Higher overcommitment to work is associated with lower norepinephrine secretion before and after acute psychosocial stress in men

Petra H. Wirtz[a],[*], Johannes Siegrist[b], Ulrike Rimmele[a], Ulrike Ehlert[a]

[a]*Department of Clinical Psychology and Psychotherapy, University of Zurich, Binzmühlestrasse 14, Box 26, CH-8050, Zurich, Switzerland*
[b]*Department of Medical Sociology, University of Duesseldorf, Germany*

Summary

Background: Overcommitment (OC) is a pattern of excessive striving. In reaction to work stress, OC has been associated with higher sympathetic nervous system activation and cortisol release, but data on neuroendocrine reactivity to standardized stressors are scarce. We investigated whether OC is associated with differential levels of the stress hormones norepinephrine and cortisol in response to acute psychosocial stress.

Methods: Fifty-eight medication-free non-smoking men aged between 20 and 65 years (mean$\pm$S.E.M.: 36.3 ± 1.8) underwent an acute standardized psychosocial stress task combining public speaking and mental arithmetic in front of an audience. We assessed OC as well as a variety of psychological control variables including vital exhaustion, perfectionism, chronic stress, and cognitive stress appraisal. Moreover, we measured plasma norepinephrine as well as salivary cortisol before and after stress and several times up to 60 min thereafter.

Results: Higher OC was associated with lower baseline norepinephrine levels ($r = -0.37$, $p < 0.01$). General linear models controlling for age, BMI, and mean arterial blood pressure revealed that higher overcommitment was associated with lower norepinephrine and cortisol levels before and after stress (p's < 0.02) as well as with lower norepinephrine stress reactivity ($p = 0.02$). Additional controlling for the potential psychological confounders vital exhaustion, perfectionism, chronic stress, and depression confirmed lower norepinephrine levels before and after stress ($p < 0.01$) as well lower norepinephrine stress reactivity ($p = 0.02$) with increasing OC. Higher OC independently explained 13% of the total norepinephrine stress response ($\beta = -0.46$, $p < 0.01$, R^2 change $= 0.13$).

*Corresponding author. Tel.: +41 44 635 7367; fax: +41 44 635 7359.
E-mail address: p.wirtz@psychologie.unizh.ch (P.H. Wirtz).

Conclusions: Our findings suggest blunted increases in norepinephrine following stress with increasing OC potentially mirroring blunted stress reactivity of the sympathetic nervous system.

1. Introduction

"Overcommitment" (OC) has been defined as an enduring cognitive-motivational pattern of maladaptive coping with demands characterized by excessive striving and an inability to withdraw from obligations (Siegrist et al., 2004). Over-committed persons are driven by their high need for control and approval, thereby repeatedly overtaxing their own resources and, thus, precipitating exhaustion and break-down in the long run (Joksimovic et al., 1999). OC has been introduced as an intrinsic component to the model of effort-reward imbalance (ERI) at work. In this context, OC is thought to magnify stressful experience resulting from high cost/low gain conditions at work because it induces exaggerated efforts which are not met by extrinsic rewards (Siegrist, 1996).

Several prospective studies suggest that OC increases coronary heart disease risk (Siegrist et al., 1990; Joksimovic et al., 1999; Kuper et al., 2002). The biological pathways through which OC might increase cardiovascular disease risk are beginning to be understood. For instance, OC has been related to major physiological cardiovascular risk factors including elevated lipid levels and hemostatic risk factors (Peter et al., 1998; Vrijkotte et al., 1999). Moreover, OC is strongly associated with the concept of vital exhaustion, an independent psychological risk factor for coronary heart disease (CHD) (Appels, 1990; Cole et al., 1999; Preckel et al., 2005).

The concept of physiological hyperreactivity to stress posits that studying short-term cardiovascular responses to controlled physiological, cognitive, and emotional chal-lenges serves as a window into complex psychological and physiological processes that are involved in the develop-ment of cardiovascular disease (Steptoe and Willemsen, 2002; Linden et al., 2003). Although not uniform (Vrijkotte et al., 2000), in reaction to work stress, OC has been associated with indicators of sympathetic nervous system activation including elevated blood pressure (Steptoe et al., 2004), shorter pre-ejection period (PEP) levels and reduced PEP variability (Vrijkotte et al., 2004). Moreover, associa-tions between OC and elevated levels of the stress hormone cortisol over the workday have been reported (Eller et al., 2006). Yet, these findings result from ambulatory monitoring studies performed in everyday life where control of potential confounders is limited.

To the best of our knowledge, experimental studies on associations between OC and physiological reactivity to standardized psychological stressors have not yet been published. According to the concept of vital exhaustion (Appels, 1997), it might be assumed that prolonged stress first leads to heightened hormonal responsiveness. Later, chronic elevations of hormones overtax an exhausted system which then might respond to this load by down-regulating the sensitivity of target tissues (Wirtz, 2002; Wirtz et al.,

2003). As a result, reduced rather than increased respon-siveness following stressful experience might occur in overcommitted persons. Indeed, the OC-related constructs vital exhaustion and ERI suggest blunted sympathetic and cortisol reactivity to acute standardized mental stressors. ERI was associated with blunted sympathetic reactivity in terms of lowered epinephrine, heart rate as well as cortisol elevations following a modified Stroop Test (Siegrist et al., 1997). Similarly, vitally exhausted persons were less likely to show large cortisol responses to a speech task (Nicolson and van Diest, 2000; Kristenson et al., 2004).

The aim of this study was to investigate associations between OC and neuroendocrine reactivity to a standar-dized psychosocial stress task in unmedicated non-smoking men. We measured the neuroendocrine parameters norepi-nephrine and cortisol as well as heart rate before and several times after stress. We favored norepinephrine over epinephrine because of its higher relevance with respect to cardiovascular disease risk (Goldstein, 1981; Rahn et al., 1999). In line with assumptions derived from the concept of vital exhaustion we hypothesized that higher OC would be associated with lower neuroendocrine stress reactivity. Moreover, to control for potential confounders, we addi-tionally assessed psychological parameters including vital exhaustion, perfectionism, chronic stress, and cognitive stress appraisal, which are related to either OC or to neuroendocrine stress reactivity.

2. Methods

2.1. Study participants

The Ethics Committee of the State of Zurich, Switzerland, formally approved the research protocol. Of a total of 64 participants we obtained complete OC scores of 58 subjects representing the final study sample. All subjects provided written informed consent. Recruitment was carried out through advertisement of the study on pin boards at the University of Zurich and by members of the research team who accompanied the mobile blood donation units of the Swiss Cross of the State of Zurich. We intentionally recruited non-smoking middle-aged men who were in excellent physical and mental health confirmed by an extensive health questionnaire (Wirtz et al., 2003) and telephone interview. Specific exclusion criteria, obtained by subjects' self-report, were: regular strenuous exercise, alcohol and illicit drug abuse; any heart disease, varicosis or thrombotic diseases, elevated blood sugar and diabetes, elevated cholesterol, liver and renal diseases, chronic obstructive pulmonary disease, allergies and atopic diathesis, rheumatic diseases, and current infectious diseases. In addition, participants were included only if they reported taking no medication, either regularly or occasionally and if their

blood pressure was in the normotensive or moderately hypertensive range (systolic BP < 160 mmHg and diastolic BP < 100 mmHg). If the personal or medication history was not conclusive, the subjects' primary care physician was contacted for verification.

2.2. Study protocol

All subjects reported to the laboratory on a single study day. Subjects were tested between 2:00 and 4:00 p.m. They had abstained from physical exercise, alcohol, and caffeinated beverages since the previous evening. We used the Trier Social Stress Test (TSST) combining a 5-min preparation phase followed by a 5-min mock job-interview, and 5-min mental arithmetic in front of an audience (Kirschbaum et al., 1993). After task completion, subjects remained seated in a quiet room for 60 min.

Blood samples for assessment of norepinephrine were taken immediately before and 0, 10, and 60 min after completion of the TSST. Samples of stimulated whole saliva (by chewing on cotton rolls) were taken immediately before the TSST as well as 0, 10, 20, 30, 40, 50 and 60 min after completion of the TSST for determination of salivary cortisol levels. Blood pressure was measured immediately before and 40 min after stress by sphygmomanometry (Omron 773, Omron Healthcare Europe B.V. Hoofddorp, The Netherlands) and mean arterial blood pressure (MAP) was calculated by the formula $(2/3 \times$ mean diastolic BP$)+(1/3$ mean systolic BP$)$.

2.3. Measurements and data analysis

2.3.1. Overcommitment
OC was assessed by a uni-dimensional scale composed by six Likert-scaled items where respondents indicated to what extent they personally agree or disagree with the given statements on a four-point rating scale. The items are as follows: (1) I get easily overwhelmed by time pressures at work; (2) As soon as I get up in the morning I start thinking about work problems; (3) When I get home, I can easily relax and "switch off" work; (4) People close to me say I sacrifice too much for my job; (5) Work rarely lets me go, it is still on my mind when I go to bed; (6) If I postpone something that I was supposed to do today I'll have trouble sleeping at night. The score ranges from 6 to 24 with higher scores reflecting higher OC (Siegrist et al., 2004). This short scale was developed from an original 29 items scale measuring different relevant aspects of this coping pattern (Siegrist, 1996; Siegrist et al., 2004). The short scale captures the core notion of the construct (inability to withdraw from work obligations), and resulted in predicted health outcomes of similar strength as those by the longer scale. Moreover, the scale exhibited the highest internal consistency in previous analyses and had an acceptable scalability (Siegrist et al., 2004). Finally, goodness of fit was appropriate in several confirmatory factor analyses (Hanson et al., 2000; Joksimovic et al., 2002; Roedel et al., 2004).

2.3.2. Vital exhaustion, perfectionism, and chronic stress
Vital exhaustion was assessed by the German version of the Shortened Maastricht Exhaustion Questionnaire (MEQ-s)

(Wirtz et al., 2003). We assessed perfectionism by measuring "concern over mistakes and doubts" (CMD, 13 Items on five-point rating scales for each item, minimum score = 13, maximum score = 65) of the German Version of the Frost Multidimensional Perfectionism Scale (MPS-d) (Frost et al., 1990; Stöber, 1998; Wirtz et al., 2007). Chronic stress was measured using the Chronic Stress Screening Scale (CSSS) (Schulz et al., 2004). The CSSS is a 12-item scale derived from a larger chronic stress questionnaire (Schulz et al., 2004) and assesses the frequency of experiencing work overload (four items), worries (four items), lack of social recognition (two items), excessive demands at work (1 item) and social overload (1 item).

2.3.3. Depression, trait anxiety, cognitive stress appraisal, and personality
The extent of depression was assessed by means of a depression scale, the short version of the "Allgemeine Depressionsskala" (ADS-K) (Hautzinger and Bailer, 1993). The ADS-K is the German version of the "Center for Epidemiological Studies Depression Scale" (CES-D). Anxiety was assessed by means of the trait version of the state-trait-anxiety-inventory (STAI) (Laux et al., 1981).

To address anticipatory cognitive appraisal processes relevant for the TSST, we assessed primary appraisal (i.e., the judgment about the significance of an event as stressful, positive, controllable, challenging or irrelevant) as well as secondary appraisal (i.e., the assessment of available coping resources and options when faced with a stressor) using a 16-item questionnaire for Primary and Secondary Appraisal (PASA) (Gaab et al., 2005), which is based on the theoretical constructs proposed by Lazarus and Folkman (1984). To assess the "big five" personality factors (agreeableness, neuroticism, extroversion, openness, and conscientiousness), we used the shortened German version of the NEO Five Factor Inventory (NEO-FFI) (Ostendorf, 1990; Schallberger and Venetz, 1999).

2.3.4. Responses of physiological parameters to TSST
Blood samples for measurement of plasma norepinephrine were obtained via an indwelling forearm catheter inserted into the non-dominant arm 45 min before start of blood sampling. Blood was drawn into EDTA-coated monovettes (ethylenediaminetetraacetic acid; Sarstedt, Numbrecht, Germany), and immediately centrifuged for 10 min at $2000 \times g$; plasma was stored at $-80\,^{\circ}$C until analysis. Plasma norepinephrine was determined by means of HPLC and electrochemical detection after liquid–liquid extraction (Smedes et al., 1982; Ehrenreich et al., 1997). The limit of detection was 10 pg/ml. Inter- and intra-assay variance was lower than 5%. To reduce error variance caused by imprecision of the intra-assay, all samples from one subject were analyzed in the same run.

For cortisol, saliva was collected using Salivette collection devices (Sarstedt, Rommelsdorf, Germany), which were stored at $-20\,^{\circ}$C until biochemical analysis. Cortisol concentrations were determined with a commercially available competitive chemiluminiscence immunoassay with high sensitivity of 0.16 ng/ml (LIA, IBL Hamburg, Germany). Intra- and inter-assay variability was less than 7.7% and 11.5%, respectively.

Heart rate data were obtained continuously via a portable heart rate monitor (Polar system, S810, Polar, Finland) (Nater et al., 2005).

2.3.5. Statistical analyses

Data were analyzed using SPSS (version 13.0) statistical software package (SPSS Inc., Chicago, IL, USA). All tests were two-tailed with level of significance set at $p \leqslant 0.05$ and level of borderline significance set at $p \leqslant 10$. The optimal total sample size to detect an expected effect size of 0.35 in regression analyses with a power between 0.85 (maximum of eight predictors) and 0.95 (minimum of four predictor) was $n = 57$.

Using the trapezoid formula, we calculated areas under the total response curve, expressed as area under the measured time-points with respect to ground (AUC) for the four repeated norepinephrine and the eight repeated cortisol measures (Pruessner et al., 2003). Prior to statistical analyses, all data were tested for normality using the Kolmogorov–Smirnov test. As an a priori fixed set of control variables, we controlled for age, BMI, and MAP in all analyses.

For assessment of associations between OC and stress hormones at rest, we calculated partial correlation analyses controlling for age, BMI, and MAP. Following previous methods, we assessed associations between OC and the neuroendocrine stress response by calculating general linear models with repeated measures of stress hormones as dependent variables and OC as continous independent variable while controlling for age, BMI, and MAP (Wirtz et al., 2006). We used OC as continous variable in all analyses to avoid artificial dichotomization which would result into a loss of statistical power.

To assess the influence of psychological factors on the association between OC and the neuroendocrine stress response, we used a three-step procedure. First, we identified potential psychological predictors by calculating partial correlation analyses controlling for age, BMI, and MAP between OC and psychological factors on the one hand and between stress hormone AUCs and psychological factors on the other hand. Second, we calculated linear regression analyses (enter method) with AUC of stress hormones as the dependent variables. As independent variables, we entered age, BMI, and MAP as well as the significant psychological correlates of step 1. Last, we entered OC. Third, we validated regression results by applying general linear models with repeated measures of the stress hormones significantly predicted by OC (from step 2) as dependent variables. As independent variables, we entered in addition to age, BMI, and MAP all potential psychological moderators of step 1 as well as OC.

Although not employed for modeling and testing, for illustrative purposes we categorized the study group into tertiles based on their OC scores.

3. Results

3.1. Subjects' characteristics

The final study sample consisted of 58 healthy men, whose medical (age, body mass index, basal blood pressures) and sociodemographic characteristics are detailed in Table 1. Table 2 depicts psychological characteristics of the study group.

3.2. Overcommitment and stress hormones at rest

Partial correlation analyses controlling for age, BMI, and MAP revealed that higher OC was significantly associated with lower baseline levels of norepinephrine ($r = -0.37$, $p < 0.01$, $n = 58$), but not of cortisol ($p = 0.17$). None of the other psychological measures significantly correlated with norepinephrine baseline levels (p's > 0.10).

Table 1 Sociodemographic and medical characteristics of the study subjects.

	N	Mean±S.E.M. (range)
Age (years)	58	36.3±1.8 (20–65)
Body mass index (kg/m^2)	58	24.6±0.4 (20.7–33.9)
Systolic blood pressure (mmHg)	58	124.3±1.7 (89.5–158)
Diastolic blood pressure (mmHg)	58	79.8±1.3 (60.5–97.0)
Mean arterial pressure (mmHg)	58	94.7±1.4 (71.2–116.0)
High school degree (Swiss "Matura") (%)	58	50.0
Full- or part-time job (%)	58	87.9

N, valid cases.

Table 2 Psychological characteristics and their correlations with overcommitment.

	Mean±S.E.M. (range)	r^p OC/N
Overcommitment (OC score)	13.03±0.33 (7–21)	
Vital exhaustion (MEQ-score)	4.12±0.46 (0–13)	*0.33*/58*
Perfectionism (CMD score)	28.13±0.97 (13–51)	*0.31*/56*
Chronic stress (TICS screening)	12.9±0.85 (2–34)	*0.57****/55*
Depression (ADS-K score)	10.25±0.53 (1–21)	*0.28*/57*
Anxiety (STAI)	34.11±1.10 (20–55)	0.23/57
Personality factors (NEO-FFI)		
1. Agreeableness	28.03±0.49 (18–36)	0.02/58
2. Neuroticism	15.67±0.55 (7–25)	0.10/58
3. Extroversion	23.36±0.69 (7–33)	0.07/58
4. Openness	25.93±0.52 (16–34)	0.18/58
5. Conscientiousness	27.19±0.66 (14–36)	0.00/58
Primary appraisal	3.66±0.11 (1.88–5.63)	0.08/58
Secondary appraisal	3.14±0.14 (1.38–5.25)	−0.17/58

N, number of valid cases; OC, overcommitment; r^p, partial correlation after correcting for age, BMI, and MAP. Significance level: *$p < 0.05$, **$p < 0.01$, and ***$p < 0.001$. Potential predictors in italics.

3.3. Overcommitment and stress responses of physiological parameters

We applied general linear models with repeated measures of stress hormones as dependent variables and OC as *continous* independent variable while controlling for age, BMI, and MAP.

Norepinephrine. The TSST caused significant increases in norepinephrine ($F(2.8/144.7) = 9.08$, $p<0.01$). Higher OC was associated with lower norepinephrine levels before and after stress (main effect OC: $F(1/52) = 14.83$, $p<0.01$) as well as with lower norepinephrine stress reactivity (interaction OC by stress: $F(2.78/144.68) = 3.49$, $p = 0.02$) (Figure 1A).

Cortisol. Similarly, in terms of repeated cortisol secretion, higher OC was associated with lower cortisol stress responses (interaction OC by stress: $F(3.03/136.3) = 3.46$, $p<0.02$). The main effect of OC on cortisol was not significant ($p = 0.26$) (Figure 1B).

Heart rate. Higher OC was associated with lower heart rates before and after stress of borderline significance (main effect OC: $F(1/51) = 3.24$, $p<0.08$) (Figure 1C).

3.4. Influence of psychological factors on the association between overcommitment and the neuroendocrine stress response

3.4.1. Identification of potential predictors and criteria: correlational analyses

To test for a potential influence of psychological measures (i.e., vital exhaustion, perfectionism, chronic stress, depression, anxiety, stress appraisal, and the "big five" personality factors) on the association between OC and the stress response of norepinephrine and cortisol, we first calculated partial correlation analyses (Table 2). We did this to reduce the number of potential predictors to be entered in subsequent regression analyses to abstain from overfitting given our sample size (Babyak, 2004).

After controlling for age, BMI, and MAP, higher OC was significantly associated with higher scores of vital exhaustion ($r = 0.33$, $p<0.02$), perfectionism ($r = 0.31$, $p = 0.02$), chronic stress ($r = 0.57$, $p<0.01$), and depression ($r = 0.28$, $p = 0.04$). While AUC of the norepinephrine stress response
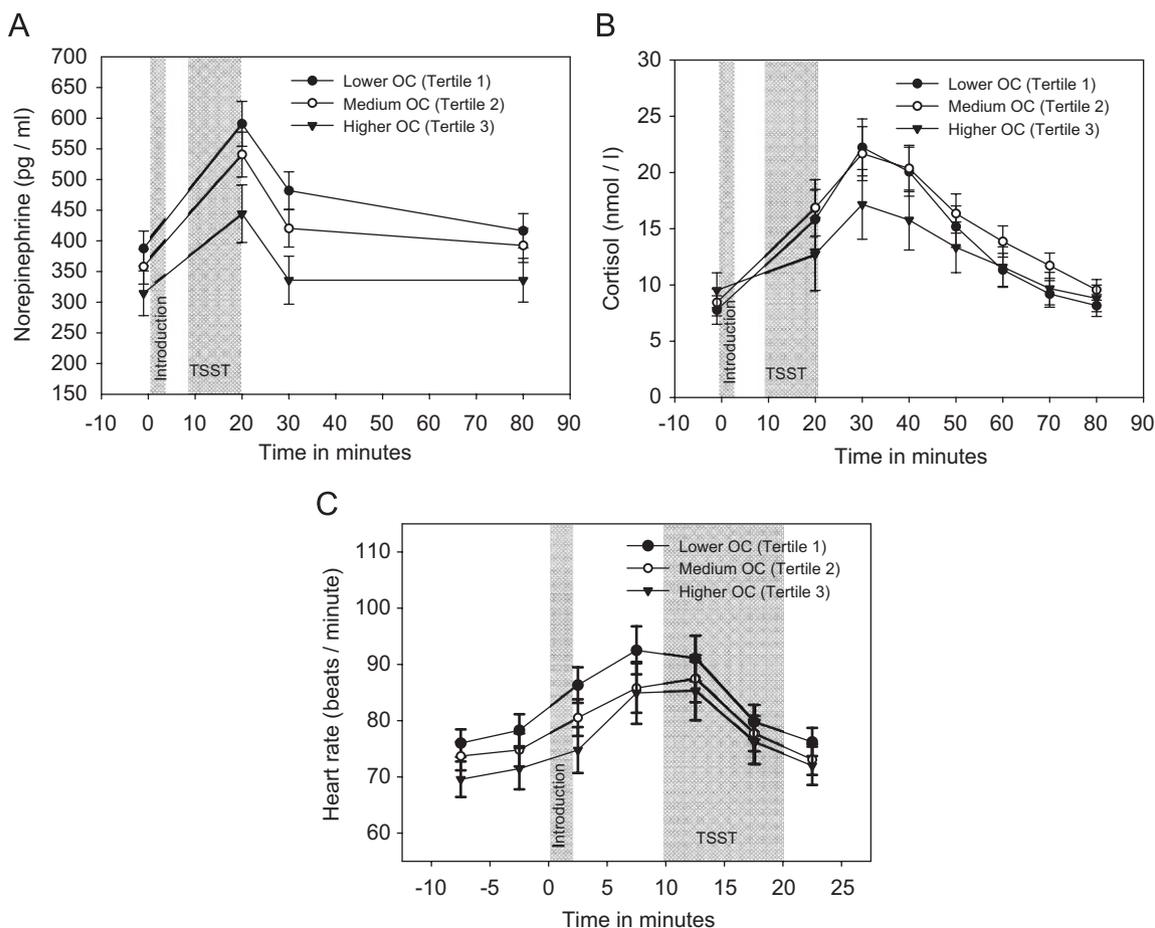

Figure 1 Norepinephrine, cortisol, and heart rate reactivity to psychosocial stress (TSST) in subjects with lower, medium, ad higher scores for overcommitment (OC). Values are means±S.E.M. We calculated general linear models with repeated measures of physiological stress parameters as dependent variables and overcommitment as continous independent variable while controlling for age, BMI, and MAP. For illustrative purposes, we depict tertiles of overcommitment. Higher overcommitment was associated with lower norepinephrine levels before and after stress ($p<0.01$, $n = 57$) as well as with lower norepinephrine stress reactivity ($p = 0.02$, $n = 57$) (A). Moreover, higher overcommitment was associated with lower cortisol stress responses ($p<0.02$, $n = 50$) (B) and lower heart rates before and after stress ($p<0.08$) (C).

was not significantly related to any psychological measure other than OC ($r = -0.48$, $p < 0.01$), higher AUC of cortisol was only associated with lower depression scores ($r = -0.33$, $p = 0.02$).

3.4.2. Regression analyses

AUC of stress hormones were entered as dependent variables. In a first step, we controlled for age, BMI, and MAP. In a second step, we entered the identified predictors vital exhaustion, perfectionism, chronic stress, and depression. In a third step, we entered OC.

Higher OC independently predicted lower norepinephrine AUC explaining 13% of the observed variance in norepinephrine AUC ($\beta = -0.46$, $p < 0.01$, $\Delta R^2 = 0.13$, $n = 51$) (Table 3). The whole regression model explained 39% of the total variance in norepinephrine AUC. Neither OC nor any other psychological measure significantly predicted cortisol AUC (p's > 0.25).

3.4.3. General linear models

To validate regression analyses, we applied general linear models with repeated measures of norepinephrine and cortisol as dependent variables and OC as continuous independent variable. Age, BMI, MAP, as well as the psychological variables vital exhaustion, perfectionism, chronic stress, and depression were controlled as covariates. Again, higher OC was associated with lower norepinephrine levels before and after stress (main effect OC: $F(1/42) = 8.51$, $p < 0.01$) as well as with lower norepinephrine stress reactivity (interaction OC by stress: $F(2.93/123.03) = 3.38$, $p = 0.02$). The association of higher OC with lower cortisol stress reactivity did not reach statistical significance (interaction OC by stress: $F(3.02/111.69) = 2.11$, $p = 0.10$).

4. Discussion

To address the hypothesis that higher OC would be associated with lower neuroendocrine stress reactivity, we studied norepinephrine and cortisol responses to public speaking stress in a group of apparently healthy non-smoking men while controlling for potentially confounding psychological variables.

The main finding of our study was that OC is associated with lower norepinephrine levels before and after stress as well as with blunted norepinephrine increases following stress. In other words, the higher OC levels of a person, the lower norepinephrine stress reactivity of that person. These findings are confirmed both, in regression analyses and in general linear models when controlling for a variety of potential psychological confounders. An impressive 13% of the total norepinephrine stress response was independently explained by OC. In terms of cortisol secretion, OC turned out to be associated with blunted cortisol stress reactivity when controlling for age, BMI, and blood pressure. However, when additionally controlling for potential psychological confounders, the OC-cortisol association became non-significant. Among the psychological variables tested higher OC turned out to be significantly associated with higher vital exhaustion, higher perfectionism, higher levels of chronic stress, and higher depression levels. The association with chronic stress was strongest ($r = 0.57$).

Reduced responsiveness of stress hormones to acute psychosocial stress was observed in persons suffering from a chronic imbalance between efforts spent and rewards received at work (Siegrist et al., 1997) and in vitally exhausted people (Nicolson and van Diest, 2000; Kristenson et al., 2004). Our finding of reduced neuroendocrine stress responsiveness in persons exhibiting higher OC is in line with these results. According to the vital exhaustion concept (Appels, 1997), an initially hightened stress response which could result from prolonged stress due to OC at early career stages may lead to bodily adaptations. As a potential consequence, the stress response is no longer hightened but lowered. Such lowered stress reactivity may result from alterations in tissue sensitivity to stress hormones (Bamberger et al., 1996; Wirtz et al., 2003). For example, excess stress hormone availability can lead to regulatory receptor down-regulation in order to keep homeostasis of the interior milieu (Lefkowitz et al., 1984; Burnstein et al., 1991; Wirtz, 2002). A contrary mechanism however could be that tissue sensitivity is enhanced leading to compensatory down-regulation of hormone production.

However, up to now we can only speculate about a potential mechanism underlying the association between reduced neuroendocrine and particularly norepinephrine stress responsiveness with OC. We did not measure the functional status of receptors involved in norepinephrine

---

Table 3 Hierarchical regression analyses for overcommitment and norepinephrine stress reactivity.

Variables entered	Standardized β-coefficient	t	p	R^2 change
Norepinephrine AUC*				
Vital exhaustion	−0.13	−0.85	0.40	0.01
Perfectionism	−0.07	−0.49	0.63	0.00
Chronic stress	0.12	0.59	0.56	0.01
Depression	0.04	0.26	0.80	0.00
Overcommitment	−0.45	−2.94	<0.01	0.13

AUC, area under the curve.
*Regression results are presented after controlling for age, body mass index, and mean arterial blood pressure in a first step.

and cortisol signal transduction. Moreover, the cross-sectional nature of our data does not permit causal conclusions to be drawn with regard to the direction of the association between OC and the psychobiological stress response pattern. Noteworthy, it appears unlikely that the level of OC is influenced by an altered physiological response pattern, given its high intraindividual stability over time (Joksimovic et al., 1999). It is also unlikely that over-committed people were less involved in, or affected by, the acute stressful challenge as we could not observe an association between OC and cognitive appraisal of the stress task. From a psychological perspective, it is more likely to assume that overcommitted people exhibit a typical pattern of coping over the course of their lifes starting with remarkable professional success, fueled by a high need for approval and control. Successful striving in combination with perfectionism may overtax their efforts of coping with multiple demands in the long run. As overcommitted people are unable to withdraw from work obligations they may run the risk of becoming exhausted both at the behavioral and at the physiological level (Appels, 1997). The significant correlations of OC with psychological constructs that mirror best such a coping career, namely vital exhaustion, perfectionism, chronic stress, or depression, are in line with such reasoning.

Our study has several limitations. First, results are restricted to a group of healthy, well-educated middle-aged men. Thus, they cannot be generalized to male groups with known cardiovascular risk factors or with less favorable social background, nor can they be generalized to women. Second, we determined our sample size to detect large effects with a power of 0.85 (four predictors) to 0.95 (eight predictors). However, it turned out that we overestimated the effect sizes as we observed effect sizes of medium and medium to large range according to effect size conventions for regression analyses or repeated ANCOVA analyses, respectively (Buchner et al., 1997). Thus, controlling for the full set of potential confounders resulted in slight statistical overcontrolling, given our sample size (Babyak, 2004). In consequence, as we cannot rule out the probability of type II error, the strength of some reported associations (e.g., the non-significant association of OC with blunted cortisol stress reactivity) may have been underestimated. Third, we cannot evaluate the possible clinical significance of a blunted stress response, e.g., whether this response indicates an elevated prospective risk of cardiovascular dysfunction.

These limitations are balanced by several strength. First, we exposed subjects to a valid standardized psychosocial stress condition, the TSST, that was previously shown to reliably evoke profound increases in a variety of physiological parameters (Kirschbaum et al., 1993; Dickerson and Kemeny, 2004; Nater et al., 2006). Second, we classified subjects according to their level of OC, a pattern of excessive striving with documented significance as a psychosocial risk factor of coronary heart disease (Siegrist et al., 1990; Joksimovic et al., 1999; Kuper et al., 2002). Third, we included a considerable number of potentially confounding psychological variables into the analysis and tested the robustness of our main finding. Fourth, in addition to norepinephrine, cortisol and heart rate were assessed as additional psychobiological markers, and we

found a similar, yet not statistically significant response pattern. Finally, the sample was relatively large and rather homogenous in terms of health status.

In conclusion, our findings suggest blunted increases in norepinephrine following stress with increasing OC which potentially mirrors blunted stress reactivity of the sympathetic nervous system. The clinical implications of our observations in health and disease remain to be demonstrated.

Role of funding source

Conflict of interest

There are no conflicts of interest.

Acknowledgment

References

Appels, A., 1990. Mental precursors of myocardial infarction. Br. J. Psychiatry 156, 465–471.

Appels, A., 1997. Exhausted subjects, exhausted systems. Acta Physiol. Scand. Suppl. 640, 153–154.

Babyak, M.A., 2004. What you see may not be what you get: a brief, nontechnical introduction to overfitting in regression-type models. Psychosom. Med. 66, 411–421.

Bamberger, C.M., Schulte, H.M., Chrousos, G.P., 1996. Molecular determinants of glucocorticoid receptor function and tissue sensitivity to glucocorticoids. Endocr. Rev. 17, 245–261.

Buchner, A., Faul, F., Erdfelder, E., 1997. G-Power: A Priori, Post hoc, and Compromise Power Analyses, Version 2.0. University of Trier.

Burnstein, K.L., Bellingham, D.L., Jewell, C.M., Powell-Oliver, F.E., Cidlowski, J.A., 1991. Autoregulation of glucocorticoid receptor gene expression. Steroids 56, 52–58.

Cole, S.R., Kawachi, I., Sesso, H.D., Paffenbarger, R.S., Lee, I.M., 1999. Sense of exhaustion and coronary heart disease among college alumni. Am. J. Cardiol. 84, 1401–1405.

Dickerson, S.S., Kemeny, M.E., 2004. Acute stressors and cortisol responses: a theoretical integration and synthesis of laboratory research. Psychol. Bull. 130, 355–391.

Ehrenreich, H., Schuck, J., Stender, N., Pilz, J., Gefeller, O., Schilling, L., Poser, W., Kaw, S., 1997. Endocrine and hemodynamic effects of stress versus systemic CRF in alcoholics during early and medium term abstinence. Alcohol Clin. Exp. Res. 21, 1285–1293.

Eller, N.H., Netterstrom, B., Hansen, A.M., 2006. Psychosocial factors at home and at work and levels of salivary cortisol. Biol. Psychol. 73, 280–287.

Frost, R.O., Marten, P., Lahart, C.M., Rosenblate, R., 1990. The dimensions of perfectionism. Cogn. Therapy Res. 14, 449–468.

Gaab, J., Rohleder, N., Nater, U.M., Ehlert, U., 2005. Psychological determinants of the cortisol stress response: the role of anticipatory cognitive appraisal. Psychoneuroendocrinology 30, 599–610.

Goldstein, D.S., 1981. Plasma norepinephrine in essential hypertension. A study of the studies. Hypertension 3, 48–52.

Hanson, E.K., Schaufeli, W., Vrijkotte, T., Plomp, N.H., Godaert, G.L., 2000. The validity and reliability of the Dutch Effort-Reward Imbalance Questionnaire. J. Occup. Health Psychol. 5, 142–155.

Hautzinger, M., Bailer, M., 1993. Allgemeine Depressionsskala. Beltz Test GmbH, Weinheim.

Joksimovic, L., Siegrist, J., Meyer-Hammer, M., Peter, R., Franke, B., Klimek, W.J., Heintzen, M.P., Strauer, B.E., 1999. Over-commitment predicts restenosis after coronary angioplasty in cardiac patients. Int. J. Behav. Med. 6, 356–369.

Joksimovic, L., Starke, D., v d Knesebeck, O., Siegrist, J., 2002. Perceived work stress, overcommitment, and self-reported musculoskeletal pain: a cross-sectional investigation. Int. J. Behav. Med. 9, 122–138.

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.

Kristenson, M., Eriksen, H.R., Sluiter, J.K., Starke, D., Ursin, H., 2004. Psychobiological mechanisms of socioeconomic differences in health. Soc. Sci. Med. 58, 1511–1522.

Kuper, H., Singh-Manoux, A., Siegrist, J., Marmot, M., 2002. When reciprocity fails: effort-reward imbalance in relation to coronary heart disease and health functioning within the Whitehall II study. Occup. Environ. Med. 59, 777–784.

Laux, L., Glanzmann, P., Schaffner, C.D., 1981. Das State-Trait-Angstinventar (Testmappe mit Handanweisung, Fragebogen STAI-G Form X 1 und Fragebogen STAI-G Form X 2. Beltz, Weinheim.

Lazarus, R.S., Folkman, S., 1984. Stress, Appraisal, and Coping. Springer Publishing Company, New York.

Lefkowitz, R.J., Caron, M.G., Stiles, G.L., 1984. Mechanisms of membrane-receptor regulation. Biochemical, physiological, and clinical insights derived from studies of the adrenergic receptors. N. Engl. J. Med. 310, 1570–1579.

Linden, W., Gerin, W., Davidson, K., 2003. Cardiovascular reactivity: status quo and a research agenda for the new millennium. Psychosom. Med. 65, 5–8.

Nater, U.M., Rohleder, N., Gaab, J., Berger, S., Jud, A., Kirschbaum, C., Ehlert, U., 2005. Human salivary alpha-amylase reactivity in a psychosocial stress paradigm. Int. J. Psychophysiol. 55, 333–342.

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

Nicolson, N.A., van Diest, R., 2000. Salivary cortisol patterns in vital exhaustion. J. Psychosom. Res. 49, 335–342.

Ostendorf, F., 1990. Sprache und Persönlichkeitsstruktur. Zur Validität des Fünf-Faktoren-Modells der Persönlichkeit. Roderer, Regensburg, Germany.

Peter, R., Alfredsson, L., Hammar, N., Siegrist, J., Theorell, T., Westerholm, P., 1998. High effort, low reward, and cardiovascular risk factors in employed Swedish men and women: baseline results from the WOLF Study. J. Epidemiol. Commun. Health 52, 540–547.

Preckel, D., von Kanel, R., Kudielka, B.M., Fischer, J.E., 2005. Overcommitment to work is associated with vital exhaustion. Int. Arch. Occup. Environ. Health 78, 117–122.

Pruessner, J.C., Kirschbaum, C., Meinlschmid, G., Hellhammer, D.H., 2003. Two formulas for computation of the area under the curve represent measures of total hormone concentration versus time-dependent change. Psychoneuroendocrinology 28, 916–931.

Rahn, K.H., Barenbrock, M., Hausberg, M., 1999. The sympathetic nervous system in the pathogenesis of hypertension. J. Hypertens. Suppl. 17, S11–S14.

Roedel, A., Siegrist, J., Hessel, A., Braehler, E., 2004. Psychometric test of the questionnaire measuring Effort-Reward Imbalance at work in a representative German sample. Zeitschrift für Differentielle und Diagnostische Psychologie 24, 227–238.

Schallberger, U., Venetz, M., 1999. Kurzversion des MRS-Inventars von Ostendorf (1990). zur Erfassung der fünf "grossen" Persönlichkeitsfaktoren. University of Zurich, Zurich.

Schulz, P., Schlotz, W., Becker, P., 2004. Trierer Inventar zum chronischen Stress. Hogrefe, Göttingen.

Siegrist, J., 1996. Adverse health effects of high-effort/low-reward conditions. J. Occup. Health Psychol. 1, 27–41.

Siegrist, J., Peter, R., Junge, A., Cremer, P., Seidel, D., 1990. Low status control, high effort at work and ischemic heart disease: prospective evidence from blue-collar men. Soc. Sci. Med. 31, 1127–1134.

Siegrist, J., Klein, D., Voigt, K.H., 1997. Linking sociological with physiological data: the model of effort-reward imbalance at work. Acta Physiol. Scand. Suppl. 640, 112–116.

Siegrist, J., Starke, D., Chandola, T., Godin, I., Marmot, M., Niedhammer, I., Peter, R., 2004. The measurement of effort-reward imbalance at work: European comparisons. Soc. Sci. Med. 58, 1483–1499.

Smedes, F., Kraak, J.C., Poppe, H., 1982. Simple and fast solvent extraction system for selective and quantitative isolation of adrenaline, noradrenaline and dopamine from plasma and urine. J. Chromatogr. 231, 25–39.

Steptoe, A., Willemsen, G., 2002. Psychophysiological responsivity in coronary heart disease. In: Stansfeld, S.A., Marmot, M.G. (Eds.), Stress and the Heart. BMJ, London, pp. 168–180.

Steptoe, A., Siegrist, J., Kirschbaum, C., Marmot, M., 2004. Effort-reward imbalance, overcommitment, and measures of cortisol and blood pressure over the working day. Psychosom. Med. 66, 323–329.

Stöber, J., 1998. The frost multidimensional perfectionism scale: more perfect with four (instead of six) dimensions. Pers. Individ. Diff. 24, 481–491.

Vrijkotte, T.G., van Doorren, L.J., de Geus, E.J., 1999. Work stress and metabolic and hemostatic risk factors. Psychosom. Med. 61, 796–805.

Vrijkotte, T.G., van Doorren, L.J., de Geus, E.J., 2000. Effects of work stress on ambulatory blood pressure, heart rate, and heart rate variability. Hypertension 35, 880–886.

Vrijkotte, T.G., van Doorren, L.J., de Geus, E.J., 2004. Over-commitment to work is associated with changes in cardiac sympathetic regulation. Psychosom. Med. 66, 656–663.

Wirtz, P., 2002. Smoking, vital exhaustion and glucocorticoid sensitivity of proinflammatory cytokine release. Cuvillier Verlag, Göttingen.

Wirtz, P.H., Von Kanel, R., Schnorpfeil, P., Ehlert, U., Frey, K., Fischer, J.E., 2003. Reduced glucocorticoid sensitivity of mono-cyte interleukin-6 production in male industrial employees who are vitally exhausted. Psychosom. Med. 65, 672–678.

Wirtz, P.H., von Kanel, R., Mohiyeddini, C., Emini, L., Ruedisueli, K., Groessbauer, S., Ehlert, U., 2006. Low social support and poor emotional regulation are associated with increased stress hormone reactivity to mental stress in systemic hypertension. J. Clin. Endocrinol. Metab. 91, 3857–3865.

Wirtz, P.H., Elsenbruch, S., Emini, L., Rudisuli, K., Groessbauer, S., Ehlert, U., 2007. Perfectionism and the cortisol response to psychosocial stress in men. Psychosom. Med. 69, 249–255.