, B.P.R. (2006). HPA- and HPT-axis alterations in chronic posttraumatic stress disorder. *Psychoneuroendocinology*, *31*, 1220-1230.

Olff, M., Langeland, W. & Gersons, B.P.R. (2005). Effects of appraisal and coping on the neuroendocrine re-

sponse to extreme stress. *Neuroscience and Biobehavioral Reviews*, *29*, 457-467.

Olff, M., Mulder, L.J.M., The, T.H., de Leij, L. & Emmelkamp, P.M.G. (1999). The psychobiological stress response in depressed patients compared to healthy controls. Proceedings of the 29th Annual Congress of the EABCT, p. 345, Dresden.

Ostrander, M.M., Ulrich-Lai, Y.M., Choi, D.C., Richtand, N.M. & Herman, J.P. (2006). Hypoactivity of the hypothalamo-pituitary-adrenocortical axis during recovery from chronic variable stress. *Endocrinology*, *147*, 2008-2017.

Pacák, K. & Palkovitz, M. (2001). Stressor specificity of central neuroendocrine responses: Implications for stress-related disorders. *Endocrine Reviews*, *22*, 502-548.

Palatini, P. & Julius, S. (2009). The role of cardiac autonomic function in hypertension and cardiovascular disease. *Current Hypertension Reports*, *11*, 199-205.

Paoli, P. & Merllié, D. (2001). Third European Survey on working conditions 2000. European Foundation for the improvement of Living and Working Conditions, 2001. Luxembourg: Office for official publications of the European Communities.

Penttilä, J., Helminen, A., Jartti, T., Kuusula, T., Huikuri, H.V., Tulppo, M.P., Coffeng, R. & Scheinin, H. (2001). Time domain, geometrical and frequency domain analysis of cardiac vagal outflow: effects of various respiratory patterns. *Clinical Physiology*, *21*, 3, 365-376.

Pike, J.L., Smith, T.L., Hauger, R.L., Nicassio, P.M., Patterson, T.L., McClintick, J., Costlow, C. & Irwin, M.R. (1997). Chronic life stress alters sympathetic, neuroendocrine, and immune responsivity to an acute psychological stressor in humans. *Psychosomatic Medicine*, *59*, 447-457.

Price, J.R. & Couper, J. (2000). Cognitive behaviour therapy for adults with chronic fatigue syndrome. *Cochrane Database Systematic Reviews*, *2*, CD001027.

Raison, C.L. & Miller, A.H. (2003). When not enough is too much: The role of insufficient glucocorticoid signaling in the pathophysiology of stress-related disorders. *American Journal of Psychiatry*, *160*, 1554-1556.

Reynolds, S. & Briner, R.B. (1994). Stress management and counselling Stress Management at work: with whom, for whom and to what ends? *British Journal of Guidance and Counselling*, *22*, 75-89.

Ring, C., Burns, V.E. & Carroll, D. (2002) Shifting hemodynamics of blood pressure control during prolonged mental stress. *Psychophysiology*, *39*, 585-590.

Rohleder, N., Nater, U.M., Wolf, J.M., Ehlert, U. & Kirschbaum, C. (2004). Psychosocial stress-induced activation of salivary alpha-amylase. An indicator of sympathetic activity? *Annals of the New York Academy of Science*, *1032*, 258-263.

Rowe, M. M. (2000). Skills training in the long-term management of stress and occupational burnout. *Current Psychology*, *19*, 215-228.

Roy, M.P., Kirschbaum, C. & Steptoe, A. (2001). Psychological, cardiovascular, and metabolic correlates of individual differences in cortisol stress recovery in young men. *Psychoneuroendocrinology*, *26*, 375-391.

Saab, P.G., Llabre, M.M., Hurwitz, B.E., Schneiderman, N., Wohlgemuth, W. Durel, L.A., Massie, C. & Nagel, J. (1993). The cold pressure test: Vascular and myocardial response patterns and their stability. *Psychophysiology*, *30*, 366-373.

Sanders, V.M., Kin, N. & Pongratz, G. (2007). Psychosocial effects on humoral immunity: Neural and neu-

roendocrine mechanisms. In: J.T. Cacioppo, L.G. Tassinary, G.G. Berntson (Eds.), *Handbook of psychophysiology* (3rd ed., pp. 367-389). Cambridge University Press, New York, United States of America.

Sapolsky, R.M., Romero, L.M. & Munck, A.U. (2000). How do glucocorticoids influence stress responses? Integrating permissive, suppressive, stimulatory and preparative actions. *Endocrine Reviews*, *21*, 55-89.

Sarid, O., Anson, O., Yaari, A. & Margalith, M. (2001). Epstein-Barr virus specific salivary antibodies as related to stress caused by examinations. *Journal of Medical Virology*, *64*, 149-156.

Schaufeli, W.B. & Buunk, B.P. (2003). Burnout: An overview of 25 years of research and theorizing. In: M.J. Schabracq, J.A.M. Winnubst, C.C. Cooper (Eds.), *The handbook of work and health psychology* (2nd ed., pp. 383–429). Wiley, West Sussex, England.

Schmidt-Reinwald, A., Pruessner J.C., Hellhammer, D.H., Federenko, I., Rohleder, N., Schurmeyer, T.H. & Kirschbaum, C. (1999). The cortisol response to awakening in relation to different challenge tests and a 12-hour cortisol rhythm. *Life Sciences*, *64*, 1653-1660.

Schuler, J.L. & O'Brien, W.H. (1997). Cardiovascular recovery from stress and hypertension risk factors: meta-analytic review. *Psychophysiology*, *34*, 649-659.

Schwartz, A.R., Gerin, W., Davidson, K.W., Pickering, T.G., Brosschot, J.F., Thayer, J.F., Christenfeld, N. & Linden, W. (2003). Toward a causal model of cardiovascular responses to stress and the development of cardiovascular disease. *Psychosomatic Medicine*, *65*, 22-35.

Segerström, S.C. & Miller, G.E. (2004). Psychological stress and the human immune system: A meta-analytic study of 30 years of inquiry. *Psychological Bulletin*, *130*, 601-630.

Selye, H. (1975). Implications of stress concept. *New-York State Journal of Medicine*, *75*, 2139-2145.

Siegrist, J. (1995). Emotions and health in occupational life: new scientific findings and policy implications. *Patient Education and Counselling*, *25*, 227-236.

Sifneos, P.E. (1996). Alexithymia: Past and present. *American Journal of Psychiatry*, *153*, 137-142.

Singh, A., Petrides, J.S., Gold, P.W., Chrousos, G.P. & Deuster, P.A. (1999). Differential hypothalamic-pituitary-adrenal axis reactivity to psychological and physical stress. The *Journal of Clinical Endocrinology & Metabolism*, *84*, 1944-1948.

Söndergaard, H.P. & Theorell, T. (2004). Alexithymia, emotions and PTSD; findings from a longitudinal study of refugees. *Nordic Journal of Psychiatry*, *58*, 185-191

Spreeuwers, D., Pal, T.M. & van der Laan, G. (Eds.) (2005). *Signaleringsrapport beroepsziekten* '05 [Report Occupational Diseases '05]. Netherlands Center for Occupational Diseases, Coronel Institute, Academic Medical Center, University of Amsterdam, The Netherlands.

Sterling, P. & Eyer, J. (1988). Allostasis: a new paradigm to explain arousal pathology. In: S. Fischer, J. Reason (Eds.), *Handbook of life stress, cognition and health* (pp. 629-649). Wiley, New York, United States of America.

Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (1996). Heart rate variability: standards of measurement, physiological interpretation and clinical use. *Circulation*, *93*, 1043-1065.

Tafet, G.E., Feder, D.J., Abulafia, D.P. & Roffman, S.S. (2005). Regulation of hypothalamic-pituitary-adrenal activity in response to cogntive therapy in patients with generalized anxiety disorder. *Cognitive, Affective,*

and Behavioral Neuroscience, *5*, 37-40.

Taylor, G. J., Bagby, R. M. & Parker, J.D.A. (1997). *Disorders of affect regulation. Alexithymia in medical and psychiatric illness.* Cambridge, Cambridge University Press, United Kingdom.

Treiber, F.A., Kamarck, T., Schneiderman, N., Sheffield, D., Kapuku, G. & Taylor, T. (2003). Cardiovascular reactivity and development of preclinical and clinical disease states. *Psychosomatic Medicine*, *65*, 46-62.

Turner-Cobb, J.M., Sephton, S.E., Koopman, C., Blake-Mortimer, J. & Spiegel, D. (2000). Social support and salivary cortisol in women with metastatic breast cancer. *Psychosomatic Medicine*, *62*, 337-345.

Ursin, H. & Eriksen, H.R. (2004). The cognitive activation theory of stress. *Psychoneuroendocrinology*, *29*, 567-592.

van der Klink, J.J.L., Blonk, R.W.B., Schene, A.H. & van Dijk, F.J.H. (2001). The benefits of interventions for work-related stress. *American Journal of Public Health*, *91*, 270-276.

van der Molen, H.F., Schop, A., Prakken, E.W., Braam I.T.J., Pal, T.M., Lenderink, A.F. & Spreeuwers, D. (2008). *Beroepsziekten in cijfers* 2008 [Occupational diseases in numbers]. Netherlands Center for Occupational Diseases, Amsterdam, The Netherlands.

van Dierendonck, D., Schaufeli, W.B. & Buunk, B.P. (1998). The evaluation of an individual burnout program: The role of inequity and social support. *Journal of Applied Psychology*, *83*, 392-407.

Vrijkotte, T.G.M., van Doornen, L.J. & de Geus, E.J.C. (2000). Effects of work stress on ambulatory blood pressure, heart rate and heart rate variability. *Hypertension*, *61*, 880-886.

Wadhwa, P.D., Dunkel-Schetter, C., Chicz-DeMet, A., Porto, M. & Sandman, C.A. (1996). Prenatal psychosocial factors and the neuroendocrine axis in human pregnancy. *Psychosomatic Medicine*, *58,* 432-446.Wilhelm, I., Born, J., Kudielka, B.M., Schlotz, W. & Wüst, S. (2007). Is the cortisol awakening rise a response to awakening? *Psychoneuroendocrinology*, *32*, 358-366.

Wofford, J.C. & Daly, P.S. (1997). A cognitive-affective approach to understanding individual differences in stress propensity and resultant strain. *Journal of Occupational Health Psychology*, *2*, 134-147.

World Health Organisation (1992). *International Classification of Diseases, ed.* 10 *(ICD*-10*).* Geneva, World Health Organisation.

Wüst, S., Federenko, I., Hellhammer, D.H. & Kirschbaum, C. (2000). Genetic factors, perceived chronic stress, and the free cortisol response to awakening. *Psychoneuroendocrinology*, *25*, 707-720.

Yalom, I.D. (1985). The therapeutic factors in group therapy. In: *The theory and practice of group psychotherapy* (3rd ed., pp. 3-18). BasicBooks, HarperCollins, United States of America.

Zhao, Z.Y., Xie, Y., Fu, Y.R., Li, Y.Y., Bogdan, A. & Touitou, Y. (2003). Circadian rhythm characteristics of serum cortisol and dehydroepiandrosterone sulphate in healthy Chinese men aged 30 to 60 years. A cross sectional study. *Steroids*, *68*, 133-138.