SHORT COMMUNICATION

Elevated hair cortisol levels in chronically stressed dementia caregivers

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1. Introduction

Long-term changes in the secretion of the glucocorticoid cortisol are considered a crucial mediator for the link between chronic stress and ill health. To obtain valid assessments of long-term cortisol levels, however, has been methodologically challenging in the past. Cortisol measured in blood, saliva or urine exhibits high situational variability and thus provides only a poor reflection of underlying long-term secretory patterns. Over the past decade, the analysis of hair cortisol concentrations (HCC) has increasingly gained acceptance as an easily obtainable index of integrated long-term cortisol secretion (reviews: Russell et al., 2012; Stalder and Kirschbaum, 2012). Considerable evidence has now supported this method in terms of its overall validity, test-retest reliability and robustness to potential confounding influences (Stalder and Kirschbaum, 2012).

KEYWORDS
Cortisol; Hair; Stress; Chronic; Caregiver; Depression; Human

Summary
Hair cortisol concentrations (HCC) are assumed to reflect integrated long-term cortisol levels and have been proposed as a promising endocrine marker of chronic psychological stress. The current study examined HCC in relation to caregiving burden, a well-established naturalistic model of chronic stress in humans. HCC and relevant psychosocial data were examined in 20 caregivers of relatives with dementia and 20 non-caregiver controls matched for age and sex. Results revealed elevated HCC in dementia caregivers compared to non-caregiver controls ($F_{(1,38)} = 4.4$, $p = .04$, $r^2_p = .10$). Further, within caregivers, a trend for a positive association of HCC with self-reported caregiving burden ($r = .43$, $p = .058$) and a positive association with depressiveness ($r = .48$, $p = .045$) were observed. No other associations between HCC and subjective measures were seen. These findings concur with the notion that HCC sensitively capture endocrine aberrations in stress-exposed groups.

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Overall, these data highlight HCC as a promising marker for endocrine correlates of chronic stress (Staufenbiel et al., 2013). However, direct enquiries in the context of chronic stress have produced diverging results: while research examining relationships of HCC with subjective stress measures has failed to report consistent results, initial studies conducted in stress-exposed groups have uniformly shown elevations in HCC (Stalder and Kirschbaum, 2012). The latter evidence concerning HCC in stress-exposed groups, however, is still based on a smaller number of studies carried out in specialized samples. Specifically, increased HCC were reported in hospitalized and ventilated infants, chronic pain patients, unemployed individuals, students with major life stressors (review: Staufenbiel et al., 2013) and members of Aboriginal First Nation communities in Canada (Henley et al., 2013). These studies feature groups in which the effect of psychological stress may not be fully distinguishable from effects of underlying medical conditions (e.g., hospitalized infants or chronic pain patients) or ethnic group differences (e.g., hair characteristics of Aboriginal people vs. whites).

This highlights the need to further investigate long-term endocrine alterations in groups with well-defined increased psychosocial stress exposure. A suitable human condition for doing so is provided by dementia caregiving burden. Caring for a demented relative constitutes a highly stressful task, characterized by changing role patterns, continuous mourning for the affected relative and demanding caring duties due to the uncontrollable nature of dementia (Schoenmakers et al., 2010). Consistently, dementia caregivers have been shown to experience higher rates of psychological stress, an increased risk for psychiatric diseases and poorer health than non-caregivers (review: Vedhara et al., 1999), and members of Aboriginal First Nation communities in Canada (Henley et al., 2013). These studies feature groups in which the effect of psychological stress may not be fully distinguishable from effects of underlying medical conditions (e.g., hospitalized infants or chronic pain patients) or ethnic group differences (e.g., hair characteristics of Aboriginal people vs. whites).

To further investigate long-term endocrine alterations in groups with well-defined increased psychosocial stress exposure, a suitable human condition for doing so is provided by dementia caregiving burden. Caring for a demented relative constitutes a highly stressful task, characterized by changing role patterns, continuous mourning for the affected relative and demanding caring duties due to the uncontrollable nature of dementia (Schoenmakers et al., 2010). Consistently, dementia caregivers have been shown to experience higher rates of psychological stress, an increased risk for psychiatric diseases and poorer health compared to other caregivers or non-caregiver peers (Pinquart and Sorensen, 2003). Further, increased activity of the endocrine stress system in dementia caregivers has been indicated (e.g., Vedhara et al., 1999), although with some inconsistency (e.g., Irwin et al., 1997).

The current study thus set out to provide a first investigation of HCC in groups of dementia caregivers and non-caregiver controls matched for age and sex. We predicted to find elevated long-term cortisol levels in dementia caregivers. To further foster interpretability of results, we also assessed dimensional relationships with self-reported caregiving burden, depressiveness, social support and sleep problems.

2. Methods

2.1. Participants

Twenty-one elderly caregivers of relatives with dementia and 22 age and sex-matched non-caregiver controls were recruited from self-help groups for dementia caregivers (caregivers) and meeting centers for the elderly (controls). The dementia caregiver group comprised individuals who were currently caring for a close relative with a general practitioner-verified diagnosis of dementia. Caregivers in this group had been caring for their spouse (n = 20) or parent (n = 1) for a mean (±SD) time of 40.8 (±30.8) months. The care settings of most participants were classified with German nursing care levels I or II which signify severe or very severe care needs, respectively. High caregiving burden in caregivers was further reflected by mean (±SD) scores of 38.2 (±13.2) on the Zarit Burden Interview (ZBI; Braun et al., 2010). A ZBI cut-off value of 26 has been proposed to mark an increased mental health risk due to high caregiving burden (Schreiner et al., 2006). The non-caregiver group comprised individuals who had never cared for a demented relative.

Participants were only included in the study (both groups) if they were not taking glucocorticoid-containing medication and had not had any medical surgery within three-months prior to hair sampling. To avoid creating an artificial sample of elderly participants, we refrained from imposing further exclusion criteria based on medical diseases or medication intake, but instead controlled for these effects statistically. All participants provided written informed consent prior to taking part in the study. The study protocol was approved by the ethics committee of the TU Dresden Medical Faculty and the study was conducted in accordance with the Declaration of Helsinki.

2.2. Self-report measures

Information on demographic and health-related variables (age, sex, body-mass-index (BMI), marital status, regular daily alcohol consumption, chronic diseases and medication intake) and hair-related characteristics (washes/week, hair treatment: coloration, bleaching, permanent wave) were measured using a self-developed questionnaire. Two ten-point rating scales were used to assess physical and mental well-being (endpoints: very low, very high) with high values signaling high well-being. The Social Readjustment Rating Scale (SRRS; German Version: Katschnig, 1980) was used to assess major life events over the past year. Depressive symptomatology over the past two weeks was assessed using the Beck Depression Inventory (BDI-II; German Version: Hautzinger et al., 2009) and the ENRICHD Social Support Inventory (ESSI; German Version: Spaderna et al., 2009) was employed to measure general perceived social support. Finally, the Jenkins Sleep Problem Questionnaire (JSPQ; Jenkins et al., 1988) was used to assess self-reported sleep problems over the previous months.

2.3. Hair cortisol analysis

Hair strands (~3 mm diameter) were cut scalp-near from a posterior vertex position. The proximal 3 cm hair segment was used for analyses. Based on an average hair growth rate of 1 cm/month, this hair segment represents hair grown over the 3-month period prior to hair sampling. Wash and steroid extraction procedures followed the laboratory protocol described in Kirschbaum et al. (2009) with 10 mg of powdered hair being used for analyses in the current study. Cortisol levels were determined using a commercially available immunoassay with chemiluminescence detection (CLIA, IBL-Hamburg, Germany). Intra- and interassay coefficients of variance were below 10%.

2.4. Statistical analysis

Analyses were performed using SPSS for Windows, version 21 (IBM, Chicago, Illinois). Box plot analyses revealed three extreme outlying HCC values exceeding three interquartile ranges from the median which were excluded from
were examined using Pearson correlations.

Professional associations between self-report measures and HCC adjusting for variables differing between groups. Dimensional associations between dementia caregivers and non-caregiver controls using one-way ANOVA and followed up by ANCOVA were conducted using $t$-tests (continuous variables) and Fisher’s exact tests (dichotomous variables). HCC were compared between dementia caregivers and non-caregiver controls. The univariate ANOVA revealed higher HCC in dementia caregivers (mean $\pm$ SD: 27.4 $\pm$ 11.3 pg/mg) than in non-caregiver controls (mean $\pm$ SD: 20.5 $\pm$ 7.3 pg/mg; $F_{(1,38)} = 4.4$, $p = .04$, $r^2_p = .10$). This effect remained significant in an ANCOVA adjusting for differences in marital status and prevalence of hypertension ($F_{(1,35)} = 4.9$, $p = .03$, $r^2_p = .12$). The effect missed statistical significance when BDI-II ($F_{(2,31)} = 2.0$, $p = .17$) or ESSI scores ($F_{(2,37)} = 2.9$, $p = .097$) were controlled for.

Correlation analyses carried out across groups revealed no significant associations between HCC and SRRS, BDI-II, ESSI and JSPQ (all $p$’s > .14). Analyses conducted within the caregiver group revealed a trend for a positive correlation of HCC with ZBI-assessed caregiving burden ($r = .43$, $p = .058$, $n = 20$) and a positive association with BDI-II scores ($r = .48$, $p = .045$, $n = 18$; see Fig. 1b and c, respectively). No further associations of HCC with self-report measures, time of caregiving or patients’ nursing care level were observed (all $p$’s > .34).

### 3. Results

Table 1 shows descriptive characteristics of the two study groups. Groups were well-matched on the examined demographic, health- and hair-related parameters, except for a significantly higher rate of married individuals in dementia caregivers. As expected for the elderly, a high percentage of participants in both groups reported chronic diseases and/or regular medication intake. Diseases included hypertension ($n = 12$), back pain ($n = 3$), ocular disorders/glaucoma ($n = 5$), diabetes ($n = 4$), allergies ($n = 3$) and osteoarthritis ($n = 3$). Most common medication types were antihypertensives ($n = 24$), thyroxin ($n = 6$) and antihyperglycemics ($n = 3$). No group differences were observed in either prevalence of chronic disease types or medication categories (all $p$’s > .34), except for a non-significant trend for a higher rate of hypertension in non-caregiver controls (Fisher’s exact, $p = .08$). As expected, dementia caregivers reported lower well-being (physical and mental) and social support as well as higher depressiveness. No significant differences in self-reported life events or sleep problems were observed.

![Fig. 1a shows HCC of dementia caregivers and non-caregiver controls. The univariate ANOVA revealed higher HCC in dementia caregivers (mean $\pm$ SD: 27.4 $\pm$ 11.3 pg/mg) than in non-caregiver controls (mean $\pm$ SD: 20.5 $\pm$ 7.3 pg/mg; $F_{(1,38)} = 4.4$, $p = .04$, $r^2_p = .10$). This effect remained significant in an ANCOVA adjusting for differences in marital status and prevalence of hypertension ($F_{(1,35)} = 4.9$, $p = .03$, $r^2_p = .12$). The effect missed statistical significance when BDI-II ($F_{(2,31)} = 2.0$, $p = .17$) or ESSI scores ($F_{(2,37)} = 2.9$, $p = .097$) were controlled for.](image-url)

### 4. Discussion

This study investigated the relationship of integrated long-term cortisol levels in hair and caregiving burden, a well-established human model of chronic psychosocial stress. Our main finding showed significantly higher HCC in dementia caregivers compared to non-caregiver controls. This concurs with previous data showing elevated HCC across a range of stress-related conditions (Stalder and Kirschbaum, 2012; Staufenbiel et al., 2013). Besides this group effect, analyses conducted within dementia caregivers also revealed positive relationships of HCC with perceived caregiving burden (at trend level) and depressiveness.
Our main finding of increased HCC in dementia caregivers concurs with previous reports of elevated salivary or blood cortisol in this group (e.g., Vedha et al., 1999). Interestingly, this pattern has not unanimously been found (e.g., Irwin et al., 1997), perhaps partly due to limitations in employed cortisol assessment methods. The fact that caring for a demented relative is highly stressful has repeatedly been shown (Pinquart and Sorensen, 2003) and was also reflected in the current data showing lower physical and mental well-being in caregivers. Given that the two groups were comparable on other examined variables, it is most likely that increased HCC in caregivers were mainly attributable to repeated cortisol reactions to stressful experiences in caregivers’ daily routines. This interpretation was further supported by our tentative dimensional finding suggesting that caregivers who reported greater caregiving burden also tended to exhibit higher HCC.

Besides increased stress exposure in caregivers, the fact that the HCC group effect missed significance after controlling for BDI-II or ESSI scores further suggests that higher depressiveness and lower perceived social support in this group also partly contributed to the observed long-term endocrine aberrations. A potential role of depressiveness was further highlighted by our finding of a positive association of HCC and depressiveness within caregivers, although this relationship was not seen across the whole sample. The finding within caregivers could be seen as suggestive of increased long-term cortisol secretion in more depressed individuals which has also been indicated by some but not all previous HCC research (review: Staufenbiel et al., 2013). However, as this association was only seen within the relatively small group of caregivers, further investigation is needed until firm conclusions can be drawn.

The latter fact that associations between HCC and self-report measures were only seen within caregivers but not across the whole sample is an interesting aspect of the current findings. It can only be speculated what may be responsible for this result. We have previously suggested that, amongst other things, individual differences in self-awareness, social desirability and retrospective bias may have had a negative effect on the quality of self-report data in previous HCC research (Stalder and Kirschbaum, 2012). It is conceivable that this has applied less to the current caregiver sample who may have been particularly sensitized to observing their stress-related living situation through frequent participation in caregiver self-help groups. This could have resulted in more accurate self-reports and thus increased the likelihood of detecting psychoneuroendocrine covariance in this group. Still, other explanations are clearly possible and future corroboration of this effect in a larger sample is expedient. Such testing may also benefit from the use of more elaborate self-assessment methods, such as ecological momentary assessments or the experience sampling method, which may further help to raise ecological validity of self-report data across the whole sample.

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Conflict of interest

None declared.

References


