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

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2 Physiological differences between burnout patients and healthy individuals: blood pressure, heart rate, and cortisol responses*

Abstract

Background: The model of sustained activation suggests that continuous or repeated exposure to stressors results in physiological changes. *Method*: We investigated whether work-related stress was associated with changes in activity of the Sympathetic-Adrenergic-Medullary (SAM) axis and the Hypothalamic-Pituitary-Adrenal (HPA) axis by comparing a sample of 22 burnout patients with 23 healthy individuals. SAM axis activity was measured by means of heart rate (HR) and blood pressure (BP). HPA axis activity was investigated by means of salivary cortisol levels. Resting levels of HR, BP, and cortisol were determined as well as the extent of reactivity and recovery of these measures during a psychosocial stressor consisting of mental arithmetic and speech tasks. In addition, morning levels of cortisol were determined. *Results*: Burnout patients showed higher resting HR than healthy individuals. BP resting values and cardiovascular reactivity and recovery during the psychosocial stressor did not differ between burnout patients and healthy individuals. Basal cortisol levels and cortisol reactivity and recovery measures were similar for burnout patients and healthy individuals. However, burnout patients showed elevated cortisol levels during the first hour after awakening in comparison to healthy individuals. *Conclusion*: The findings provided limited proof that SAM axis and HPA axis activity are disturbed in work-related stress. Elevated HR and elevated early morning cortisol levels are in support of sustained activation.

Although originally exclusively related to social professions, burnout is nowadays commonly accepted as a stress state characterised by symptoms such as emotional exhaustion and physical fatigue, detachment from work, diminished sense of competence, loss of energy, increased irritability and sleep and concentration problems which can occur irrespective of the type of profession (Maslach, Schaufeli & Leiter, 2001). The symptoms of burnout are also known as subjective health complaints (Eriksen, Olff, Murison & Ursin, 1999), since up till now, no objective signs of illness have been found for these complaints. Comparable symptom clusters, with exclusion of the work-related complaints, are also characteristic of Chronic Fatigue Syndrome (CFS; Wessely, 1990) and Post-Traumatic Stress Disorder (PTSD; American Psychiatric Association, 1994). Although burnout is not considered to be a 'classical' stress disorder, it is often preceded by periods of prolonged work-related stress (Maslach et al., 2001).

Concerning the relation between stress and health complaints, attention is paid within psychobiological research to the association between failure to effectively cope with stressors and physiological responses (Linden, Earle, Gerin & Christenfeld, 1997). Two physiological stress systems are commonly distinguished: the Sympathetic-Adrenergic-Medullary (SAM) axis and the Hypothalamic-Pituitary-Adrenal (HPA) axis (Henry, 1992; Linden et al., 1997; Peters et al., 1998). Simply stated, the SAM axis coordinates immediate sympathetic activation preparing an individual to deal with a stressor, resulting in for example increased heart rate (HR) and blood pressure (BP) and release of catecholamines such as epinephrine and norepinephrine. SAM axis activation occurs within seconds as a result of a stressor and permits adaptive responding to a stressor. The HPA axis is a slower response system involving release of corticosteroids such as corticotropin releasing hormone, adrenocorticotropic hormone and cortisol. HPA axis activation is associated with inability to cope, helplessness, affective distress, and perceived uncontrollability (Henry, 1992; Linden et al., 1997; Peters et al., 1998; Ursin & Olff, 1993). Generally, low SAM and HPA axis activation is seen in persons with high levels of effective coping and control (Olff, 1999a; Olff, Brosschot & Godaert, 1993; Olff et al., 1995).

According to the model of 'sustained activation', sustained or frequently repeated activation of the stress-systems without the possibility to recover may contribute to the development of illness (Eriksen et al., 1999). Sustained activation can be a result of prolonged or repeated exposure to stressors, with which a person cannot adequately cope. Consequently, the SAM axis and HPA axis stay persistently activated and new set-points may develop. Lasting changes in the neuroendocrine system are thought to be particularly health threatening (Cacioppo, 1998; Dienstbier, 1989; Frankenhaeuser, 1991).

Elevated BP or hypertension may be considered a sign of dysregulation of the SAM axis while hypersecretion or hyposecretion of cortisol is indicative of dysregulation of the HPA axis. Associations between SAM and HPA functioning on the one hand, and workload, job strain and chronic stress on the other, have been repeatedly observed. Elevations in BP (Evans & Steptoe, 2001; Fredrikson, Tuomisto, Lundberg & Melin, 1990; Goldstein, Shapiro, Chicz-DeMet & Guthrie, 1999; Steptoe, Roy & Evans, 1996) and HR (Evans & Steptoe, 2001; Goldstein et al., 1999) during the

workday were shown in various populations and professions. In addition, positive associations were found between job strain and BP (Kawakami, Haratani & Araki, 1998; Schnall, Schwartz, Landbergis, Waaren & Pickering, 1998) job strain and hypertension (Tsutsumi, Kayaba, Tsutsumi & Igarashi, 2001) and between chronic stress and cardiovascular basal levels (Benschop et al., 1994). Furthermore, relations were observed between cortisol and workload or job strain (Steptoe, Cropley, Griffith & Kirschbaum, 2000; Steptoe et al., 1998). Actual support for sustained activation after a working day has also been reported (Steptoe, Cropley & Joekes, 1999; Sluiter, van der Beek & Frings-Dresen, 1998).

Since burnout symptoms highly resemble symptoms that are characteristic of CFS, Frankenhaeuser (1989) suggested that burnout patients as CFS patients (Demitrack, 1997; Demitrack et al., 1991) may show lower basal HPA axis activity resulting for example in hyposecretion of cortisol. Basal hyposecretion of cortisol has also been observed in individuals who developed PTSD after an extreme stressor as compared to healthy individuals or other psychiatric patients (Boscarino, 1996; Golier & Yehuda, 1998; Yehuda, 1990). However, studies concerning chronic stress due to high job strain, work overload and/or vital exhaustion show both decreases (Ockenfels, 1995; Pruessner, Hellhammer & Kirschbaum, 1999) and increases (Kristenson et al., 1998; Melamed et al., 1999; Schultz, Kirschbaum, Pruessner & Hellhammer, 1998; Steptoe et al., 2000) in cortisol levels. Results from the study of Melamed et al. (1999) suggested that within a sample of employees, a longer history of burnout complaints, implying chronicity, was associated with higher cortisol levels.

With respect to the relationship between stress and health, it appears relevant to investigate reactivity to and recovery from stressors, rather than looking at basal activity of the SAM axis and HPA axis alone (Linden et al., 1997). Different reactivity may be reflected in the magnitude and/or the duration of the response. Likewise, recovery may not occur to the same extent and/or within the same time frame. McEwen (1998) has stated that delayed recovery following a stressor is indicative of sustained activation. Kristenson et al. (1998) found that elevated cortisol levels among persons reporting job strain and vital exhaustion were associated with attenuated cortisol reactivity to stress-inducing tasks. Roy et al. (1998) found that in healthy fire fighters reporting a higher density of recent life events, high social support was associated with stronger HR en BP reactivity and quicker recovery to stress-inducing tasks in comparison with low social support. According to Roy et al., swifter recovery, despite increased reactivity, may be seen as adequate adaptation.

It should be noted that the above mentioned studies were carried out among participants who could still carry out their daily activities. Thus, although participants reported chronic stress or even burnout symptoms, these conditions were not impairing their daily functioning to a large extent. To our knowledge, so far, studies concerning SAM axis and HPA axis functioning in burnout patients who are unable to work are absent.

The objective of the present study was to investigate differences between burnout patients and healthy individuals concerning SAM axis and HPA axis functioning as indicated by both basal values and reactivity and recovery measures. Therefore, burnout patients and healthy individuals were exposed to a psychosocial stressor consisting of mental arithmetic and speech tasks. During

the psychosocial stressor, cardiovascular measures and cortisol levels were determined. In addition, participants collected morning saliva to obtain information about the cortisol response to awakening, which, according to Pruessner et al. (1997), shows good intra-individual stability over time and can serve as an indicator for HPA axis activity. We expected to find dysregulation of the SAM axis and the HPA axis in burnout patients.

Method

Participants

We recruited 22 burnout patients and 23 healthy individuals. Group characteristics, including gender distribution, mean age, education level, and type of occupation, are presented in Table 1. Healthy individuals were younger ($t(43) = 4.0$, $p < .001$) and higher educated ($t(42) = -2.0$, $p < .05$) than burnout patients.

Burnout patients were recruited through occupational health practitioners and general practitioners. Burnout patients were included in the study when 1) they reported continuous mental and/or physical fatigue and increased fatigability, and at least two other stress complaints out of the following: dizziness, dyspepsia, muscular aches or pains, tension headaches, inability to relax, irritability, and sleep disturbance; 2) the complaints were considered to be predominantly work-related; and 3) participants reported (partial) sick leave of at least 2 weeks, but less than 6 months,

Table 1: *Characteristics of the burnout group and the healthy group.* [a]

	Burnout patients (*n* = 22)	Healthy individuals (*n* = 23)
Gender		
Men / Women	14 (64%) / 8 (36%)	10 (43%) / 13 (57%)
Age	42 (10.2)	31 (7.6) [b]
Education (scale: 1-6) [c]	3.4 (1.2)	4.2 (1.3) [b]
Cigarette smokers	9 (41%)	7 (30%)
Burnout complaints (UBOS)		
Emotional exhaustion	4.2 (1.0)	1.3 (0.8) [b]
Depersonalisation	3.1 (1.2)	1.4 (0.9) [b]
Professional competence	4.1 (1.0)	4.3 (1.0)
Fatigue (CIS total score)	105.4 (19.7)	47.8 (22.8) [b]
Duration of complaints		
< 6 months / > 6 months	4 (18%) / 18 (82%)	-

Note: UBOS: Utrecht Burnout Scale; CIS: Checklist Individual Strength
[a] Values are counts (%) and *M* (*SD*s).
[b] Difference with patient group is significant at α = .05.
[c] 1 = Primary school, 6 = University grade.

because of burnout complaints. A semi-structured diagnostic interview was administered by a clinical psychologist. Primary Axis I disorders were excluded using a short version of the Composite International Diagnostic Interview (CIDI; World Health Organisation, 1987), a structured interview covering depression, social phobia, panic disorder, somatoform disorder other than undifferentiated, posttraumatic stress disorder, obsessive-compulsive disorder, hypomania, and psychotic disorders. Additionally, the Beck Depression Inventory (BDI; Beck & Steer, 1987) was used to exclude severe depression. Since depressive symptoms such as difficulty concentrating and loss of energy are also characteristic of burnout, the cut-off score was set conservatively at 25. Other exclusion criteria were: having experienced a traumatic event in the past six months, pregnancy, and a history of immune-, diabetic or other medical disease that could possibly explain fatigue. Two burnout patients were using anti-hypertensive medication of the type beta-blockers. Burnout patients received refund of their travel expenses and a printed report of their baseline BP and HR.

Healthy individuals were recruited by flyers in libraries and other public places and among part-time working psychology students. Healthy individuals were screened by an interview administered by telephone. Participants in good physical health and working for at least eight hours a week were included in the study. Exclusion criteria were: scoring both within the clinical range of the Emotional Exhaustion Scale of the Maslach Burnout Inventory (i.e., > 2.60; Schaufeli & van Dierendonck, 2000) and within the clinical range of the total fatigue score of Checklist Individual Strength (i.e., > 76; Bültmann et al., 2000) currently taking sick leave, psychiatric illness, having experienced a traumatic event in the past six months, and pregnancy. All healthy participants, except for three women who were on oral contraceptives, were medication-free. Healthy subjects were paid 20 euro and received a printed report of their baseline BP and HR after attending the laboratory session, completion of the questionnaires, and delivering the morning saliva samples.

Procedure

All participants in the study gave written informed consent. Participants collected morning saliva, visited the laboratory in order to be exposed to the psychosocial stressor, and filled out questionnaires concerning biographic characteristics and work-related stress complaints. At the day of morning saliva collection and at the day of stress test performance, participants filled out a state questionnaire pertaining to mood, physical activity, and smoking. Participants were asked to refrain from smoking and coffee consumption for at least 60 minutes before the start of the psychosocial stress procedure. In order to reliably differentiate the experimentally induced cortisol from the strong early morning elevation, which is inherent to the circadian rhythm of the morning cortisol secretion (Linkowski et al., 1993; Schmidt-Reinwald et al., 1999), the psychosocial stress procedures were planned in the afternoon, starting at 13.30hrs.

To prevent effects of anticipatory stress for the laboratory session on morning cortisol levels, morning saliva was collected on another day than the psychosocial stress procedure. With the exception of five participants, all burnout patients collected the morning saliva on the day before the day they visited the laboratory. The healthy group collected the morning saliva within five days

after their visit to the laboratory. By instructing participants to collect morning saliva on a weekday we avoided disturbing influences due to different sleeping habits in the weekend.

Materials and Measures

Psychosocial stressor
The psychosocial stress procedure consisted of a) a resting period (30 min.), b) speech task preparation (5 min.), c) a mental arithmetic task (5 min.), d) a speech task (5 min.) followed by e) a recovery period (30 min.). In the resting period the participant was introduced to the procedures and the blood pressure instrumentation. Furthermore, he/she watched a documentary-like movie for 15 minutes. In the speech task preparation period the participant was instructed to read a short description of a situation in which he/she was unfairly accused of causing damage. The participant was told to imagine him/herself in that particular situation and to think how he/she would react behaviourally, emotionally, etc. He/she was also told to prepare a consistent story, which he/she had to tell in front of a camera later that afternoon. The mental arithmetic task entailed adding and subtracting rows of five tot seven integers while only writing down the final solution per row. The participant was instructed to solve the sums as quickly as possible, without making mistakes. For the speech task, the participant was told to tell his/her story, which had to last five minutes. If the participant silenced before the five minutes had passed, he/she was told to keep talking and if he/she silenced a second time, the experimenter reported how much time there was left. In the following recovery period, participants again watched the subsequent part of the documentary-like movie. During the whole experimental session, participants remained seated. Similar psychosocial stress procedures have been shown to induce subjective stress as well as changes in endocrine and immune parameters (Kirschbaum, Pirke & Hellhammer, 1993; Olff, Mulder, The, de Leij & Emmelkamp, 1999b).

SAM axis activity
To measure activity of the SAM axis, we used the cardiovascular measures heart rate and blood pressure. Heart rate and blood pressure were computed from continuous finger blood pressure using a Finapres (Ohmeda Finapress type 2300[E], Blood Pressure Monitor). Basal values were obtained by calculating mean values during the final ten minutes of the resting period. Task reactivity was determined by calculating mean values over each task (preparation, mental arithmetic, speech task) separately. Short- and long-term recovery were measured by averaging values over the first and second resting periods respectively, each lasting 10 minutes (with exclusion of saliva collection).

HPA axis activity
We used cortisol to measure HPA axis activity. During the psychosocial stress session, saliva was collected five times: 1) at baseline, i.e., immediately before the start of the speech preparation task

(time (t) = -4 min.); 2) immediately after the speech preparation phase (t = 5 min.); 3) directly after the speech task (t = 19 min.); 4) after the first part of the recovery period (t = 33 min.); and 5) after the second part of the recovery period (t = 47).

Saliva was collected following the method described by Navazesh (1993), in which the participant refrains from swallowing for a period of four minutes, allowing the saliva to accumulate in the floor of the mouth. The collection starts with the instruction to void the mouth of saliva by swallowing. The participant spits out into a cup every 60 s. Fifteen minutes before the experiment, the participant rinses the mouth with water. After collection, saliva samples were stored upon ice until the end of the experiment. Immediately after the experiment, saliva was clarified by centrifugation (10.000 G., 4 min). The clear supernatant was divided in 0.5 ml aliquots and stored at -20°C until analysis.

With respect to morning cortisol levels, participants were instructed to collect saliva at the time of awakening, 30 minutes, and 60 minutes thereafter, and at 12.00 AM. Cortisol values at midday were used as indicators for basal cortisol levels. Saliva was collected in non-coated Salivettes™ (Sarstedt, Nümbrecht, Germany) placed under the tongue or between cheek and teeth for three minutes. If the swab was not saturated, subjects were permitted to slowly move the swab around in the mouth without chewing on it. Participants were instructed not to have breakfast nor to brush their teeth within 15 minutes before a sample was collected. Additionally, participants were instructed to store all samples in the fridge until next day's visit to the laboratory (burnout patients) or postage/deliverance (healthy individuals). All samples were centrifuged at (5000 G., 5 min.) and stored at -20°C until analysis. The amount of free cortisol was determined by enzyme immunoassay (DSL, Veghel, The Netherlands). Sensitivity of the assay was 1 ng/ml.

Work-related stress complaints

The Dutch version of the Maslach Burnout Inventory-General Survey (MBI-GS) was used to measure burnout (Utrechtse Burnout Schaal: UBOS; Schaufeli & van Dierendonck, 2000). The UBOS consists of 15 items regarding Emotional exhaustion, Depersonalisation, and Professional competence, which are scored on a seven-point Likert scale ranging from 1 (never) to 7 (always/daily).

Fatigue was measured with the Checklist Individual Strength (CIS; Vercoulen, Alberts & Bleijenberg, 1999). The CIS consists of 20 items referring to four dimensions of fatigue: a) Subjective feeling of fatigue and physical fitness, b) Activity level, c) Motivation, and d) Concentration, which are scored on a seven-point Likert scale ranging from 1 (false) tot 7 (true). A total fatigue score is calculated by adding up all item scores and can thus range from 20 to 140.

Subjective stress responses

The subjective response during the laboratory session was measured by means of the Vigor and Tension subscales of the Profile Of Mood Scale (POMS), consisting of five and six items respectively (McNair, Lorr & Droppleman, 1971). Items are scored on a five-point scale ranging from 0

(not at all) to 4 (very much). The Vigor subscale is indicative of psychological activation and the Tension subscale contains items referring to tension and anxiety. These mood-dimensions have been previously used to measure subjective responses during stress-inducing tasks (Roy, Kirschbaum & Steptoe, 2001). The mood questionnaires were completed five times during the laboratory session, while saliva was collected.

Education
Education level was assessed as the highest completed education on a six-point scale ranging from 1 (Primary school) to 6 (University grade).

Statistical analyses
Background characteristics and complaints levels were compared between the patient group and the healthy group using Chi-square-tests and t-tests. Group differences in resting values of cardiovascular measures were assessed by comparison of mean values during the last five minutes of the pre-stressor resting period by means of analysis of variance (ANOVA), using a one between-subjects factor (group) design. Group differences in basal cortisol levels were examined by comparing mean cortisol levels at midday (fourth sample of the morning saliva samples) using ANOVA including group as one between-subjects factor.

Reactivity and recovery during the psychosocial stress procedure were analysed by means of ANOVA for repeated measures, using a one within- (time), one between-subjects factor (group) design, for the cardiovascular measures, the cortisol outcomes, and the subjective stress responses separately. Early morning cortisol response was analysed likewise. When the assumption of sphericity was violated, corrected results according to he Greenhouse-Geisser method were presented. Post-hoc contrasts were employed to reveal group differences concerning changes between subsequent measurements with use of the repeated contrasts within ANOVA for repeated measures procedure. Analyses were performed with and without relevant covariates. Both age and gender have consistently been associated with cardiovascular measures and cortisol levels (Allen, Stoney, Owens & Matthews, 1993; Girdler, Turner, Sherwood & Light, 1990; Kirschbaum, Kudielka, Gaab, Schommer & Hellhammer, 1999; Tsutsumi et al., 2001; Van Cauter, Leproult & Kupfer, 1996) and were therefore added as covariates, despite the fact that the difference of gender distribution was not statistically significant between the burnout patients and healthy individuals.

Some data were missing due to equipment problems or to lost saliva samples. Analysis of blood pressure and heart rate was based on 22 burnout patients and 22 healthy individuals, with the exception of basal values during the resting period, which was based on 23 healthy individuals. In addition, analysis of cortisol during the psychosocial stress procedure was based on 21 burnout patients and 23 healthy individuals. Furthermore, analysis of morning cortisol was carried out for 20 burnout patients and 23 healthy individuals, with exception of baseline comparison at 12.00 hrs, which was based on 21 burnout patients and 23 healthy individuals.

Results

Initial analyses

Burnout patients scored significantly higher than healthy individuals on the Emotional exhaustion subscale and the Depersonalisation subscale of the UBOS ($t(43) = 11.0$, $p < .001$; $t(43) = 5.3$, $p < .001$), and on the CIS ($t(43) = 9.1$, $p < .001$) (see Table 1). Within the group of burnout patients, the majority (82%) reported chronic burnout complaints, i.e., complaints of more than six months duration.

Cardiovascular measures

Figures 1a-c show mean systolic and diastolic BP and HR values during the different phases of the psychosocial stress procedure. Burnout patients had higher resting HR than healthy individuals ($F(1,43) = 7.17$, $p < .05$). After correction for age and gender, the difference for HR during the resting phase remained statistically significant ($F(1,41) = 4.21$, $p < .05$). The result is in support of a higher level of basal HR in the burnout group.
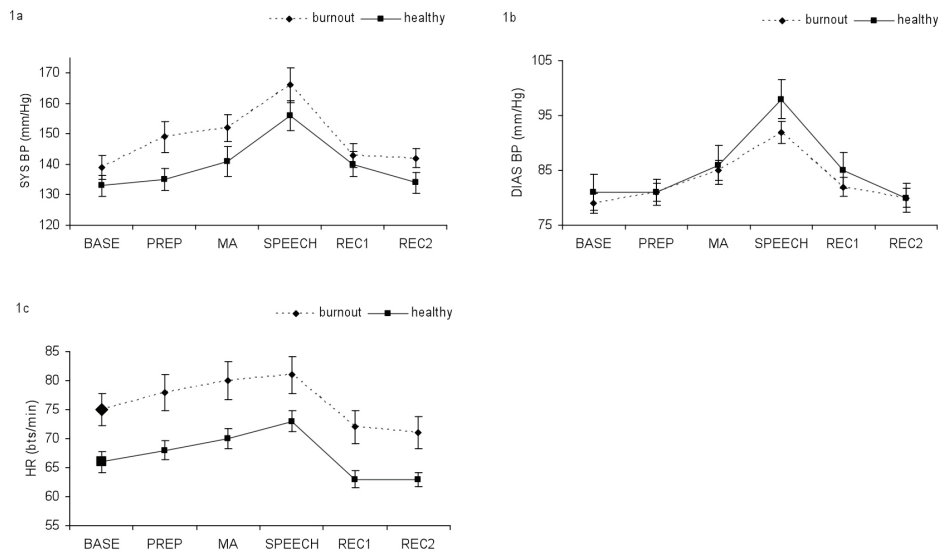
Figures 1a-c: *Systolic blood pressure, diastolic blood pressure, and heart rate (M ± S.E.M.) in burnout patients and healthy individuals during the psychosocial stress procedure.*

Note: 1a-c: BASE = baseline, i.e., pre-stressor resting phase, PREP = speech task preparation, MA = mental arithmetic, SPEECH = speech task, REC1 = first recovery phase, REC2 = second recovery phase; 1a: time main effect: $p < .05$; group main effect: $p > .05$; time x group interaction effect: $p > .05$; 1b: time main effect: $p < .05$; group main effect: $p > .05$; time x group interaction effect: $p > .05$; 1c: time main effect: $p < .05$; group main effect: $p < .05$; time x group interaction effect: $p > .05$; the statistically significant group difference (cross-sectionally) of HR resting values is indicated by enlargement of group indicators.

Systolic BP, diastolic BP, and HR differed during the six phases of the psychosocial stress procedure indicating change over time (within-subjects effect of time: $F_{(5,210)} = 35.72$, $p < .001$; $F_{(5,210)} = 58.09$ $p < .001$; $F_{(5,210)} = 46.23$, $p < .001$, respectively). Post-hoc analyses revealed that differences between subsequent phases of the psychosocial stress procedure were all statistically significant, with exception of diastolic BP between the resting and speech preparation phase and HR between the first and second recovery phase. After correction for age and gender, the within-subjects time effect remained statistically significant for systolic and diastolic BP ($F_{(5,200)} = 4.29$, $p < .01$; $F_{(5,200)} = 4.34$, $p < .01$, respectively), and became marginally significant for HR ($F_{(5,200)} = 2.30$, $p < .10$). The results support physiological change through stress induction.

No between group differences were found during the psychosocial stress procedure for systolic and diastolic BP (between-subjects group effect: systolic BP: $F_{(1,42)} = 2.38$, $p > 0.05$, diastolic BP: $F_{(1,42)} = 0.34$, $p > 0.05$). After adjustment for age and gender, the between-subjects group effects for systolic and diastolic BP were still non-significant. However, burnout patients had higher HR during the entire psychosocial stress procedure (between-subjects group effect: $F_{(1,42)} = 6.66$, $p < 0.05$), which, in absence of a time x group interaction effect, further supports a higher basal HR in the burnout group. After adjustment for age and gender, the between-subjects group effect for HR remained statistically significant ($F_{(1,40)} = 4.12$, $p < .05$).

No between-group differences were observed with respect to change over time for any of the cardiovascular measures during the laboratory session (time x group interaction: systolic BP: $F_{(5,210)} = 1.99$, $p > .05$; diastolic BP: $F_{(5,210)} = 1.04$, $p > .05$; HR: $F_{(5,210)} = 0.25$, $p > .05$). After adjustment for age and gender, time x group interaction effects remained statistically non-significant. Hence, no indications were found for between-group differences in cardiovascular reactivity and recovery.

Cortisol
Cortisol values during the psychosocial stress procedure are presented in Figures 2a & b. Basal values of cortisol measured at 12.00hrs revealed no differences between burnout patients and healthy individuals ($F_{(1,42)} = 0.24$, $p > .05$). Correction for age and gender did not affect the non-significance of the results. During the psychosocial stress procedure, cortisol changed over time (within-subjects time effect: $F_{(4,168)} = 17.80$, $p < .001$). Post-hoc analyses of the overall within-subjects time effect revealed that differences between subsequent phases of the laboratory session were all statistically significant, with exception of the difference between the post speech preparation and the post speech-task samples. After correction for age and gender, the within-subjects time effect became marginally significant ($F_{(4,160)} = 2.57$, $p < .10$).

No overall groups-differences emerged (between-subjects group effect: $F_{(1,42)} = 2.27$, $p > .05$). After adjustment for age and gender, non-significance of the group effect was unaffected. Burnout patients showed a different development of cortisol during the psychosocial stress procedure in comparison to healthy individuals (time x group interaction effect: $F_{(4,168)} = 4.16$, $p < .05$). The time x group interaction effect could not be attributed to a particular phase, but was probably a result of the overall steeper decrease in cortisol of burnout patients than healthy individuals during
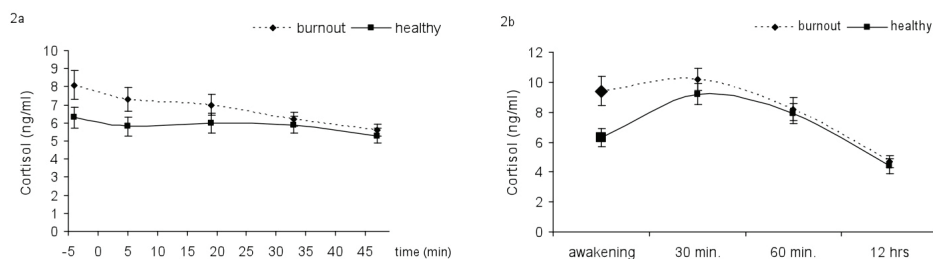
Figures 2a-b: *Concentrations of salivary free cortisol (M, ± S.E.M.) in burnout patients and healthy individuals during the psychosocial stress procedure (a) and during the morning (b).*

Note: 2a: t = -4: baseline sample; t = 5: post speech preparation sample; t = 19: post speech sample; t = 33: resting phase sample 1; t = 47: resting phase sample 2; 2b: 30 min.: 30 minutes after awakening; t = 60: one hour after awakening; 2a: time main effect: $p < .05$; group main effect: $p > .05$; time x group interaction effect: $p < .05$; 2b: time main effect: $p < .05$; group main effect: $p < .10$; time x group interaction effect: $p > .05$; The statistically significant group difference (cross-sectionally) of cortisol values at awakening is indicated by enlargement of group indicators.

the psychosocial stress procedure. After adjustment for age and gender, the time x group interaction effect remained statistically significant ($F(4,160) = 3.75$, $p < .05$).

Morning cortisol levels changed over time (within-subjects time effect: $F(3,123) = 28.25$, $p < .001$), which is in support of the cortisol awakening response. Post-hoc analysis of the overall time effect showed significant differences between every subsequent measurement. After correction for age and gender, the time effect remained significant ($F(3,117) = 5.14$, $p < .01$).

Burnout patients tended to have higher overall cortisol levels than healthy individuals ($F(1,41) = 3.79$, $p < .10$). After adjustment for age and gender, the group effect became statistically significant ($F(1,39) = 4.87$, $p < .05$). Figure 2b shows that the burnout group has higher morning cortisol values at the moment of awakening, however, one hour after awakening and at midday cortisol values of both groups have become nearly equal.

No evidence for a different development of morning cortisol for the two groups emerged (time x group interaction effect: $F(3,123) = 1.96$, $p > .05$). After adjustment for age and gender, the time x group interaction effect remained non-significant.

Exploratory associations between cortisol and complaints
Associations between morning cortisol and the core complaints of burnout, i.e., emotional exhaustion and fatigue, were further explored. Regression analyses were conducted associating early morning cortisol at the moment of awakening and emotional exhaustion and fatigue, using data of both groups. A positive relationship emerged between cortisol level at awakening and emotional exhaustion (B = 0.16, SE = 0.06, $\beta = 0.37$, $t = 2.57$, $p < .05$) and between maximal cortisol level during the first hour after awakening and emotional exhaustion (B = 0.15, SE = 0.07, $\beta = 0.32$, $t = 2.20$,

$p < .05$). After correction for age and gender the relation between cortisol level at awakening and emotional exhaustion became somewhat weaker (B = 0.11, SE = 0.06, β = 0.25, t = 1.85, $p < .10$) as did the relation between maximal cortisol level and emotional exhaustion (B = 0.14, SE = 0.06, β = 0.29, t = 2.24, $p < .05$). The cortisol level at awakening was also positively associated with general fatigue (B = 2.65, SE = 1.29, β = 0.30, t = 2.06, $p < .05$), however, the association between maximal cortisol level during the first hour after awakening and fatigue did not reach significance (B = 2.19, SE = 1.47, β = 0.22, t = 1.49, $p > .05$). After correction for age and gender, the associations became non-significant (B = 1.86, SE = 1.25, β = 0.21, t = 1.50, $p > .05$; B = 2.09, SE = 1.36, β = 0.22, t = 1.54, $p > .05$, respectively).

Subjective stress responses

The subjective stress responses are presented in Figures 3a and b. Psychological activation (Vigor subscale of the POMS) changed over time during the psychosocial stress procedure (within-subjects time effect: $F_{(4,172)}$ = 13.25, $p < .001$). Post-hoc analyses showed significant differences between the speech preparation measurement and the measurement after the speech task and between the measurement after the speech task and the first recovery measurement. After correction for age and gender the time effect remained significant ($F_{(4,164)}$ = 2.64, $p < .05$). No overall difference between the groups was found ($F_{(1,43)}$ = 1.60, $p > .05$). After adjustment for age and gender the difference between groups became marginally significant ($F_{(1,41)}$ = 3.63, $p < .10$). There was no support for a different development of psychological activation during the laboratory session between burnout patients and healthy individuals (time x group interaction effect: $F_{(4,172)}$ = 1.34, $p > .05$). After adjustment for age and gender, the time x group interaction was unaffected.
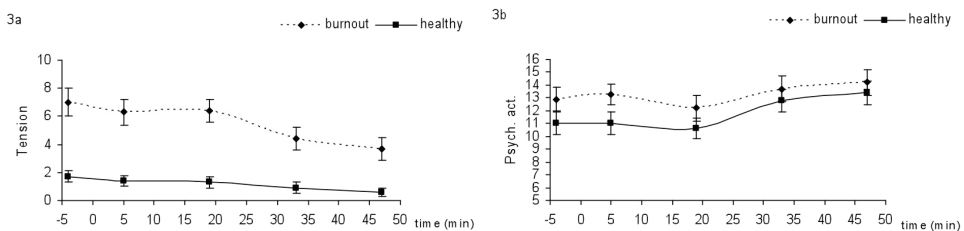
Figures 3a-b: *Descriptive information about the subjective stress response (M, ± S.E.M.) in burnout patients and healthy individuals during the psychosocial stress procedure.*

Note: 3a,b: t = -4: baseline measurement; t = 5: post speech preparation measurement; t = 19: post speech measurement; t = 33: resting phase measurement 1; t = 47: resting phase measurement 2; 3a: time main effect: $p < .05$; group main effect: $p < .05$; time x group interaction effect: $p < .05$; 3b: time main effect: $p < .05$; group main effect: $p > .05$; time x group interaction effect: $p > .05$.

Tension (Tension subscale of the POMS) also changed during the psychosocial stress procedure (within-subjects time effect: $F_{(4,172)} = 18.2$, $p < .001$). Post hoc analyses showed significant differences between the measurement after the speech task and the first recovery measurement and between the two recovery measurements. After correction for age and gender the time effect remained significant ($F_{(4,164)} = 2.87$, $p < .05$). Furthermore, burnout patients had overall higher tension scores than healthy individuals (between-subjects group effect: $F_{(1,43)} = 26.23$, $p < .001$). After correction for age and gender, the group effect remained statistically significant ($F_{(1,41)} = 14.36$, $p < .001$). In addition, burnout patients and healthy individuals showed a different development of tension during the laboratory session (time x group interaction effect: $F_{(4,172)} = 5.25$, $p < .01$). After adjustment for age and gender, the time x group interaction effect was still statistically significant ($F_{(4,164)} = 4.26$, $p < .05$). These results indicate that the tension scores of the healthy group were relatively low and did not change during the laboratory session, while the tension scores of the patient group were considerably higher, showing a decrease after the stress-inducing tasks.

Discussion

The aim of the present study was to investigate differences between burnout patients and healthy individuals regarding basal physiological values and physiological stress responses by examining measures of the SAM axis (HR and BP) and the HPA axis (cortisol). With respect to basal values of cardiovascular measures, burnout patients showed higher HR than healthy individuals. The results are in support of sustained activation. Our results are in line with previous studies on associations between chronic stress or workday and elevated HR (Benschop et al., 1994; Evans & Steptoe, 2001; Goldstein et al., 1999). However, we found no elevated BP levels as reported by others (Benschop et al., 1994; Evans & Steptoe, 2001; Fredrikson et al., 1990; Goldstein et al., 1999; Kawakami et al., 1998; Schnall et al., 1998; Steptoe et al., 1999; Steptoe et al., 1996; Tsutsumi et al., 2001). The conclusion may be that hyperactivity of the SAM axis was limited in our burnout patients. On the other hand, the lack of finding substantial differences in basal BP may also indicate that the hyperactivity of the SAM axis had partially abated, as a result of the rest obtained during sick leave. This recovery could have occurred since burnout patients were tested several weeks after they had called themselves sick. An alternative suggestion may be that two burnout patients used anti-hypertensive medication. Post-hoc analysis with exclusion of these patients did not change our findings with respect to any effect of any of the cardiovascular measures. However, mean BP and HR of the patient group could have been somewhat higher, if data of untreated hypertension of these particular patients had been at hand.

With respect to cardiovascular reactivity and recovery values during the psychosocial stress procedure, no differences between burnout patients and healthy individuals were obtained. Both groups showed considerable cardiovascular increases during the stress-inducing tasks, at least as high as the effects obtained in other studies using a laboratory stressor (Carroll et al., 2001; Larson,

Ader & Moynihan, 2001), and recovered within thirty minutes after termination of the stressor. It seemed that having been exposed to work stress does not extensively affect cardiovascular reactivity or recovery. Again, an alternative explanation may be that potential changes in reactivity and recovery may have normalised within the weeks of rest after having called themselves sick. Also in these analyses, attention was paid to anti-hypertensive medication, and again post hoc analysis excluding these patients did not change any of the results. Our results are consistent with findings of Benschop et al. (1993), who found no association between cardiovascular reactivity and chronic stress, despite the fact that they obtained both elevated basal BP and HR among persons reporting chronic stress in comparison to persons not reporting chronic stress.

No differences between basal cortisol levels were obtained between burnout patients and healthy individuals. These findings are partly in accordance with other findings. Steptoe et al. (2000) did not find any differences during the day between high and low job strain groups. Melamed et al. (1999), however, obtained higher cortisol levels in a chronic burnout group compared to a non-chronic burnout-group and a group without burnout complaints. The absence of a difference in the present study could not be ascribed to relatively large inter-individual differences in measurements in the afternoon, as suggested by Schmidt-Reinwald et al. (1999).

With respect to cortisol reactivity and recovery, no differences emerged between burnout patients and healthy individuals. The outcomes are in accordance with results published by Roy et al. (1998), addressing life events and cortisol reactivity and recovery. Other studies, however, reported associations between daily stressors or job strain and vital exhaustion and cortisol reactivity (Kristenson et al., 1998; Roy et al., 2001). An explanation for these inconsistent results may be that general cortisol reactivity obtained in the current study and by Roy et al. (1998) was smaller than reported by others (Kirschbaum et al., 1993; Kirschbaum et al., 1995; Schmidt-Reinwald et al., 1999). Consequently, group differences may remain unnoticed. A possible explanation for a somewhat smaller cortisol response to the stressor may be that the nature of the tasks used in the present study differed to some extent from other psychosocial stress procedures, including the Trier Social Stress Test (Kirschbaum et al., 1993). For example, a camera was used during the speech task instead of a real audience. However, despite the fact that Roy et al. (2001) as well obtained relatively small cortisol reactivity, while also using a camera instead of a real audience during the speech task, they found an association between reactivity and daily stress. Another explanation for the relatively flat cortisol pattern during the psychosocial stress procedure may be the timing of the measurement. According to Schmidt-Reinwald et al. (1999), who investigated the 12-hour cortisol rhythm during daytime, cortisol concentrations show a relatively strong decrease between 13.00 hrs and 15.00 hrs characterised by relatively large inter-individual differences. These differences are probably largely due to variance in the consistence of the midday meal, which is known to affect cortisol concentrations (Gibson et al., 1000). As a result, increases in cortisol following the stress-inducing tasks may remain unnoticed. A flat response may, though, be considered a response, which might have shown a steeper slope without exposure to the stress test as is suggested by Roy et al. (2001).

Burnout patients showed elevated early morning cortisol levels in comparison with healthy

individuals. Our findings are consistent with the studies of Melamed et al. (1999), Schultz et al. (1998), and Steptoe et al. (2000) concerning people with high job strain, high workload, or burnout symptoms and with the results of Kristenson et al. (1998), concerning people reporting vital exhaustion. These findings suggest a dysregulation of the HPA axis in burnout patients. The fact that the difference seems most pronounced at the moment of awakening, burnout patients may not have recovered fully during the night, which may be a sign of 'sustained activation'.

It is remarkable that although burnout patients reported severe emotional exhaustion, scored in the clinical range and comparable to CFS patients on general fatigue (Bültmann et al., 2000), and reported chronic burnout complaints, they did not have blunted cortisol levels as have been found in CFS patients (Demitrack, 1997; Demitrack et al., 1991). In addition, the severity of emotional exhaustion was positively associated with the cortisol level at awakening. These outcomes suggest that the burnout syndrome is essentially different from CFS. Another explanation may be that the neuroendocrine changes develop over time and thus can only be found in patients who suffer from burnout complaints for a certain long-lasting period. Unfortunately, the size and distribution of the current sample did not allow us to do subgroup analysis to investigate differences in cortisol response between more and less chronic burnout patients.

The present study has several limitations. Firstly, the sample size was relatively small in comparison to similar studies using physiological measures, resulting in limited statistical power. Consequently, small effect sizes could not be detected. Secondly, the stress-inducing tasks might not have caused sufficient distress to result in substantial HPA axis activation, thus possibly thwarting the discovery of different reactivity and recovery patterns between burnout patients and healthy individuals.

In conclusion, the results of the present study suggest that there is some dysregulation of the SAM axis, as indicated by elevated basal HR in burnout patients. The results are also supportive of dysregulation of the HPA axis in burnout patients as indicated by elevated early morning cortisol levels. Both elevated HR and elevated morning cortisol is indicative of sustained activation. The outcomes of burnout patients are more similar to the results observed in persons reporting substantial job strain or vital exhaustion, than to the pattern found in patients with chronic fatigue or patients suffering from post-traumatic stress. The specific underlying mechanisms and exact meaning of these findings, however, remain to be clarified.

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