



## Short Communication

## Associations of work stress with hair cortisol concentrations – initial findings from a prospective study

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## ABSTRACT

There is ample evidence supporting the link between stress at the workplace and physical and mental health. One of the pathways potentially mediating those associations may involve the hypothalamic-pituitary-adrenal (HPA) axis, with cortisol as an end product. While theoretically plausible, findings on the association of self-reported work stress with hair cortisol concentrations (HCC) are inconclusive, being potentially biased by omitted pertinent factors. This issue can be addressed, among others, by eliminating time-invariant factors through consideration of variation within persons over time. To this end, the present study examined the association between variation in HCC and perceived work stress – as assessed by the Effort-Reward-Imbalance (ERI) model – between two points in time (t1 and t2) over one year in a sample of 40 male factory workers. Neither a cross-sectional association, nor a link between change in ERI and HCC levels at t2 was observed. There was however a robust association of the change in ERI with the change of HCC. This effect was independent of baseline HCC and other confounders (Beta = 0.414, S.E. = 0.155,  $p = 0.012$ ). Accordingly, this is the first study revealing prospective evidence for the associations of work stress with HCC, while excluding potentially time-stable confounding factors, like genetic factors or phenotypic hair color.

## 1. Introduction

The hypothalamic-pituitary-adrenal (HPA) axis represents an essential part of the (work) stress response and embodies a key biophysiological mechanism underlying ill-health. The end products of the HPA axis are glucocorticoids, which encompass the stress hormone cortisol. Cortisol levels are subject to diurnal variations and short-term changes (e.g., in response to stressors), which affect measurements in plasma and saliva. Measuring hair cortisol concentrations (HCC) is a more recent approach which retrospectively assesses the cumulative cortisol levels of several months, which is therefore not affected by diurnal variation, and has been regarded as a promising biomarker of chronic stress exposure (Russell et al., 2012). Empirical findings of the association of HCC with perceived stress in general (for a review see Stalder et al., 2017) and with work stress in particular are however inconclusive (Gidlow et al., 2015; Herr et al., 2017; Janssens et al., 2016; Qi et al., 2014; Steinisch et al., 2014). Those mixed findings may

partly be explained by limited consideration of all contributing factors (i.e., confounders). Very recent studies revealed, e.g., HCC to be sensitive to genetic factors, and, in addition, to phenotypic hair color (Neumann et al., 2017; Tucker-Drob et al., 2017). While controlling for such factors in cross-sectional studies appears difficult – if not impossible – a longitudinal examination can eliminate such time-invariant factors by exploiting within-person variation (Wooldridge, 2010). Exploiting within-person variation in the data inherently eliminates any time-invariant factor from the analysis including characteristics of the investigated/surveyed individual. To our knowledge, this study is the first to examine the variation of perceived work stress and HCC between two time points.

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## 2. Methods

### 2.1. Participants

This study uses two waves of a cohort followed up after a preceding stress management intervention. In 2006/7 all production line employees with leadership responsibility (lower and middle management) of a metal manufacturing plant in Southern Germany were invited to enroll in a stress management training program. Management responsibilities at the interface between production and higher management are known to be particularly stressful. The aim of the stress management training program was to improve participants' ability to identify and cope with stressors at the workplace, focusing especially on the extrinsic component of the Effort-Reward-Imbalance (ERI) model, the mismatch between efforts and rewards, and recovery from the intrinsic component over-commitment. The training comprised a tailored group-orientated stress prevention seminar, applying psychodynamic, conflict- and emotion-focused principles, but also elements of behavioral cognitive techniques (for details, please see Limm et al., 2011). Participants were followed up in 2008, 2015, and 2016. In the last two waves (i.e., 2015 [here: t1] and 2016 [here: t2]) ERI and hair cortisol concentration (HCC) were measured at both time points, which therefore provided the data for the current study.

In the present analyses men (the original sample included only one female respondent) with valid HCC data and ERI data at both waves were included ( $n = 48$ ). Participants with asthma and those using cortisol medication ( $n = 2$ ), or those reporting a chronic mental illness (i.e., post-traumatic stress disorder, depression, or burnout;  $n = 5$ ), or HCC outliers (more than  $\pm 3.5$  standard deviation around the mean;  $n = 1$ ) were excluded. The final sample comprised 40 individuals. All participants provided written informed consent and the local Ethical Committee approved the study.

The average age of individuals in the sample was 47.9 years (standard deviation (S.D.) = 6.30), the mean body mass index (BMI) was 28.15 kg/m<sup>2</sup> (S.D. = 4.32), and 35% of the participants were segment managers. Participants worked 43.4 h a week (S.D. = 4.28) on average. The majority of the sample (82%) did not smoke and did no shift work (64%). The mean cortisol values were 8.37 pg/mg (S.D. = 6.50) at t1, and 9.19 pg/mg (S.D. = 7.32) at t2. The E-R ratio was 0.57 (S.D. = 0.24) at t1, and 0.55 (S.D. = 0.22) at t2.

### 2.2. Measures

#### 2.2.1. Work stress

Work stress was operationalized at both time points using the established effort-reward-imbalance (ERI) model (Siegrist et al., 2004), which is associated with HPA axis measures (Eddy et al., 2017). Effort was measured with six items, and reward was measured with eleven items with responses being provided on a 5-point Likert scale. The measurement of over-commitment (OC) consisted of six items and a 4-point response scale (Siegrist et al., 2004). Sum scores were calculated with higher scores indicating higher effort, reward, or OC, respectively. In addition, a weighted ratio between the effort and reward was calculated to obtain the E-R ratio, with higher values indicating higher work stress (Siegrist et al., 2004).

#### 2.2.2. Hair cortisol analysis

Participants provided a 3-cm hair segment (when available, but not less than 1 cm) cut closely to the scalp from the back of the head at both time points. HCC was measured by an online solid phase extraction liquid chromatography-tandem mass spectrometry method based on fragments of second order MS<sup>3</sup> (SPE LC-MS/MS/MS) according to the procedure described by Quinete et al. (2015). Intra- and inter-assay coefficients of variation of the method ranged between 1.4 and 14%.

### 2.3. Statistical analyses

The core of the statistical analysis is based on linear regressions of first-differenced data:  $Y_{i2} - Y_{i1}$ , with Y indicating both dependent variables as well as explanatory variables, subscripts i indicating the individual and 1 and 2 referring to time points 1 and 2, respectively. This allows to eliminate all time-invariant confounders (between t1 and t2) which is similar to using fixed-effects specifications in a  $t > 3$  panel (for further details, see Wooldridge, 2010)). That is, instead of estimating a cross-sectional relationship of the form  $HCC_i = const + \beta * ERI_i + \omega * X_i + \varepsilon$ , our main results are based on:

$$(HCC_{i2} - HCC_{i1}) = const + \beta * (ERI_{i2} - ERI_{i1}) + \omega * (X_{i2} - X_{i1}) + \varepsilon_i.$$

HCC refers to the level of hair cortisol at each time point and  $(HCC_{i2} - HCC_{i1})$  refers to the change in HCC levels between t1 and t2. ERI stands for the weighted ratio between effort and reward (E-R ratio) and the vector X includes a number of confounders included in some of the models. In our analyses, the first model (Model 1) included no confounder. The second model (Model 2) contained potential confounders, which conceivably affect changes in HCC or ERI, these are: age (continuous), body mass index (continuous, BMI), current smoking (yes vs no), job position (segment manager vs other), and changes in weekly working hours and shift work. This model also adjusted for HCC baseline values to consider potential floor or ceiling effects.

HCC was logarithmically transformed and all variables were z-transformed and standard errors are robust to heteroscedasticity. Analyses were performed using StataSE 13.

## 3. Results

### 3.1. Replication of previous findings

There were no significant cross-sectional associations between the E-R ratio with HCC (t1: Beta = -0.052, S.E. = 0.167,  $p = 0.755$ ; Fig. 1 Panel A; t2: Beta = 0.035, S.E. = 0.157,  $p = 0.825$ ). The change of the E-R ratio between the two time points had a small, albeit non-significant, effect on HCC levels at t2 (Beta = 0.315, S.E. = 0.196,  $p = 0.117$ ).

### 3.2. Prospective analyses

Introducing the change of HCC as dependent variable, the change in E-R ratio had a significant effect (Table 1; Model 1; Fig. 1, Panel B). This effect was independent of confounding factors (age, BMI, smoking, job position, and changes in working hours and shift work), and HCC baseline values (Beta = 0.368, S.E. = 0.150,  $p = 0.021$ ; Model 2). In the sub-dimensions, the effect of effort decreased after adjustment (Model 1: Beta = 0.591, S.E. = 0.215,  $p = 0.009$ , Model 2: Beta = 0.306, S.E. = 0.179,  $p = 0.099$ ), while the effect of reward became more pronounced (Model 1: Beta = -0.274, S.E. = 0.206,  $p = 0.192$ , Model 2: Beta = -0.335, S.E. = 0.126,  $p = 0.013$ ). For over-commitment effects remained comparable (Table 1). (An instrumental variable estimation additionally controlling for all unobserved time-variant factors revealed even more pronounced effect for E-R ratio (Model 2: Beta = 0.887, S.E. = 0.336,  $p = 0.014$ ), as well as for the components (Table A.1.); see Appendix for further details).

## 4. Discussion

This study is the first examining the prospective association of work stress with HCC. Using first-differenced data, thereby excluding time-invariant factors like genetic variation or hair pigmentation, linear regressions revealed an increase in work stress to be related to an increase in HCC. These findings can, however, only be seen as a first indication, as the sample was quite small, and the study was restricted to two measurement points, not permitting classical longitudinal analysis

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