Psychoneuroendocrinology 109 (2019) 104399

Contents lists available at ScienceDirect

Psychoneuroendocrinology

journal homepage: www.elsevier.com/locate/psyneuen

Effort-reward imbalance at work is associated with hair cortisol concentrations: Prospective evidence from the Dresden Burnout Study

Marlene Penz[a,*], Johannes Siegrist[b], Magdalena K. Wekenborg[a], Nicole Rothe[a], Andreas Walther[a], Clemens Kirschbaum[a]

[a] Institute of Biological Psychology, Technische Universität Dresden, Germany
[b] Centre for Health and Society, Faculty of Medicine, Heinrich-Heine-University Düsseldorf, Germany

ARTICLE INFO

Keywords:
Work stress
Effort-reward imbalance
Hair cortisol concentrations
Prospective measures
Blunted cortisol

ABSTRACT

Chronic stress experienced at work is considered a major health challenge for modern societies. In fact there is ample evidence that deleterious work environments, based on high efforts in relation to few rewards, substantially augment the risk for a number of highly prevalent diseases (e.g. ischemic heart disease, stroke). One potential pathway mediating these associations involves the stress-related activation of the hypothalamus-pituitary-adrenocortical (HPA) axis with proceeding alterations in the secretion of its main effector hormone cortisol.

In this study we assessed a prospective, two-year effect of effort-reward imbalance (ERI) on cortisol secretion, based on a sub sample (N = 150; mean ± SD age: 42.4 ± 11.1; 84.0% female) of the ongoing Dresden Burnout Study (DBS). The provided ERI measures were collected as part of the online baseline and first follow up assessment. Further, cortisol secretion patterns over prolonged periods of time were evaluated in three consecutive years of laboratory baseline and follow up visits.

Our findings suggest prospective associations between ERI and cortisol, indicating a blunted cortisol secretion in response to long-term work stress ($p < 0.001$). Given the regulatory properties of cortisol on various central and peripheral target tissues (e.g. cardiovascular system, liver, adipose tissue), a long-term decrease of cortisol availability can be hypothesized to cause multiple health-challenging consequences. Based on our findings, providing work environments where high efforts are always linked with high rewards have to be considered an important issue for employees health.

1. Introduction

Scientific evidence demonstrates that stressful work increases the risk of a number of diseases that are highly prevalent among adult populations of modern societies. More specifically, a work stress-related burden of disease was identified most convincingly in case of ischemic heart disease and stroke (Dragano et al., 2017; Kivimäki and Steptoe, 2018), depression (Rugulies et al., 2017; Theorell et al., 2015), and metabolic disorders (Chandola et al., 2006). This new knowledge resulted mainly from prospective epidemiologic cohort studies, where work stress was assessed by validated measures of one of several established theoretical models. One of these models is effort-reward imbalance (ERI). ERI builds on the norm of social reciprocity that lies in the core of the work contract. The recurrent experience of failed reciprocity in terms of high efforts spent and low rewards received in turn elicits strong negative emotions and stress reactions among employees, in response to the perceived violation of this basic social norm of exchange (Siegrist, 1996). In this model, three reward transmitters are distinguished (money, esteem, social status). It is assumed that high-cost, low-gain conditions at work occur frequently if people have no alternative choice in the labour market or are exposed to heavy competition. In addition, a personal pattern of coping with demands, characterized by over-commitment (OC), contributes to the recurrent experience of this imbalance (Siegrist, 1996).

Knowledge on adverse effects of effort-reward imbalance at work on workers' health is not confined to results from epidemiologic investigations. Quasi-experimental and experimental studies provide additional information on potential psychobiological pathways linking this type of stressful experience with elevated disease susceptibility. For instance, effort-reward imbalance was associated with reduced heart rate variability (Falk et al., 2018; Jarczok et al., 2013), elevated blood pressure (Gilbert-Ouimet et al., 2014), markers of reduced immune

* Corresponding author.
E-mail address: marlene.penz@tu-dresden.de (M. Penz).

https://doi.org/10.1016/j.psyneuen.2019.104399
Received 14 March 2019; Received in revised form 18 June 2019; Accepted 29 July 2019

competence and increased inflammation (Bellingrath and Kudielka, 2016; Nakata et al., 2011), and with altered cortisol release (Eddy et al., 2018).

In this line of research, the recurrent stress-induced activation of the hypothalamus-pituitary-adrenocortical (HPA) axis with its release of glucocorticoids (mainly cortisol) and its effects on immune and inflammatory responses is of particular importance (Chrousos and Gold, 1992; Nicolaides et al., 2015; Sapolsky et al., 2000). Referring to the HPA axis, activation is often reflected in elevated cortisol concentrations, but several studies observed reduced rather than increased cortisol excretion in association with stressful experience (Bellingrath and Kudielka, 2008; Maina et al., 2009; Siegrist et al., 1997). Theories to explain these inconsistencies are based on a time-course model of cortisol excretion. Such models hypothesize increased levels of cortisol for an early stage of chronic stress exposure, followed by decreased levels as a result of functional adaptation to long-term excessive exposure (Miller et al., 2007; Rohleder, 2018; Siegrist et al., 1997; Steudte-Schmiedgen et al., 2016).

Previous studies linking effort-reward imbalance at work with cortisol secretion produced divergent findings. This divergence may be due to different cortisol measures (e.g. cortisol awakening response; Maina et al., 2009; diurnal profiles of cortisol secretion; Steptoe et al., 2004; HPA axis feedback sensitivity; Bellingrath et al., 2008), and/or different occupational groups under study (e.g. factory workers; Steinisch et al., 2014; line managers; Siegrist et al., 1997; call center employees; Maina et al., 2009; teachers; Bellingrath et al., 2008; Qi et al., 2014). Moreover, few studies up to now used hair cortisol concentrations (HCC), a measure representing cumulative cortisol excretion over several weeks or months (Stalder and Kirschbaum, 2012). With one exception (Herr et al., 2018), these few studies were restricted to a cross-sectional design (Qi et al., 2014; Steinisch et al., 2014; van der Meij et al., 2018).

With this paper we set out to analyse associations of chronic work stress, as measured by two consecutive assessments of effort-reward imbalance, with prospective hair cortisol concentrations (HCC), a measure of cumulative cortisol secretion over periods of hair growth (Stalder and Kirschbaum, 2012). Contrary to most previous studies we include a population representing a variety of professions and occupations. More specifically, we test the following research hypotheses: First, a one-year change in work stress (a summary measure defined by the effort-reward ratio) predicts a two-year change in hair cortisol concentration (HCC), after adjustment for relevant confounders. Due to the inconclusiveness of previous results and hypothesis (e.g. Eddy et al., 2018; Miller et al., 2007), no hypothesis concerning the direction of change (direct or inverse) was formulated. Secondly, hypothesis 1 holds equally true for each single component of the work stress model (with high effort, and high over-commitment pointing to the same direction of association as the ratio measure, discriminative to high reward).

2. Materials and methods

2.1. Study population

This report is based on data from the ongoing Dresden Burnout Study (DBS; Penz et al., 2018b), a large-scale prospective cohort study assessing health-related risk factors of work stress. The DBS has been developed in accordance with the Declaration of Helsinki, and has been approved by the local ethics committee of the University of Dresden (project number: EK 236062014). The study population includes a nation-wide online sample, providing questionnaire data in annual study waves, and a sub sample of participants living in or near the city of Dresden that was recruited to additionally participate in laboratory research, collecting a set of biomarkers (see below). This report is essentially based on this sub sample (N = 150), but descriptive characteristics of the overall online sample (including all participants who provided an ERI measure at baseline and follow up) are reported in addition (N = 1375). Table 1 provides demographics and job characteristics for both samples. To give a profound overview of the study sample, estimates of psychological health and well-being are additionally included in Table 1, but were not part of our analyses.

Table 1
Sample characteristics for baseline online and laboratory sample.

	baseline			
	online (N = 1375)		laboratory (N = 150)	
	M (SD)	Range	M (SD)	Range
demographics				
age (years)	43.4 (10.7)	18.0 – 68.0	42.4 (11.1)	23.0 – 64.0
female (%)	65.1			
body mass index (kg/m²)	25.7 (4.9)	13.1 – 45.0	25.0 (4.6)	17.7 – 40.9
underweight (%; BMI < 18.5)	1.5		1.3	
normal (%; BMI 18.5 – 24.9)	51.1		59.7	
overweight (%; BMI 25.0 – 29.9)	30.1		25.5	
obesity (%; BMI ≥ 30)	17.3		13.4	
university degree (%)	38.8		40.0	
psychological health factors				
MBI-GS sum score	2.4 (1.2)	0.1 – 5.7	2.4 (1.1)	0.2 – 5.2
≤ 1.49 (%)	26.6		25.3	
1.50 – 3.49 (%)	54.1		58.0	
≥ 3.5 (%)	19.3		16.7	
EE	3.1 (1.6)	0.0 – 6.0	3.1 (1.6)	0.0 – 6.0
Cy	2.2 (1.5)	0.0 – 6.0	2.1 (1.5)	0.0 – 6.0
rE	1.6 (1.1)	0.0 – 6.0	1.6 (1.2)	0.0 – 6.0
PHQ-9 sum score	8.8 (5.5)	0.0 – 27.0	8.6 (5.2)	0.0 – 23.0
< 15 (%)	84.0		86.0	
≥ 15 (%)	16.0		14.0	
LSC-R sum score (N = 80)	–	–	4.3 (4.0)	0.0 – 15.0
≤ 5 (%)	–	–	61.3	
≥ 6 (%)	–	–	38.7	
CTQ sum score (N = 79)	–	–	27.4 (10.5)	14.0 – 55.0
emotional abuse	–	–	4.1 (4.3)	0.0 – 17.0
physical abuse	–	–	1.0 (1.8)	0.0 – 17.0
sexual abuse	–	–	0.8 (2.2)	0.0 – 13.0
emotional neglect	–	–	15.9 (3.9)	10.0 – 24.0
physical neglect	–	–	5.5 (2.1)	4.0 – 15.0
job characteristics				
working hours	39.4 (10.3)	5.0 – 65.0	38.8 (10.0)	2.0 – 60.0
side job (%)	16.6		13.1	
shiftwork (%)	14.1		10.1	
main earner (%)	61.8		54.7	
years in current job	9.4 (8.8)	0.0 – 42.0	9.5 (9.1)	0.5 – 40
income (netto/month)				
< 1500	26.6		34.0	
1500–2000	21.5		28.0	
2000–3000	31.6		27.3	
3000–4000	11.9		6.0	
> 4000	8.4		4.7	
cortisol				
HCC baseline (N = 150; pg/mg)	–	–	14.0 (12.5)	0.4 – 60.3
HCC first follow up (N = 83)	–	–	7.9 (6.7)	0.1 – 30.0
HCC second follow up (N = 95)	–	–	10.0 (8.3)	2.2 – 35.4

Note. Standard deviations are in parentheses. MBI-GS = Maslach Burnout Inventory-General Survey, EE = emotional exhaustion, Cy = cynicism, rE = reduced efficacy, PHQ = Patient Health Questionnaire, LSC-R = Life Stressor Checklist revised, CTQ = Childhood Trauma Questionnaire, HCC = hair cortisol concentrations.

The study started in 2015, inviting volunteers to participate, provided they were aged between 18 and 68 years and were sufficiently fluent in German language (more details of the study protocol are given elsewhere; Penz et al., 2018b).

Besides the general DBS study criteria concerning age and language,

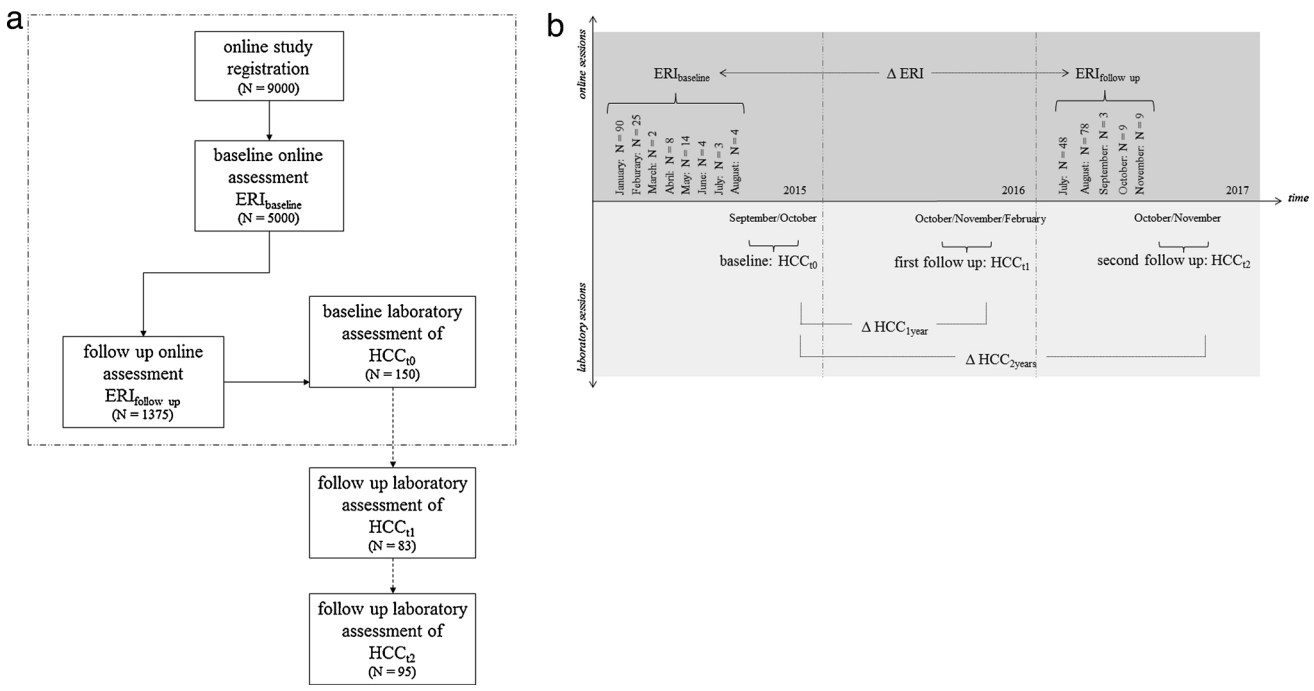

Fig. 1. (a) Sample recruitment and selection procedure (b) Data collection scheme for ERI and HCC.
Note. ERI = effort-reward imbalance; HCC = hair cortisol concentrations.
t_0 = baseline; t_1 = 1. follow up; t_2 = 2. follow up.
Note. Δ ERI = $ERI_{follow\ up} - ERI_{baseline}$. Δ HCC_{1year} = $HCC_{t1} - HCC_{t0}$; Δ HCC_{2years} = $HCC_{t2} - HCC_{t1}$.

inclusion to the current sub sample was based on online pre-selection. Participants were included if they registered via the study homepage (www.dresden-burnout-study.de) and provided ERI measurements at online baseline and follow up assessment. Further, it was obligatory to participate in the baseline laboratory assessment of biomarkers. Fig. 1a and b give an overview of the timetable (Fig. 1a) and the recruitment and selection procedure (Fig. 1b).

2.2. Measurements

2.2.1. Work stress

ERI was measured with the standardized 16-item short version (Siegrist et al., 2009). It is composed by the two extrinsic scales 'effort' (3 items) and 'reward' (7 items, including esteem, job security, and job promotion), and by the intrinsic scale 'over-commitment' (6 items). All items are answered on a 4-point Likert-scale (1 = strongly agree, 2 = agree, 3 = disagree, 4 = strongly disagree). Sum scores are computed for each scale, where high scores indicate high 'effort', high 'reward', and high 'over-commitment'. In line with the theoretical assumption that the imbalance between high effort and low reward matters most, the construction of an 'effort-reward ratio' has been proposed in addition to the single scales. This ratio (ERI) quantifies the mismatch between effort (nominator) and reward (denominator), adjusted for unequal number of items, at individual level (Siegrist and Wahrendorf, 2016). The short ERI version has been used in many epidemiologic and experimental studies. Its scales provide satisfactory internal consistency, and the factorial validity has been repeatedly confirmed by structural equation modelling in studies, among others, from France (Siegrist et al., 2018), Germany (Li et al., 2012), and Italy (Magnavita et al., 2012). Moreover, these studies supported the criterion validity of the scales, given consistent associations with selected health indicators.

2.2.2. Hair cortisol concentrations

At each laboratory visit, hair strains were cut as close as possible to the scalp from the posterior vertex position, provided that hair length did not undercut 3 cm. Hair cortisol concentrations (HCC) were provided from the 3 cm most proximal to the scalp. Due to the average hair growth of 1 cm per month (Wennig, 2000) this reflects a measure of cumulative cortisol secretion for the period of 3 months prior to sampling (Stalder and Kirschbaum, 2012). Washing procedure and cortisol extraction were conducted in accordance with the laboratory protocol by Gao et al. (2013). All samples were analysed by liquid chromatography coupled with tandem mass spectrometry (LC–MS/MS).

The DBS study design provides for an ongoing recruitment and open study pool. As a consequence, participants of the present sub sample registered and provided baseline measurements (e.g. $ERI_{baseline}$) with an inter-individual variation of several months (January to August 2015; Fig. 1b). Independent of the moment of study registration, all participants were re-invited for the online follow up assessment in July 2017 and were provided with a timeframe of several weeks to participate. To decrease the influence of seasonal effects on cortisol concentrations (Spiga et al., 2014), laboratory assessments were conducted yearly in autumn and winter. Due to this reason, there is also inter-individual variation in the time intervals between online and laboratory assessments. To reduce the possibility of systematic effects due to these time variations, all statistical models were adjusted by the variable `time interval´. The variable represents the distance between online baseline and follow up assessment, which further defines the amount of distance between online and laboratory assessments (`time interval´ = date $ERI_{follow\ up}$ - date $ERI_{baseline}$).

2.3. Data processing and statistical analyses

Logarithmic transformations were performed for $ERI_{baseline}$ and $ERI_{follow\ up}$. Consequently, the change value between baseline and follow up was calculated based on the log-transformed values [Δ ERI = $\log(ERI_{follow\ up}) - \log(ERI_{baseline})$]. Notably, the three individual scales ('effort', 'reward', and 'over-commitment') were used for analyses in their original categorical format.

HCC were log-transformed to provide a normal distribution and outliers were excluded, defined as above or below 3 standard deviations from the mean of the log-scaled outcome. 5 values (3.3%) had to be

excluded for laboratory baseline, 1 (0.7%) for the first and 3 (2%) for the second follow up. A change score was calculated for HCC, analogous to the change in ERI.

According to our hypothesis, we analysed associations between a summary measure of stressful work [Δ ERI = log($ERI_{follow\ up}$) − log($ERI_{baseline}$)] and a summary measure of prospective change in HCC (Δ HCC_{2years} = HCC_{t2} − HCC_{t0}; see Fig. 1). In addition, associations with the subsequent HCC_{t2} measure were analysed. While these calculations were essential for our hypothesis, additional combinations of relationships between all available work stress and HCC measures as well as analyses including the moderator ERI*OC were explored and documented (see supplement).

All analyses were conducted by using SPSS Statistics 25 (SPSS Inc., IL, USA).

2.3.1. Primary analyses

As mentioned, our main analyses assessed the associations between Δ ERI and Δ HCC_{2years} as well as the associations between Δ ERI and HCC_{t2}. Sequential multiple regression analyses were conducted to this end. To avoid potential floor or ceiling effects, regression models were adjusted for the baseline HCC value (HCC_{t0}; Herr et al., 2018). All regression models were adjusted for the inter-individual confounders sex, age, and body mass index (meta-analysis: Stalder et al., 2017). Further, two additional confounders were entered into the regression model: `medication´ (51% of participants reported regular use of medication, including oral contraceptives, antidepressants, antihistamines, and intake of thyroid hormones) and `time interval´ between online baseline and follow up assessment. All confounders were entered *en bloc* into the model.

Significance for main analyses was defined by the Bonferroni-corrected threshold of $p < \alpha = 2.5\%$ (two-sided) to maintain a family-wise error rate of 5%.

2.3.2. Secondary analyses

Further, the contribution of each individual scale was analysed analogous to the primary analyses. Instead of Δ ERI, Δ Effort, Δ Reward, and Δ OC were computed by the same equation to estimate their predictive value towards Δ HCC_{2years} and HCC_{t2}. The same confounders were entered *en bloc* to the model. Significance for secondary analyses was defined by the Bonferroni-corrected threshold of $p < \alpha = 1.67\%$ (two-sided).

3. Results

Main study variables (ERI and individual scales) are reported in Tables 2a and 2b for both samples.

Table 2b
Main study variables for the respective study sample.

	laboratory sub sample (N = 150)					*Cohen´s d*
	baseline		follow up		*t*	
	M (SD)	Range	M (SD)	Range		
effort	9.3 (1.8)	4.0 – 12.0	8.9 (2.1)	3.0 – 12.0	2.25*	0.18
reward	17.7 (3.8)	9.0 – 12.0	18.1 (3.8)	7.0 – 28.0	−1.33	0.11
esteem	5.0 (1.5)	2.0 – 8.0	5.0 (1.5)	2.0 – 8.0	−0.10	0.01
promotion	6.8 (1.9)	3.0 – 12.0	7.0 (1.9)	3.0 – 12.0	−1.52	0.12
security	5.9 (1.6)	2.0 – 8.0	6.0 (1.5)	2.0 – 8.0	−1.08	0.09
OC	15.4 (3.9)	6.0 – 24.0	14.6 (3.7)	6.0 – 24.0	3.52**	0.29
ERI	1.3 (0.4)	0.5 – 2.8	1.2 (0.5)	0.3 – 4.0	1.58	0.13
≤1 (%)	27.3		37.3			
> 1 (%)	72.7		62.7			

Note. Standard deviations are in parentheses. OC = over-commitment. ERI = effort-reward imbalance; ***p < 0.001, **p < 0.01, *p < 0.05.

3.1. Primary analyses

Δ ERI highly significantly predicted the change in HCC over the period of two years (Δ HCC_{2years}: $R^2 = 0.58$, $F(7,86) = 17.21$, $\Delta R^2 = 0.08$, β = -0.28, $p < 0.001$) and the point measure of HCC at second follow up (HCC_{t2}: $R^2 = 0.30$, $F(7,86) = 5.15$, $\Delta R^2 = 0.13$, β = -0.37, $p < 0.001$). The reported inverse associations are displayed by Fig. 2a and b, which exemplify the linear fit between Δ ERI and Δ HCC_{2years}/HCC_{t2}.

3.2. Secondary analyses

Δ Effort did not significantly predict Δ HCC_{2years} or HCC_{t2}, but was indicated as a trend in both models (Δ HCC_{2years}: $R^2 = 0.53$, $F(7,86) = 13.78$, $\Delta R^2 = 0.03$, β = -0.16, $p = 0.04$; HCC_{t2}: $R^2 = 0.20$, $F(7,86) = 3.12$, $\Delta R^2 = 0.04$, β = -0.21, $p = 0.04$). Δ Reward was significantly associated with Δ HCC_{2years} ($R^2 = 0.55$, $F(7.86) = 14.96$, $\Delta R^2 = 0.05$, β = 0.22, $p < 0.01$) and with HCC_{t2} ($R^2 = 0.24$, $F(7,86) = 3.82$, $\Delta R^2 = 0.08$, β = 0.28, $p < 0.01$). By contrast, Δ OC neither significantly explained variance in Δ HCC_{2years} nor in HCC_{t2}.

As shown by the supplementary material, the remaining associations support the primary and secondary results. Additionally, inverse associations between the follow up variables ERI and effort, and the moderator ERI*OC with HCC_{t2} are likewise suggested.

Table 2a
Main study variables for the overall online sample.

	online assessment (N = 1375)					*Cohen´s d*
	baseline		follow up		*t*	
	M (SD)	Range	M (SD)	Range		
effort	9.4 (1.9)	3.0 – 12.0	9.2 (2.1)	3.0 – 12.0	3.62***	0.10
reward	17.4 (3.9)	7.0 – 28.0	18.0 (4.1)	7.0 – 28.0	−6.37**	0.17
esteem	4.8 (1.5)	2.0 – 8.0	4.9 (1.5)	2.0 – 8.0	−3.08**	0.08
promotion	6.7 (1.9)	3.0 – 12.0	7.0 (2.0)	3.0 – 12.0	−6.33**	0.17
security	5.8 (1.5)	2.0 – 8.0	6.0 (1.5)	2.0 – 8.0	−4.02***	0.11
OC	15.9 (4.0)	6.0 – 24.0	15.0 (4.0)	6.0 – 24.0	10.08***	0.27
ERI	1.3 (0.5)	0.3 – 3.7	1.3 (0.5)	0.3 – 4.0	5.19***	0.14
≤1 (%)	25.7		32.3			
> 1 (%)	74.3		67.7			

Note. Standard deviations are in parentheses. OC = over-commitment. ERI = effort-reward imbalance; ***p < 0.001, **p < 0.01, *p < 0.05.

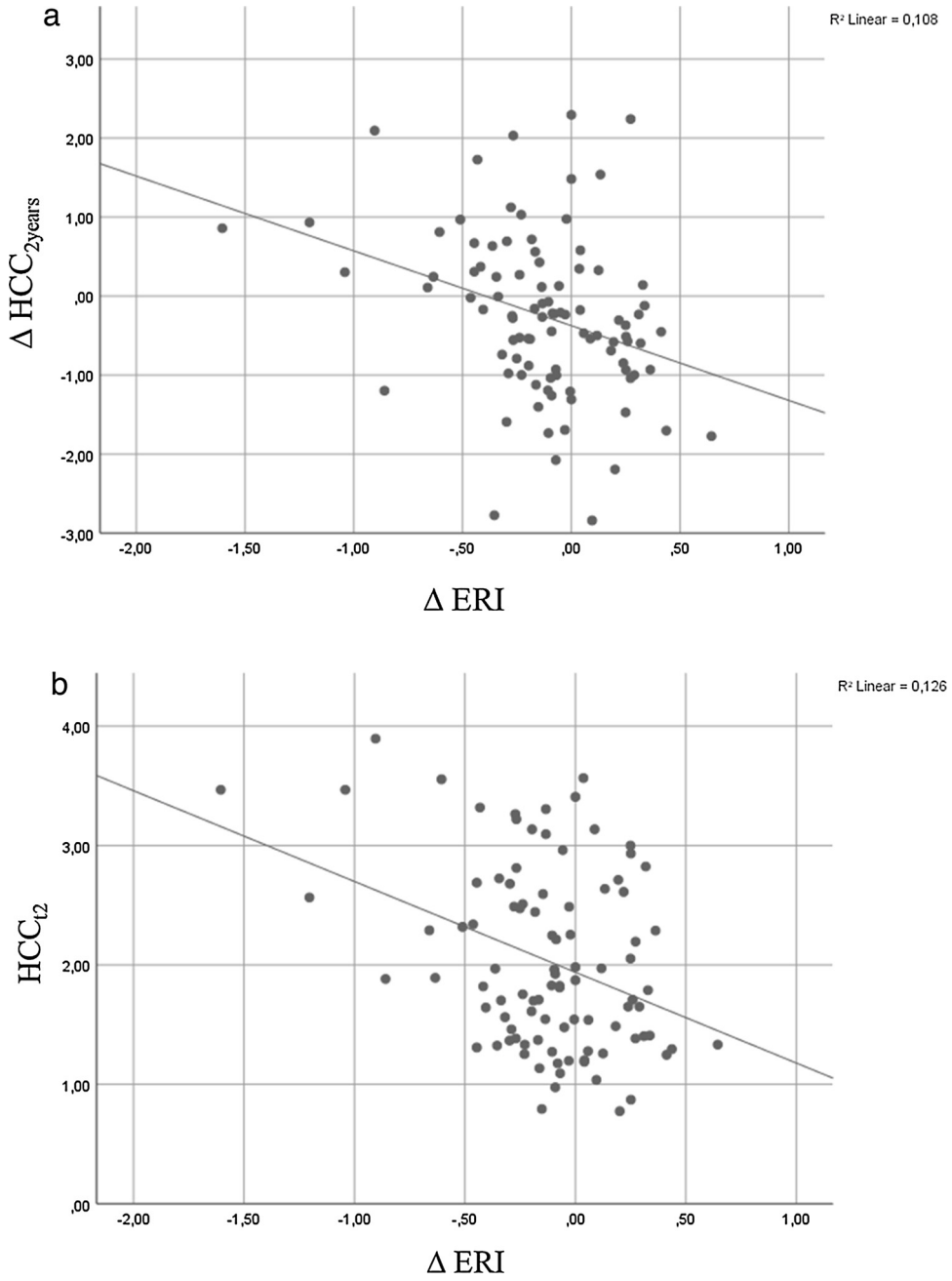

Fig. 2. (a) Linear fit between Δ ERI and Δ HCC_{2years} (b) Linear fit between Δ ERI and HCC_{t2}.
Note. ERI = effort-reward imbalance; HCC = hair cortisol concentrations; Δ ERI = $ERI_{follow\ up} - ERI_{baseline}$; Δ HCC_{2years} = $HCC_{t2} - HCC_{t1}$; t2 = 2. follow up.

4. Discussion

This study indicates prospective associations between a summary measure of work stress (one-year change in effort-reward imbalance: Δ ERI) and two prospective hair cortisol measures (Δ HCC_{2years}; HCC_{t2}). A one-year increase in ERI was predictive of a two-year decrease in HCC, thus suggesting a blunted cortisol secretion (Fig. 2a). Furthermore, the one-year increase in ERI was inversely associated with HCC at second follow up (HCC_{t2}), supporting the notion of reduced long-term cortisol secretion (Fig. 2b). Supplementary analyses using both individual ERI measures instead of the change score point to the same direction: high long-term ERI is related to low prospective cortisol secretion. Concerning secondary analyses referring to the sub components of the ERI model, reward was the only measure with consistent associations with cortisol. In line with our hypothesis, the association between reward and HCC pointed to the opposed direction as the association between ERI and HCC. The direct association supports the idea that low reward represents a stressor, likewise ERI, which can lead to HPA axis alteration in the long term. Contrary to our hypothesis, the change of reward was not associated with the long-term change of HCC. Notably, additional analyses (supplement) using the individual point measures instead of a change score suggest a long-term inverse association between the subcomponent effort and HCC: Both individual and combined point measures ($effort_{baseline}$ and $effort_{follow\ up}$) suggested an inverse association with cortisol. It can therefore be speculated that not just the ratio measure (ERI) but also the individual subcomponents (effort, reward) activate a physiological stress reaction. Interestingly, neither secondary nor supplementary analyses indicate a long-term effect of OC on cortisol excretion.

Our main findings contradict the hypothesis of a direct association

between level of ERI and level of cortisol secretion, that was suggested by a recent meta-analysis (Eddy et al., 2018). However, discrepant findings, pointing to a blunted cortisol response following exposure to chronic work stress due to ERI, were reported as well (Bellingrath et al., 2008; Maina et al., 2009; Siegrist et al., 1997). Generally, the current results are difficult to compare with previous findings, for the following reasons: As already mentioned in the introduction section, study designs providing available data on the association between ERI and cortisol secretion differ immensely. Differing to the DBS, most previous studies focused on specific professions (e.g. call centre operators, teachers), and it might be concluded that participants faced a specific level, duration or kind of general work strain, depending on a certain profession. Further, reported cortisol measures varied. Bellingrath et al. (2008) for instance reported stronger cortisol suppression after dexamethasone application referring to HPA axis feedback sensitivity, while Maina et al. (2009) found ERI associated with lower CAR and daily cortisol profiles. The only prior study measuring the association between ERI and HCC in a prospective design indicated the opposite to our results (direct long-term association between ERI and HCC; Herr et al., 2018). Indeed, findings were based on a small sample, a short follow-up period, and a group of male workers with low level of work stress (Herr et al., 2018).

As our results support the notion of blunted cortisol secretion following long-term exposure to work stress, the question arises of how this finding deviating from the common pattern can be interpreted. Importantly, a meta-analysis conducted by Miller et al. (2007) supports the notion of a two-stage process of HPA axis activation, in case that a stressor is prolonged for an undefined duration of months or even years. In a first stage, increased cortisol secretion following exposure to a stressor is observed. A long-term heightened exposure to the hormone is then hypothesized to activate counter-regulatory mechanisms, such as an altered biosynthesis of respective releasing factors or structural change of its receptors (Fries et al., 2005). As a consequence, a second stage with decreased HPA axis responsiveness and cortisol secretion might arise and is discussed as missing link to explain inconsistent findings in regard to cortisol and stress exposure (Rohleder, 2018; Steudte-Schmiedgen et al., 2016).

We interpret the inverse associations between ERI and HCC in our sample to be in line with a two-stage theory of HPA axis activation. We therefore hypothesize that compared to studies showing the opposite pattern of direct associations (e.g. Herr et al., 2018), our sample in average represents a higher level of burden and chronification. The long-term suffering from failed reciprocity at work might have caused long-term over-activation of the HPA axis, challenging receptor sensitivity and feedback regulation, leading to the consequence of an overall blunted cortisol excretion.

5. Study limitations

Although the reported results are based on sound statistics and adjusted for potential confounders, our study shows some shortcomings and limitations. First, the sample is characterised by a rather high level of imbalance between effort and reward, compared to other populations (e.g. Hoven et al., 2015; Jood et al., 2018; Wege et al., 2018). It is therefore likely that participants were susceptible to blunted cortisol responses due to longer-term exposure to stressful experience. Moreover, we cannot exclude a sample selection bias over time, such that highly stressed participants were more likely to complete all online and laboratory assessments. Neither can we exclude a potential moderator effect of other prior and/or co-occurring life stressors (Table 1). Second, the majority of participants were women, due to the fact that the requested hair length for HCC assessment was available to a lower extent among men than among women. Therefore, generalization of our findings to both sexes is limited. In this regard it has to be mentioned that the use of contraceptives was assessed only based on an overall medication estimate (`Do you regularly take medicine?´, if yes: `which one?´). Even if the longitudinal design perfectly controls for inter-individual confounders, results are not ideally adjusted for the variation explained by the use of contraceptives or regular medication. Third, as mentioned, due to the recruitment strategy of the DBS (Penz et al., 2018b) our data collection implies high inter-individual variation of time intervals between online and laboratory assessments (e.g. view days up to several months between ERI and HCC assessment). Even if we minimized potential bias by statistical adjustment for these differences, we cannot preclude a systematic effect caused by these differences.

A further limitation concerns the lack of conclusive evidence supporting the two-stage process of HPA axis activation. Even if the theory is supported by meta-analytic findings (Miller et al., 2007), longitudinal data assessing a stress-guided switch from one phase to another is so far missing. Our supplementary analyses indirectly support such a switch, by suggesting a long-term change from `no association´ towards inverse associations between the stressor and HCC. Certainly, there is no evidence for a preceding state of direct association, as suggested by the theory.

Last but not least, the notion of a blunted cortisol secretion following a work-related stressor (ERI) might appear contrary to a direct association between burnout and HCC related to the same laboratory baseline assessment (reported in Penz et al., 2018a). We interpret this discrepancy to be due to the assessments of two theoretically related but different concepts with restricted comparability (various additional antecedents of burnout except ERI are conceivable). Another interpretation is based on a two-stage process of HPA axis activation, where HPA axis over-activation due to an aversive work situation changes into blunted cortisol excretion at a later stage of stress chronification. Such a process was already reported and discussed by Fernández-Sánchez et al. (2018) for different levels of burnout.

6. Conclusions

In conclusion, this study revealed strong prospective associations of chronic work stress, as measured by effort-reward imbalance, with a summary measure of cortisol (HCC). The inverse associations suggest a blunted cortisol secretion in response to longer-term exposure to stressful work. If supported by future research, this finding may contribute to an improved identification and protection of persons susceptible to stress-related physiological dysregulation and its potential adverse effects on health.

Declaration of Competing Interest

The authors have no conflicts of interest to declare.

Acknowledgements

We thank the whole research team, which contributed to the collection and analyses of this data. Especially we want to thank Angelika Buske-Kirschbaum, Tobias Stalder, and Robert Miller for sharing their expertise. We further thank our participants, who were willing to come to the laboratory once a year to provide us with longitudinal information.

Funding

This work was supported by an intramural research grant issued by the TU Dresden (Support the Best programme, part of the TUD Institutional Strategy, Excellence Initiative, awarded to CK).

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.psyneuen.2019.

104399.

References

Bellingrath, S., Kudielka, B.M., 2008. Effort-reward-imbalance and overcommitment are associated with hypothalamus–pituitary–adrenal (HPA) axis responses to acute psychosocial stress in healthy working schoolteachers. Psychoneuroendocrinology 33, 1335–1343.

Bellingrath, S., Weigl, T., Kudielka, B.M., 2008. Cortisol dysregulation in school teachers in relation to burnout, vital exhaustion, and effort–reward-imbalance. Biol. Psychol. 78, 104–113.

Bellingrath, S., Kudielka, B.M., 2016. Psychobiological pathways from work stress to reduced health: naturalistic and experimental studies on the ERI model. In: Siegrist, J., Wahrendorf, M. (Eds.), Work Stress and Health in a Globalized Economy: The Model of Effort-Reward Imbalance. Springer, pp. 145–170.

Chandola, T., Brunner, E., Marmot, M., 2006. Chronic stress at work and the metabolic syndrome: prospective study. BMJ 332, 521–525.

Chrousos, G.P., Gold, P.W., 1992. The concepts of stress and stress system disorders: overview of physical and behavioral homeostasis. JAMA 267, 1244–1252.

Dragano, N., Siegrist, J., Nyberg, S.T., Lunau, T., Fransson, E.I., Alfredsson, L., et al., 2017. Effort–reward imbalance at work and incident coronary heart disease: a multicohort study of 90,164 individuals. Epidemiology (Cambridge, Mass.) 28, 619.

Eddy, P., Wertheim, E.H., Hale, M.W., Wright, B.J., 2018. A systematic review and meta-analysis of the effort-reward imbalance model of workplace stress and hypothalamic-pituitary-adrenal axis measures of stress. Psychosom. Med. 80, 103–113.

Falk, A., Kosse, F., Menrath, I., Verde, P., Siegrist, J., 2018. Unfair pay and health. Manage. Sci. 64, 1477–1488.

Fernández-Sánchez, J.C., Pérez-Mármol, J.M., Blásquez, A., Santos-Ruiz, A.M., Peralta-Ramírez, M.I., 2018. Association between burnout and cortisol secretion, perceived stress, and psychopathology in palliative care unit health professionals. Palliat. Support. Care 16, 286–297.

Fries, E., Hesse, J., Hellhammer, J., Hellhammer, D.H., 2005. A new view on hypocortisolism. Psychoneuroendocrinology 30, 1010–1016.

Gao, W., Stalder, T., Foley, P., Rauh, M., Deng, H., Kirschbaum, C., 2013. Quantitative analysis of steroid hormones in human hair using a column-switching LC–APCI–MS/MS assay. J. Chromatogr. B 928, 1–8.

Gilbert-Ouimet, M., Trudel, X., Brisson, C., Milot, A., Vezina, M., 2014. Adverse effects of psychosocial work factors on blood pressure: systematic review of studies on demand-control-support and effort-reward-imbalance models. Scand. J. Work Environ. Health 40, 109–132.

Herr, R.M., Almer, C., Loerbroks, A., Barrech, A., Elfantel, I., Siegrist, J., et al., 2018. Associations of work stress with hair cortisol concentrations–initial findings from a prospective study. Psychoneuroendocrinology 89, 134–137.

Hoven, H., Wahrendorf, M., Siegrist, J., 2015. Occupational position, work stress and depressive symptoms: A pathway analysis of longitudinal SHARE data. J. Epidemiol. Community Health 69, 447–452.

Jarczok, M.N., Jarczok, M., Mauss, D., Koenig, J., Li, J., Herr, R.M., Thayer, J.F., 2013. Autonomic nervous system activity and workplace stressors – a systematic review. Neurosci. Biobehav. Rev. 37, 1810–1823.

Jood, K., Karlsson, N., Medin, J., Pessah-Rasmussen, H., Wester, P., Ekberg, K., 2018. The psychosocial work environment is associated with risk of stroke at working age. Scand. J. Work Environ. Health 43, 367–374.

Kivimäki, M., Steptoe, A., 2018. Effects of stress on the development and progression of cardiovascular disease. Nat. Rev. Cardiol. 15, 215.

Li, J., Loerbroks, A., Jarczok, M.N., Schöllgen, I., Bosch, J.A., Mauss, D., et al., 2012. Psychometric properties and differential explanation of a short measure of effort–reward imbalance at work: a study of industrial workers in Germany. Am. J. Ind. Med. 55, 808–815.

Magnavita, N., Garbarino, S., Siegrist, J., 2012. The use of parsimonious questionnaires in occupational health surveillance: psychometric properties of the short Italian version of the effort/reward imbalance questionnaire. Sci. World J. 2012.

Maina, G., Bovenzi, M., Palmas, A., Filon, F.L., 2009. Associations between two job stress models and measures of salivary cortisol. Int. Arch. Occup. Environ. Health 82, 1141–1150.

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. Psychol. Bull. 133, 25–45.

Nakata, A., Takahashi, M., Irie, M., 2011. Effort-reward imbalance, overcommitment, and cellular immune measures among white-collar employees. Biol. Psychol. 88, 270–279.

Nicolaides, N.C., Kyratzi, E., Lamprokostopoulou, A., Chrousos, G.P., Charmandari, E., 2015. Stress, the stress system and the role of glucocorticoids. Neuroimmunomodulation 22, 6–19.

Penz, M., Stalder, T., Miller, R., Ludwig, V.M., Kanthak, M.K., Kirschbaum, C., 2018a. Hair cortisol as a biological marker for burnout symptomatology. Psychoneuroendocrinology 87, 218–221.

Penz, M., Wekenborg, M.K., Pieper, L., Beesdo-Baum, K., Walther, A., Miller, R., et al., 2018b. The Dresden Burnout Study: protocol of a prospective cohort study for the bio-psychological investigation of burnout. J. Methods Psychiatr. Res. e1613.

Qi, X., Zhang, J., Liu, Y., Ji, S., Chen, Z., Sluiter, J.K., Deng, H., 2014. Relationship between effort–reward imbalance and hair cortisol concentration in female kindergarten teachers. J. Psychosom. Res. 76, 329–332.

Rohleder, N., 2018. Burnout, hair cortisol, and timing: Hyper-or hypocortisolism? Psychoneuroendocrinology 87, 215–217.

Rugulies, R., Aust, B., Madsen, I.E., 2017. Effort–reward imbalance at work and risk of depressive disorders. A systematic review and meta-analysis of prospective cohort studies. Scand. J. Work Environ. Health 43, 294–306.

Sapolsky, R.M., Romero, L.M., Munck, A.U., 2000. How do glucocorticoids influence stress responses? Integrating permissive, suppressive, stimulatory, and preparative actions. Endocr. Rev. 21, 55–89.

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

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

Siegrist, J., Wahrendorf, M., 2016. Work Stress and Health in a Globalized Economy: the Model of Effort-reward Imbalance. Springer.

Siegrist, J., Wahrendorf, M., Goldberg, M., Zins, M., Hoven, H., 2018. Is effort–reward imbalance at work associated with different domains of health functioning? Baseline results from the French CONSTANCES study. Int. Arch. Occup. Environ. Health 1–14.

Siegrist, J., Wege, N., Pühlhofer, F., Wahrendorf, M., 2009. A short generic measure of work stress in the era of globalization: effort–reward imbalance. Int. Arch. Occup. Environ. Health 82, 1005–1013.

Spiga, F., Walker, J.J., Terry, J.R., Lightman, S.L., 2014. HPA axis-rhythms. Compr. Physiol. 4, 1273–1298.

Stalder, T., Kirschbaum, C., 2012. Analysis of cortisol in hair–State of the art and future directions. Brain Behav. Immun. 26, 1019–1029.

Stalder, T., Steudte-Schmiedgen, S., Alexander, N., Klucken, T., Vater, A., Wichmann, S., et al., 2017. Stress-related and basic determinants of hair cortisol in humans: a meta-analysis. Psychoneuroendocrinology 77, 261–274.

Steinisch, M., Yusuf, R., Li, J., Stalder, T., Bosch, J.A., Rahman, O., et al., 2014. Work stress and hair cortisol levels among workers in a Bangladeshi ready-made garment factory–results from a cross-sectional study. Psychoneuroendocrinology 50, 20–27.

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.

Steudte-Schmiedgen, S., Kirschbaum, C., Alexander, N., Stalder, T., 2016. An integrative model linking traumatization, cortisol dysregulation and posttraumatic stress disorder: Insight from recent hair cortisol findings. Neurosci. Biobehav. Rev. 69, 124–135.

Theorell, T., Hammarström, A., Aronson, G., Träskman Bendz, L., Grape, T., Hall, C., 2015. A systematic review including metaanalysis of work environment and depressive symptoms. BMC Public Health 15, 738.

van der Meij, L., Gubbels, N., Schaveling, J., Almela, M., van Vugt, M., 2018. Hair cortisol and work stress: importance of workload and stress model (JDCS or ERI). Psychoneuroendocrinology 89, 78–85.

Wege, N., Li, J., Siegrist, J., 2018. Are there gender differences in associations of effort–reward imbalance at work with self-reported doctor-diagnosed depression? Prospective evidence from the German Socio-Economic Panel. Int. Arch. Occup. Environ. Health 91, 435–443.

Wennig, R., 2000. Potential problems with the interpretation of hair analysis results. Forensic Sci. Int. 107, 5–12.