Use of hair cortisol analysis to detect hypercortisolism during active drinking phases in alcohol-dependent individuals

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ABSTRACT

The assessment of cortisol levels in human hair has recently been suggested to provide a retrospective index of cumulative cortisol exposure over periods of up to 6 months. The current study examined the utility of hair cortisol analysis to retrospectively detect hypercortisolism during active drinking phases in alcoholics in acute withdrawal ($n = 25$), the normalisation of cortisol output in abstinent alcoholics ($n = 20$). Scalp-near 3-cm hair segments were sampled and analysed for cortisol content. Results showed three to fourfold higher cortisol levels in hair samples of alcoholics in acute withdrawal than in those of abstinent alcoholics ($p < .001$) or controls ($p < .001$), with no differences between the latter two groups. The current hair cortisol findings closely mirror results of previous research using well-established measures of systemic cortisol secretion and thus provide further validation of this novel method.

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1. Introduction

Activity of the hypothalamus–pituitary–adrenal (HPA) axis is frequently examined in psychobiological research. Here, a particular interest often lies in obtaining estimates of systemic cortisol exposure over extended periods of time. The adequate assessment of long-term cortisol levels, however, is difficult given that common measurement strategies only reflect acutely circulating cortisol levels, however, is difficult given that common measurement strategies only reflect acutely circulating cortisol levels. This is further exacerbated by the fact that cortisol secretion is characterised by high reactivity, marked circadian changes and considerable day-to-day variability within an individual (Hellhammer et al., 2007). This means that in order to obtain a reliable assessment of long-term cortisol exposure, sampling has to be frequently repeated – a procedure associated with considerable research and participant burden.

In this context, the analysis of cortisol concentrations in human hair may constitute a major methodological advancement. As cortisol is incorporated into the hair shaft during hair growth, the examination of cortisol concentrations in a specific hair segment is believed to provide a retrospective measure of systemic secretion over the respective hair growth period (see Gow et al., 2010). Given an average hair growth rate of approximately 1 cm/month (Wennig, 2000), the examination of 3 cm hair segments allows the assessment of cumulative cortisol levels over a 3 months period – a window of time which would have been virtually impossible to cover adequately using previous measures. Whilst this highlights the potential of hair cortisol analysis, the validity of this method for assessing long-term systemic exposure has only been examined in a small number of human studies so far, e.g. to detect hypercortisolism in Cushing’s syndrome patients (Thomson et al., 2010) or during the third trimester of pregnancy (Kirschbaum et al., 2009). Further validation of this method in humans is thus clearly needed.

One approach to examining the validity of hair cortisol analysis is to investigate conditions that have been well documented to be associated with HPA axis alterations (i.e. hypo- or hypercortisolism). Alcohol dependence, a prevalent disorder associated with considerable health and economic costs (Spanagel, 2009), constitutes such a condition. In studies using different paradigms and assessment methods, alcohol intoxication/dependence was consistently shown to be associated with hypercortisolism. This has been demonstrated in early studies of experimentally induced ethanol intoxication in alcoholic participants (Mendelson and Stein, 1966; Mendelson et al., 1971) as well as in more recent evidence indicating an upregulation of different aspects of HPA axis activity in heavy drinkers, e.g. the cortisol awakening response (Badrick et al., 2008), overnight urinary cortisol (Thayer et al., 2006), or single assessments of plasma (Gianoulakis et al., 2003) or salivary (Adinoff et al., 2003) cortisol concentrations. Besides intoxication,
acute alcohol withdrawal has also been related to increased cortisol secretion (Iranmanesh et al., 1989; Adinoff et al., 1991; Esel et al., 2001), whilst cortisol output returns to normal levels after about 7 days of abstinence (Adinoff et al., 1991). Together, this suggests that alcohol dependence provides a well-suited model for examining the adequacy of hair cortisol analysis as a method to detect long-term aberrations of cortisol production. Based on the reviewed evidence, the present study aimed to examine the relationship between alcohol intoxication and cortisol concentrations in hair segments. In order to be able to investigate both the effects of alcohol intoxication and its normalisation with abstinence, hair cortisol concentrations were compared between three participant groups. Given the retrospective nature of hair analysis, samples of (i) alcoholics in acute withdrawal were assumed to cover the time period of repeated alcohol intoxication prior to the commencement of withdrawal. On the other hand, hair samples of (ii) long-term abstinent alcoholics and (iii) healthy control participants were assumed to reflect periods with no, or only modest, alcohol consumption. In addition, self-report measures of relevant demographic and psychological variables were obtained to allow the investigation of potential confounding influences as well as effects of mood disturbances associated with alcohol dependence.

2. Methods

2.1. Participants

Participants were 30 alcoholics in acute withdrawal (2nd to 12th day: mean age ± standard deviation (SD): 44.3 years ± 10.9 years), 25 abstinent alcoholics (mean age ± SD: 45.6 years ± 8.2 years), and 21 age- and gender-matched control participants (mean age ± SD: 43.6 years ± 10.9 years). Alcoholics in acute withdrawal were recruited through inpatient addiction treatment programs of specialized hospitals or mixed psychiatric units in the Leipzig and Dresden areas of Germany. Abstinent alcoholics (at least 14 weeks of abstinence) were also recruited from inpatient addiction treatment programs (n = 16), or from alcoholics anonymous meetings in or near the Leipzig area (n = 9). All alcoholics in acute withdrawal and all hospital-treated abstinent alcoholics met KCD-10 criteria for alcohol dependence. Abstinence of hospital-treated participants was controlled by means of a breathalyser as well as through the measurement of liver enzyme and carbohydrate-deficient transferrin levels. Both groups of alcohol-dependent subjects were screened for psychiatric comorbidity. Control participants were also screened to exclude psychiatric morbidity within the previous 12 months or a lifetime history of substance abuse or addiction using a standardised interview (SKID I, Wittchen et al., 1997). According to self-report, the mean (±SD) daily intake of alcohol during periods of active drinking was 253.7 g (±150.8 g) in alcoholics in acute withdrawal, 265.2 (+204.2 g) in presently abstinent alcoholics, as well as 27.3 (±29.3 g) in control participants. All alcoholics in acute withdrawal and all hospital-treated abstinent alcoholics met KCD-10 criteria for alcohol dependence. Abstinence of hospital-treated participants was controlled by means of a breathalyser as well as through the measurement of liver enzyme and carbohydrate-deficient transferrin levels. Both groups of alcohol-dependent subjects were screened for psychiatric comorbidity. Control participants were also screened to exclude psychiatric morbidity within the previous 12 months or a lifetime history of substance abuse or addiction using a standardised interview (SKID I, Wittchen et al., 1997). According to self-report, the mean (±SD) daily intake of alcohol during periods of active drinking was 253.7 g (±150.8 g) in alcoholics in acute withdrawal, 265.2 (+204.2 g) in presently abstinent alcoholics, as well as 27.3 (±29.3 g) in control participants.

All participants provided written informed consent prior to taking part in the study. The study protocol was approved by the ethics committee of the Dresden Technical University Medical Clinic and the study was conducted in accordance with the Declaration of Helsinki.

2.2. Clinical and psychological measures

Relevant sociodemographic variables (sex, age, smoking status, body mass index) were recorded. In addition, self-reports of participants’ health, well-being as well as information on the use of alcohol and drugs were obtained using a self-developed questionnaire. As part of this, physical and mental well-being were rated on ten-point Likert scales (1 “bad” to 10 “very good”) and participants were asked about any significant physical illness or operations over the past 12 months and about the regular use of drugs for either medical or recreational purposes over this time period. Depressive symptoms were assessed using the Beck Depression Inventory (BDI-II; Haertinger et al., 2006), the Perceived Stress Scale (PSS; Cohen et al., 1983) was employed as a self-report measure of perceived stress and the trait form of the State-Trait Anxiety Inventory (STAI-T; Laux et al., 1981) was used to assess trait anxiety. In addition, information regarding physical and psychiatric illnesses was obtained from attending psychiatrists and psychologists.

2.3. Hair cortisol analysis

Hair strands of a diameter of approximately 3 mm were taken scalp-near from a posterior vertex position. Cortisol concentrations were determined from the 3 cm hair segment most proximal to the scalp. Based on an average hair growth rate of 1 cm/month (Wennig, 2000), this hair segment was assumed to represent hair grown over the 3-month period prior to hair sampling. Wash and steroid extraction procedures followed the laboratory protocol described in detail in Kirschbaum et al. (2009) with 25 mg of powdered hair being used for analyses in the present study. Cortisol levels were determined using a commercially available immunoassay with chemoluminescence detection (CLIA; IBL-Hamburg, Germany). The intra and interassay coefficients of variance were both below 10%.

2.4. Data exclusion and statistical analysis

Hair samples were obtained from 76 participants (30 alcoholics in acute withdrawal, 25 abstinent alcoholics, and 21 controls). Data from seven participants of the acute withdrawal group was excluded from analyses due to the last alcohol consumption dating back more than 12 days (n = 2) or the participant having received treatment for alcohol dependence over the past 2 months (n = 5). In addition, data from one control participant was excluded because of previous treatment for alcohol dependence. This resulted in a total of 68 hair samples.

Group comparisons regarding sociodemographic, clinical/psychological and hair-related characteristics were conducted using univariate ANOVAs (continuous variables) or c² contingency tables (dichotomous variables). Kolmogorov–Smirnov tests revealed that cortisol data were not normally distributed. Log transformations were applied which effectively reduced the skewness statistic. Univariate ANOVAs were used to examine differences in hair cortisol levels between the three studied groups. Findings of significant main effects were followed up by post hoc comparisons using Tukey honest significant difference tests. To control for potential confounding effects of participant depressiveness, perceived stress or trait anxiety, analyses were repeated using the score of the BDI-II, PSS or STAI-T as covariates.

Associations between these measures and hair cortisol levels were also explored using correlation analyses.

3. Results

Table 1 presents demographic and psychological characteristics of alcoholics in acute withdrawal, abstinent alcoholics and control participants. It can be seen that the three groups were well-matched on the examined demographic characteristics. As expected, significant differences in self-reported depressive symptoms (BDI-II), perceived stress (PSS), trait anxiety (STAI-T) as well as physical and mental well-being were found between the three groups. Post hoc analyses revealed that both alcoholic groups scored significantly higher on self-reports of depressive symptoms, perceived stress and trait anxiety and significantly lower on physical and mental well-being than healthy control participants.

Hair cortisol concentrations were found to differ significantly between the three groups (see Fig. 1; F₂,6₄ = 17.80, p < .001, r² = .37). Post hoc analyses revealed that both alcoholic groups had about three to fourfold higher hair cortisol concentrations than abstinent alcoholics (mean ± SD: 51.99 ± 43.30 pg/mg) had about three to fourfold higher hair cortisol concentrations than abstinent alcoholics (mean ± SD: 13.98 ± 10.63 pg/mg; p < .001) or control participants (mean ± SD: 16.35 ± 12.59 pg/mg; p < .001). No significant differences were found between hair cortisol concentrations of abstinent alcoholics and control participants (p = .906). Hair cortisol levels were not found to be significantly associated with scores of the BDI-II (r = .19, p = .15), PSS (r = .11, p = .41) or STAI-T (r = .07, p = .61). Controlling for scores on these measures also did not alter ANOVA results.

4. Discussion

The present findings show that cortisol levels in scalp-near 3 cm hair segments of alcoholic participants in acute withdrawal are three to fourfold elevated compared to those of abstinent alcoholics or healthy control participants, respectively. Based on an average growth rate of 1 cm per month, the cortisol values of alcoholics in acute withdrawal should reflect the 3 months when participants were still drinking. In contrast, the hair cortisol levels of abstinent alcoholics and control participants should cover periods with no or only modest alcohol consumption. The current finding of higher hair cortisol levels in acutely withdrawing alcoholics is in line with previous evidence showing that periods of alcohol intoxication are associated with increased cortisol levels (Mendelson and
Stein, 1966; Mendelson et al., 1971; Gianoulakis et al., 2003; Thayer et al., 2006; Badrick et al., 2008). On the other hand, the present finding that hair cortisol concentrations in abstinent alcoholics were comparable to those of healthy controls is consistent with previous evidence indicating that cortisol concentrations return to normal levels with the abstinence from alcohol (Adinoff et al., 1991).

Whilst the magnitude of group differences in hair cortisol levels in the current study is comparable to effects of one previous study (Adinoff et al., 2003), it is considerably larger than effects reported by most other research in which heavy drinking groups have been found to show marginally higher overnight urinary cortisol levels (Thayer et al., 2006) or just below twofold increased cortisol awakening responses (Badrick et al., 2008) and cortisol levels in a single morning blood sample (Gianoulakis et al., 2003). A potential explanation for these quantitative differences is that two of these studies (Thayer et al., 2006; Badrick et al., 2008) examined alcohol intoxication in otherwise healthy and non-dependent participants, whereas in the current study and in the work of Adinoff et al. (2003) alcohol intoxication in alcohol-dependent participants was studied. In addition, it is conceivable that hair cortisol levels, which are assumed to retrospectively reflect cumulative cortisol exposure, might be less influenced by measurement error due to intra-individual variability or cortisol reactivity to the measurement situation than previous methods. If corroborated by future research, this might indicate that hair cortisol levels can provide a more sensitive measure of chronic states of hyper- or hypocortisolism.

A potential limitation of the current study lies in its cross-sectional nature which means that no definite inferences with regard to changes in hair cortisol levels over time can be made. Nevertheless, the clear-cut differences in hair cortisol levels between acutely withdrawing and abstinent alcoholics as well as the close resemblance of hair cortisol profiles of abstinent alcoholics and control participants support the interpretation that these differences were indeed due to the effects of repeated alcohol intoxication as well as a lack of alcohol intoxication during abstinence, respectively. This interpretation is further supported by the fact that both alcoholic groups were well-matched with regard to demographic and psychological characteristics. A further noteworthy point is that since hair samples of acutely withdrawing participants were obtained between the second and twelfth day of withdrawal, it cannot be excluded that increased cortisol secretion related to the acute withdrawal process might have partly contributed to the hair cortisol levels of this group. Similarly, as it was not recorded whether participants of this group had attempted to withdraw from alcohol over the 3-month period prior to hair sampling, a potential influence of previous withdrawal attempts on hair cortisol levels remains a possibility.

Overall, the results of the current study add further support to the notion that hair cortisol analysis provides a valuable retrospective measure of cortisol secretion over prolonged periods of time. These findings thus highlight the potential for this method to become an important tool in psychobiological research. Given the unique information and the convenience of hair sampling and storage, hair cortisol analysis might be applicable to research questions which have previously been difficult to examine. Amongst others, these might include clinical designs that would otherwise require costly prospective cortisol assessments, or studies aiming to measure long-term cortisol levels on a larger epidemiological level. Further research extending the examination of fundamental characteristics of cortisol incorporation into human hair are needed to document the full potential of this promising new research tool.

References


