Comprehensive Psychoneuroendocrinology 11 (2022) 100155

Contents lists available at ScienceDirect

Comprehensive Psychoneuroendocrinology

journal homepage: www.sciencedirect.com/journal/comprehensive-psychoneuroendocrinology

Do subjective and objective measures of stress agree in a clinical sample of youth and their parents?

Sydney Whitney [a], Chloe Bedard [a,*], John Mielke [a], Dillon T. Browne [b], Mark A. Ferro [a]

[a] School of Public Health Sciences, University of Waterloo, 200 University Ave W, Waterloo, ON, N2L3G1, Canada
[b] Department of Psychology, University of Waterloo, 200 University Ave W, Waterloo, ON, N2L3G1, Canada

ARTICLE INFO

Keywords:
Stress-related measurement
Perceived stress
Adolescents
Mental health
Hair cortisol

ABSTRACT

This study explored agreement and potential relationships among perceived stress (self-reported using the Perceived Stress Scale), hair cortisol concentration (HCC), and mental disorders in a clinical sample of youth and their parents. Data were collected from a cross-sectional sample of 48 youth (38 females; mean age = 15.6 years) with a mental disorder and 72 parents (65 females; mean age = 45.49 years). Agreement was assessed using Bland-Altman plots and intraclass correlation coefficients. Multiple regression was used to model the association between covariates and HCC and perceived stress for youth and parents. Agreement between perceived stress and HCC was low for both youth and parents (ICC = 0.15 to 0.31). Among youth, lower income (β = 0.24) and parent psychopathology (β = 0.42) were associated with higher HCC. Female sex (β = 0.42) and higher parent psychopathology (β = 0.28) were associated with higher perceived stress, whereas chronic physical illness was associated with lower perceived stress (β = −0.24). Among parents, female sex (β = −0.21) was associated with lower HCC and family functioning (β = 0.46) was associated with higher perceived stress. In youth, higher HCC was associated with generalized anxiety (OR = 1.14) and higher perceived stress was associated with major depressive episode (OR = 1.33), generalized anxiety (OR = 1.10), and separation anxiety (OR = 1.14). Among parents, higher HCC was associated with depression (β = 0.27) and perceived stress was associated with depression (β = 0.53) and anxiety (β = 0.45). This exploratory study shows that agreement between psychological and physiological stress is low in a clinical sample of youth and their parents. Sociodemographic and psychosocial factors, and mental health, are differentially associated with psychological and physiological stress.

Funding information

This work was supported by Hamilton Health Sciences (NIF-14363).

Disclosure statement

The authors report there are no competing interests to disclose.

Data availability statement

Research ethical approval for this study does not permit the public sharing of study data. However, requests to access data should be made in writing by contacting the corresponding author by email to initiate discussions regarding potential research projects.

Credit author statement

Sydney Whitney: Conceptualization, methodology, formal analysis, writing – original draft. Chloe Bedard: writing – review and editing. John Mielke: methodology, writing – review and editing. Dillon T Browne: methodology, writing – review and editing. Mark A Ferro: conceptualization, methodology, resources, writing – review and editing, supervision, funding acquisition.

1. Introduction

A coordinated psychological and physiological response occurs in individuals after exposure to a stressor which works to improve the ability to withstand the stressor and return them to a state of homeostasis [1,2]. The psychological response involves the appraisal of

* Corresponding author.
E-mail addresses: swhitney@uwaterloo.ca (S. Whitney), c3bedard@uwaterloo.ca (C. Bedard), jgmielke@uwaterloo.ca (J. Mielke), dillon.browne@uwaterloo.ca (D.T. Browne), mark.ferro@uwaterloo.ca (M.A. Ferro).

https://doi.org/10.1016/j.cpnec.2022.100155
Received 18 April 2022; Received in revised form 8 July 2022; Accepted 8 July 2022
Available online 14 July 2022
2666-4976/© 2022 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

stressors as threats and an assessment of countervailing resources, while the physiological response involves the activation of the hypothalamic-pituitary-adrenal (HPA) axis and the release of cortisol, which induces physiological and behavioural changes to help the body cope with the stressor. Stress is recognized as a major influence on health [3]; however, obtaining measures of stress that are valid and reliable can be challenging [4].

Measures of psychological stress are typically self-reported questionnaires which ask an individual about how stressful they feel their lives, or certain life events, are during a specified period [5]. In contrast, physiological assessments of stress frequently measure cortisol levels within the body [4]. Acute physiological stress is often measured using salivary cortisol, and chronic physiological stress is quantified using hair cortisol concentration (HCC), which can provide an estimate of cortisol levels averaged over several months [6]; this is a key advantage of the use of hair cortisol compared to salivary or plasma cortisol which measures only acute stress in the previous hours. As psychological stress is often recalled over a certain number of weeks or months, hair cortisol levels may be compared over the same period depending on the amount of hair collected. Reductions in the invasiveness of biological sample collection (e.g., hair sampling) and improvements in laboratory processing and assaying have resulted in the expansion of using objective measures of physiological stress [4,7].

Given that the psychological and physiological components of the stress response appear to act in a coordinated manner, the possibility exists that HCC could be used as an objective proxy measure of perceived stress [2,4,8]. Indeed, this hypothesis is supported by the link between the HPA axis and the brain structures controlling the psychological stress response [2,8]. However, in the available literature, the association between perceived stress and HCC has been inconsistent [8,9]. For example, in a population-based study of adolescents, Oldehinkel and colleagues (2011) found covariation between psychological and physiological measures of stress. While a negative association was found between HCC and psychological stress among mothers living in a low-income neighborhood [10]. When examining young adults, Heinze and colleagues (2016) found no association between HCC and perceived stress among either those seeking help for mental health problems or those without any mental health concerns. Furthermore, while there are few studies among children and youth, the associations are similarly inconsistent. For example, Milam and colleagues [11] found no association between HCC and perceived stress among a small school-based sample of adolescents, whereas Vanaelst and colleagues [12] found a positive association among elementary school females, and a negative association was found among young adults by Gerber and colleagues (2013). The diversity in study design and sample composition precludes the ability to determine whether these differences are due to methodological differences (length of hair sample, measurement of psychological stress), heterogeneity in mental health status of participants (those with mental illness vs healthy controls), or sample age (adolescent vs adult).

Evidence suggests that perceived stress and HCC may be associated with factors such as age, sex, income, family functioning, and negative health outcomes, including mental disorder [13], however, the direction and magnitude of these associations are mixed and remain under study. Age, sex, income, and chronic illness have been identified as correlates of both HCC [14] and perceived stress [15–17]. The association between HCC and family functioning is far less studied despite the known relationship between family functioning and perceived stress [18] and psychopathology [19], particularly among children with a chronic illness; however one study found no association with HCC, though notably, was underpowered [20]. While mental disorder is typically associated with higher levels of perceived stress [21,22], the association between mental disorder and HCC is not clear. A 2021 systematic review of HCC among mental disorders in adults concluded that the association between HCC and depression and anxiety is still mixed [23]. Generalized anxiety disorder tended to be associated with lowered HCC compared to controls; however, this association was influenced by comorbid depression and other anxiety disorders (i.e., social anxiety, obsessive compulsive disorder) appear to have different cortisol responses. Similarly inconsistent findings were reported on the association between HCC and depression, depending on the type of depression (atypical vs melancholic) and the timing of sampling with both low and high levels of HCC associated with depression. Among young adults, HCC has been found to have a negative association with depressive symptoms [24], however, more recent findings have suggested a curvilinear relationship exists such that HCC at the low and high end of the distribution are associated with depressive symptoms [25]. Limited research in children has focused on the association between HCC and posttraumatic stress disorder [26], externalizing disorders [27], and environmental stress from childhood adversities such as maltreatment [28] and chronic physical illness [29]. Similarly, mixed results are evident in the literature among children with lowered HCC found after childhood maltreatment [28] and in children with posttraumatic stress symptoms [26], no association between HCC and internalizing or externalizing problems among preschoolers [27], and increased HCC associated with both internalizing and externalizing disorder among children ages 6–16 years with a chronic physical illness [29], and with lowered health-related quality of life among children with a co-morbid physical and mental illness [30].

Given the inconsistencies in the literature regarding the concordance between perceived stress and HCC and the factors influencing both, this study explored the interrelationships among measures of perceived stress and HCC in a clinical sample of youth with mental disorder and their parents. The specific objectives were to (1) estimate the agreement between measures of perceived stress and HCC, (2) identify the sociodemographic and psychosocial factors associated with levels of perceived stress and HCC, and (3) quantify the association between mental disorder and perceived stress and HCC. Given both the inconsistency of the previous literature and the exploratory nature of these analyses, no hypotheses were proposed.

2. Methods

2.1. Data source

Data come from a cross-sectional study designed to investigate physical comorbidity and mental health service use among youth with mental disorder [31]. Youth were eligible for the study if they were ages 4–17 years, were classified as having major depressive episode, generalized anxiety disorder, separation anxiety, social phobia, specific phobia, attention-deficit hyperactivity disorder, oppositional defiant disorder, or conduct disorder, were currently receiving inpatient or outpatient mental health services, and had parents with sufficient English skills to complete the questionnaires. Analyses for the current study restricted the youth sample to those ≥14 years of age, as they were able to provide self-reported data. Youth were excluded if their current mental state limited their ability to complete the interview and questionnaires. The parents included in the study were the primary caregiver of the youth. Only one parent per child was included in the study. A total of 259 eligible youth were identified, of which, 144 (56%) provided informed consent, and 100 (39%) participated in the study. Eight youth did not complete the questionnaires, resulting in 92 (36%) youth-parent dyads. Restricting this sample to youth aged ≥14 years resulted in 48 youth and 72 parents with complete survey data and valid hair samples.

2.2. Data collection

Research staff identified eligible inpatient youth in consultation with the hospital staff. Interested youth gave research staff permission to contact their parents and obtain verbal consent. Youth outpatient rosters, containing contact information of age-eligible youth and parents who agreed to be contacted about research studies, were also provided to research staff for the purpose of recruitment. Research staff scheduled

a time for parents to complete the interview, questionnaires, and provide hair samples, which occurred during hospital visits, or when the youth was discharged. All data collection and consent for outpatients occurred at the research office between September 2015 and March 2017. Parents provided written consent for themselves and their children <16 years of age. Children 8–15 years provided written assent and children ≥16 years provided written consent. The study was approved by the Hamilton Integrated Research Ethics Board (15–197).

2.3. Measures

2.3.1. Youth perceived stress

Perceived stress was measured in youth 14–17 years using the Perceived Stress Scale (PeSS). The PeSS is a 10-item self-report scale measuring the perception of stress during the previous month [32]. Responses were scored from '0' (never) to '4' (very often) for a total score between 0 and 40, with higher scores indicating greater appraisal of life situations as stressful. The PeSS has been validated in a variety of populations, with a Cronbach's alpha >.70 [33].

2.3.2. Parent perceived stress

Parent perceived stress was measured using the Parental Stress Scale (PaSS) [34]. Items on the PaSS ask about parents' typical relationship with their child and aims to capture both the demands and rewards of parenting. The 18 items are scored from '1' (strongly disagree) to '5' (strongly agree) for a total score between 18 and 90, with higher scores indicating higher levels of parental stress. The PaSS has shown strong psychometric properties in populations of parents of children with and without chronic illness [35,36] and is strongly correlated with scores on Cohen's Perceived Stress Scale [37].

2.3.3. Hair cortisol concentration

Hair cortisol concentration was used to measure physiological stress in both youth and their parents. Research staff collected hair samples from parents and youth. For participants with longer hair, the first 3 cm of approximately 50–60 hairs were cut from the posterior vertex, as close to the scalp as possible. Participants with shorter hair had 15-20 hairs collected from four-to-five different locations. Samples were clipped to cardstock indicating the direction of hair growth. Hair samples were analyzed using a standardized protocol for washing, extraction, and cortisol assays which has previously been used successfully [29,38]. Samples were analyzed using the High Sensitivity Salivary Cortisol Immunoassay Kit (Cat# 1–3002, Salimetrics, Pennsylvania), as per manufacturer instructions. Cortisol levels are expressed as pg/mg of hair with 0.35 pg/mg as the lowest detectable value. Intra and inter-assay coefficients of variance were <10% [38].

2.3.4. Youth mental disorder

The Mini International Neuropsychiatric Interview for Children and Adolescents (MINI-KID) was used to assess the most common internalizing disorders (major depressive episode, separation anxiety, social phobia, specific phobia, and generalized anxiety) and externalizing disorders (attention-deficit hyperactivity, oppositional defiant, and conduct) (Georgiades et al., 2019). The MINI-KID is a structured diagnostic interview that assesses mental disorders in youth <18 years (Sheehan et al., 2010). The MINI-KID was administered to youth, answering questions about themselves, and parents, answering questions about their child. The MINI-KID has demonstrated strong psychometric properties (Duncan et al., 2018; McDonald et al., 2021) and has been validated against the Schedule for Affective Disorders and Schizophrenia for School Aged Children-Present and Lifetime Version (Sheehan et al., 2010). Due to the limited sample size available for these analyses and low prevalence of some disorders, social phobia and specific phobia were combined into a single category (referred to as 'phobia') and oppositional defiant disorder and conduct disorder were combined into a single category ('referred to as 'oppositional defiant/conduct disorder').

2.3.5. Parent psychopathology

Symptoms of depression and anxiety were measured using the Center for Epidemiological Studies Depression Scale (CES-D) and the State Trait Anxiety Inventory (STAI). The CES-D is a 20-item self-report scale designed to assess depressive symptoms over the previous week in adults [39]. It uses a four-point scale and total scores range from 0 to 60, with higher scores indicating greater impairment. The CES-D has been validated [35,40]. The STAI is a 40-item measure for measuring anxiety in adults [41]. The 20 items measuring trait anxiety were used in this study which assess how individuals "generally feel". Responses are scored from '1' (almost never) to '4' (almost always) for a total score between 20 and 80, with higher scores indicating higher levels of anxiety. The STAI has been validated [35,41]. Due to the limited sample size available for this study, the limited number of covariates that could be included, and the high correlation between the two scales ($r = 0.72$), for analyses in youth only, parent CES-D and STAI scores were summed to create a composite measure of parent psychopathology; for analyses in parents, both scores were considered in separate models.

2.3.6. Family functioning

Family functioning was measured using the General Functioning subscale of the McMaster Family Assessment Device (FAD), completed by parents. The FAD is a 12-item self-report measure of the overall health/pathology of the family [42]. Responses were scored on a four-point scale and summed for a total score out of 36, with higher scores representing better family functioning. The FAD has been validated [43] and the construct validity of the General Functioning subscale has been established [44].

2.3.7. Sociodemographic and health characteristics

Youth and parent age and sex, and household income were collected. Household income was coded as annual household income above, or below $90,000. Presence of chronic physical illness was parent reported using an item adapted from the Canadian Community Health Survey-Mental Health [45].

2.4. Data analysis

Bland-Altman plots were constructed to assess the agreement between HCC and perceived stress for both youth and parents. Both HCC and PeSS/PaSS scores were transformed to z-scores before being plotted using the Bland-Altman method. The intraclass correlation coefficient (ICC) and corresponding confidence intervals (CIs) were calculated.

Multiple linear regression was used to model the association between selected covariates and HCC and perceived stress scores for youth and parents. Two groups of models were generated for each subgroup with either perceived stress, or HCC as the outcome variable. Log-transformed HCC values were used in the models because distributions were non-normal. To compare the relative effect of each covariate, the method of variance estimates recovery (MOVER) was used to calculate the differences in regression estimates and associated 90% CIs. The MOVER is a general approach to estimating confidence intervals between effect measures using the confidence intervals of each effect separately [46].

Multiple logistic regression was used to model the association between perceived stress, or HCC and mental disorder in youth. Two models were created for each mental disorder with either PeSS, or HCC as the predictor variable; models were adjusted for youth age and sex. Linear regression was used to model the association between perceived stress, or HCC and psychopathology in parents. Two models were created with either PaSS, or HCC as the predictor, for each outcome (CES-D and STAI); models were adjusted for parent age and sex.

All statistical analyses were conducted with SAS Studio 9.0.4. Due the exploratory nature of this study, all analyses were conducted using a

significance level of α = 0.10 [47].

3. Results

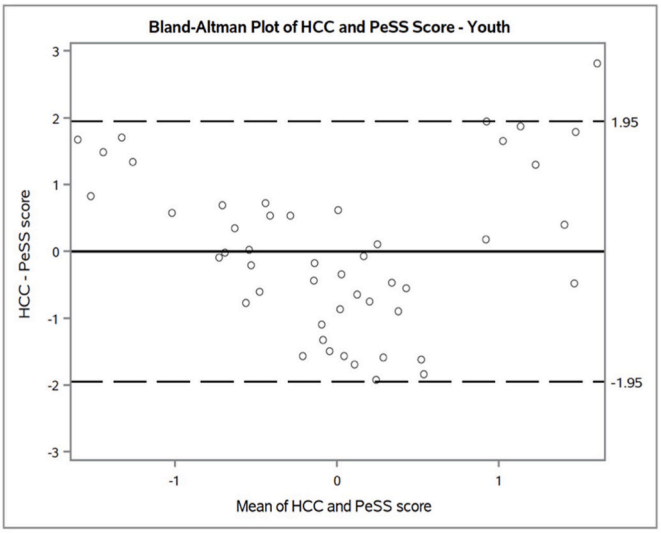
Forty-eight youth ages 14–17 years and 73 parents provided a hair sample and completed the PeSS or PaSS, respectively. One parent was determined to have an out-of-range HCC and was excluded from analyses. Sample characteristics are presented in Table 1. Youth had a mean age of 15.6 years (SD 1.2), 81% were female, and 26% had a chronic physical illness. Parents had a mean age of 45.5 (SD 6.7) years, and 90% were female. The Bland-Altman plots showing agreement between HCC and perceived stress in youth and parents are shown in Fig. 1. The ICC between HCC and perceived stress was low in youth and parents (0.31 [90% CI 0.08, 0.51] and 0.15 [90% CI -0.04, 0.33], respectively).

Results of the regression analyses among youth are shown in Table 2. A household income of < $90,000 and higher parent psychopathology were associated with higher HCC. Female sex and higher parent psychopathology were associated with higher perceived stress, while the presence of a chronic physical illness was associated with lower perceived stress. When comparing models, a significant difference was found for youth sex, which was more strongly associated with PeSS than HCC (Table 2). Results of the regression analyses among parents are shown in Table 3. Female sex was associated with lower HCC and family functioning was associated with higher perceived stress. When comparing models, a significant difference was observed for family functioning, which was more strongly associated with PaSS than HCC (Table 3).

Results of the logistic regression analyses between HCC/PeSS score and mental disorder in youth are shown in Table 4. Adjusting for age and sex, higher HCC was associated with increased odds of generalized anxiety and higher PeSS was associated with increased odds of major depressive episode, generalized anxiety, and separation anxiety. Results of the regression analyses between HCC/PaSS and CES-D and STAI score among parents are shown in Table 5. Adjusting for age and sex, higher HCC was associated with higher CES-D scores and higher PaSS scores were associated with higher CES-D and STAI scores.

4. Discussion

This exploratory study was the first to assess agreement between perceived stress and HCC in a clinical sample of youth with mental disorder and their parents. Although the level of agreement was low in both the youth and parent subgroups, our findings align with other studies that found weak, or no associations between perceived stress and HCC across populations [6,7,17,22,48]. Despite the theoretical link



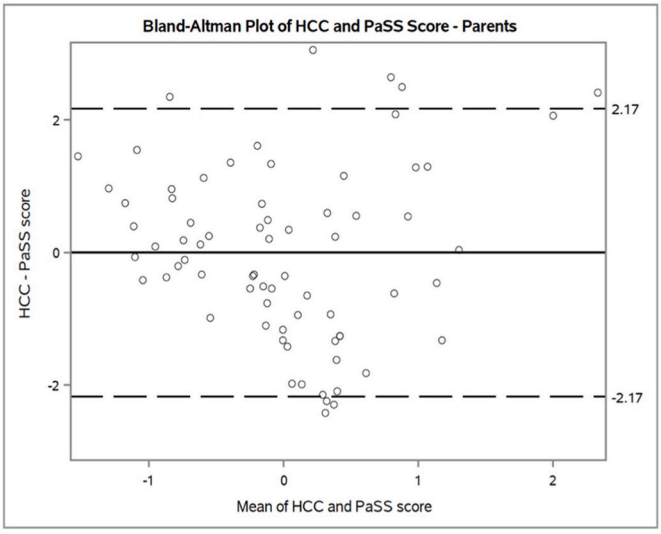


Fig. 1. Bland-Altman plot for HCC and PeSS in (a) youth and (b) parents.

Table 1
Characteristics of the study sample.

Variable	Youth Subgroup (N = 48)	Parent Subgroup (N = 72)
	N (%) or Mean (SD)	N (%) or Mean (SD)
Age (years)	15.63 (1.16)	45.49 (6.74)
Female	38 (80.85%)	65 (90.28%)
Household income < $90,000	30 (62.50%)	44 (61.11%)
Presence of a chronic physical illness/ Child with a chronic physical illness	12 (25.53%)	19 (26.39%)
Parent's combined CES-D + STAI score	65.91 (16.81)	
Child's age (years)		13.58 (3.24)
Female child		48 (66.67%)
FAD score		20.22 (5.95)
HCC (pg/mg)	9.80 (8.90)	9.63 (7.68)
PeSS score	26.40 (7.97)	
PaSS score		51.65 (12.72)
Major depressive disorder	38 (79.17%)	
Generalized anxiety disorder	32 (66.67%)	
Separation anxiety	13 (27.08%)	
Phobia	36 (75.00%)	
Attention-deficit hyperactivity disorder	18 (37.50%)	
Oppositional defiant/conduct disorder	20 (41.67%)	
CES-D score		20.27 (10.11)
STAI score		43.92 (7.38)

Table 2
Correlates of HCC and PeSS scores in youth.

	B coefficient (90% CI)	Δ*B* (90% CI)
HCC		
Adjusted R^2	0.23	
Age	0.20 (−0.04, 0.44)	0.11 (−0.22, 0.44)
Female sex	−0.18 (−0.42, 0.06)	−0.60 (−0.93, −0.27)
Household income < $90,000	0.24 (0.01, 0.47)	0.14 (−0.10, 0.63)
Parent psychopathology	0.42 (0.19, 0.64)	0.14 (−0.19, 0.45)
Chronic physical illness	0.04 (−0.19, 0.26)	0.28 (−0.05, 0.59)
PeSS		
Adjusted R^2	0.23	
Age	0.09 (−0.13, 0.32)	
Female sex	0.42 (0.19, 0.65)	
Household income < $90,000	0.10 (−0.33, 0.13)	
Parent psychopathology	0.28 (0.06, 0.51)	
Chronic physical illness	−0.24 (−0.46, −0.01)	

Δ*B* is the difference in the standardized estimates for each covariate between the HCC and PeSS models. Parent psychopathology = CES-D + STAI score.

Table 3
Correlates of HCC and PaSS scores in parents.

	B coefficient (90% CI)	Δ*B* (90% CI)
HCC		
Adjusted R^2	0.04	
Age	0.16 (−0.07, 0.39)	0.11 (−0.20, 0.43)
Female sex	−0.21 (−0.42, −0.01)	−0.12 (−0.40, 0.16)
Household income < $90,000	0.19 (−0.01, 0.39)	0.22 (−0.06, 0.49)
Child age	0.02 (−0.21, 0.25)	0.06 (−0.25, 0.37)
Female child	0.08 (−0.13, 0.29)	0.11 (−0.18, 0.40)
Child with chronic physical illness	−0.08 (−0.29, 0.12)	−0.17 (−0.38, 0.11)
Family Functioning score	0.03 (−0.18, 0.24)	−0.43 (−0.71, −0.14)
PaSS		
Adjusted R^2	0.14	
Age	0.05 (−0.17, 0.26)	
Female sex	−0.09 (−0.28, 0.10)	
Household income < $90,000	−0.03 (−0.21, 0.16)	
Child age	−0.04 (−0.25, 0.17)	
Female child	−0.03 (−0.23, 0.17)	
Child with chronic physical illness	0.09 (−0.10, 0.27)	
Family Functioning score	0.46 (0.26, 0.65)	

Δ*B* is the difference in the standardized estimates for each covariate between the HCC and PeSS models. Family Functioning score = Family Assessment Device (FAD) score.

Table 4
Multiple regression of HCC and PeSS scores on mental disorder in youth.

	HCC	PeSS
Major depressive disorder	1.05 (0.95, 1.16)	1.33 (1.12, 1.57)
Generalized anxiety disorder	1.14 (1.01, 1.28)	1.10 (1.01, 1.19)
Separation anxiety	1.04 (0.98, 1.10)	1.14 (1.03, 1.25)
Phobia	1.01 (0.94, 1.08)	1.06 (0.98, 1.14)
Attention deficit hyperactivity disorder	0.98 (0.92, 1.04)	1.03 (0.96, 1.11)
Oppositional defiant/conduct disorder	0.98 (0.93, 1.04)	0.99 (0.93, 1.06)

Values denote odds ratio (90% CI).

Table 5
Multiple regression of HCC and PeSS scores on CES-D and STAI scores in parents.

	HCC	PaSS
CES-D	0.27 (0.06, 0.48)	0.53 (0.35, 0.71)
STAI	0.15 (−0.07, 0.37)	0.45 (0.26, 0.64)

Values denote standardized *B* coefficient (90% CI).

between perceived stress and HCC, they are likely not suitable proxies for each other, or measures that can be individually used to determine how stress has affected a person.

In part, the low levels of agreement between subjective and objective measures of stress that we observed may be attributed to the different reference periods the questionnaires (past month) and hair samples (past three months) captured [48,49]. Adding to the potential for disagreement, some studies have reported that perceived stress levels may be stable over periods of up to two years [50], whereas others have found changes in perceived stress in as little as six weeks [33]. As well, further variability in the agreement between perceived stress and HCC may be attributable to the observation that exposure to adverse life events, or trauma can lead to HPA axis dysfunction and altered (chronic hypo, or hyper) cortisol secretion [3,51]; notably, we do not know how many participants in our sample may have had altered HPA axis responses due to previous exposure to adverse life events, or trauma.

In agreement with previous reports, female sex was associated with higher perceived stress in youth [52,53]. A large body of research demonstrates that adolescent females perceive higher levels of stress compared to their male peers [16]. This sex difference generally appears in adulthood as well [54], however, we did not observe this difference in the current study; this may be related to all parents in the study being the primary caregiver for their child, given previous evidence suggesting that the primary caregiving role may be a more important determinant of psychological distress than biological sex [55]. The results also found female sex to be associated with lower HCC in parents, which is consistent with previous research [49,56].While not observed in the current study, the parallel association in females of higher perceived stress and lower HCC suggests that prolonged exposure to stress is leading to HPA axis dysfunction such that there is increased negative feedback sensitivity and thus cortisol concentrations are attenuated [57]. The lack of association between sex and HCC in youth fits within the inconsistent evidence of the relationship between sex and HCC as a previous report [7] found higher cortisol levels in adolescent females, however, a 2018 systematic review found higher HCC among males [14]. The smaller sample size and use of a clinical population in the current study may have contributed to the lack of an observed difference.

Lower income was associated with higher HCC among youth, which was consistent with previous reports [58] and is thought to be related to life burden associated with lower income [58]. Similarly, parent psychopathology was associated with higher HCC and perceived stress among youth, which is consistent with recent work showing that youth HCC mediated the association between parent psychopathology and youth mental disorder [38] and reaffirms the influence of environment and heritability on HPA axis regulation and the mental health of children.

In youth, the presence of a chronic physical illness was associated with significantly lower perceived stress scores. Although the finding was unexpected, as worsening symptoms of physical illnesses have previously been reported to be associated with perceived stress [59], the current study specifically asked about physical illnesses that were diagnosed prior to mental disorder. A diagnosis of physical illness can place strain on both youth and their families and many subsequently develop adaptive coping strategies to manage these strains and reduce stress [60]. As a result, when the youth in our sample went on to face mental illness, they may have already had effective coping strategies and resources in place, such as a greater ability to navigate the healthcare system [31], which may have allowed them to better cope with their mental disorder and reduce stress.

Higher family functioning scores were associated with higher levels of perceived stress in parents. It is possible that this sample, comprised of parents of children receiving mental health treatments, has a higher degree of family functioning which led to a greater awareness of their child's illness and increased their stress levels. Indeed, Oltean and colleagues (2020) found that higher levels of affective involvement in parents was associated with increased odds of major depressive disorder in their children and suggested the parental support needed by children with major depressive disorder contributed to greater conflict and emotional withdrawal in the parent.

The MOVER analysis comparing the strength of the associations between each of the covariates and HCC/perceived stress suggested that sociodemographic and psychosocial factors may have a stronger association with perceived stress than with HCC, providing further evidence that there is a lack of psychoendocrine covariance between measures of psychological and physiological stress.

In parents, higher perceived stress was associated with higher scores on both the CES-D and STAI; in youth, higher perceived stress was associated with an increased odds of the presence of major depressive episode, generalized anxiety, and separation anxiety. The observed associations between higher levels of perceived stress and mental disorder aligns with previous studies that found psychological stress is associated with both depression and anxiety [22].

In youth, higher HCC was only associated with increased odds of

generalized anxiety, which was unexpected as previous studies have typically observed lower HCC in individuals with generalized anxiety disorder [61]. However, the hypocortisolism typically observed in patients with generalized anxiety disorder is thought to result from the gradual attenuation of the stress response following an initial increase in cortisol release [61], and our sample may have captured youth experiencing the initial increase in cortisol secretion [62]. Such a possibility aligns with recent findings that patients with shorter duration anxiety disorders have elevated HCC, while patients with a longer duration of illness do not [63].

In parents, higher HCC was associated with higher CES-D scores but was not associated with STAI scores. The association between HCC and CES-D scores in parents aligns with previous studies which have found increased HCC to be associated with depression [6] and provides additional evidence that depression is associated with HPA axis dysfunction. However, no association was found between major depressive episode and HCC in youth. Notably, there is some emerging evidence that the association between depression and HCC may be curvilinear, with both high and low levels of cortisol being associated with depression [25], which is plausible given the thought that HPA axis dysfunction manifests as both under- and over-activation of the cortisol response. Since this study was not designed to detect curvilinear relationships, future studies are warranted.

5. Limitations

The findings of this study should be considered in the context of the following limitations. First, as an exploratory study, the sample size was limited. Therefore only a small number of potential risk factors for high levels of perceived stress, or HCC could be examined and, the effects of comorbidity could not be assessed. Additionally, the limited sample size indicates that findings should be treated with caution. Second, all participants were recruited from a single site and thus findings may not be generalizable. Third, the Parental Stress Scale captures stress specifically related to parenting and may not fully reflect overall perceived stress among parents. Fourth, due to some missing data (not all parents and children completed all assessments), the children and parents included are not completely matched, therefore we were unable to model the association of child-level variables on parent-level outcomes and vice versa. Finally, due to the cross-sectional nature of the study, the directionality of observed associations could not be established.

6. Conclusions

This study makes an important contribution to the discussion around the level of agreement that might be expected between perceived stress and HCC. The results indicate that these measures should not be used as proxies of one another and that both are needed to properly evaluate the stress response. Future studies should continue to explore the agreement between psychological and physiological measures of stress to confirm the low level of agreement found in this study and explore potential factors that may be contributing to the lack of agreement, such as exposure to adverse life events. Understanding how the associations observed in this study may change over time is warranted and would make an important contribution to the field.

References

[1] G.P. Chrousos, Stress and disorders of the stress system, Nat. Rev. Endocrinol. 5 (2009) 374–381, https://doi.org/10.1038/nrendo.2009.106.

[2] W. Schlotz, R. Kumsta, I. Layes, S. Entringer, A. Jones, S. Wüst, Covariance between psychological and endocrine responses to pharmacological challenge and psychosocial stress: a question of timing, Psychosom. Med. 70 (2008) 787–796, https://doi.org/10.1097/PSY.0b013e3181810658.

[3] G.E. Miller, E. Chen, E.S. Zhou, If it goes up, must it come down? Chronic stress and the hypothalamic-pituitary-adrenocortical axis in humans, Psychol. Bull. 133 (2007) 25.

[4] B. Vanaelst, T. De Vriendt, I. Huybrechts, S. Rinaldi, S. De Henauw, Epidemiological approaches to measure childhood stress, Paediatr. Perinat. Epidemiol. 26 (2012) 280–297, https://doi.org/10.1111/j.1365-3016.2012.01258.x.

[5] M.S. Kopp, B.K. Thege, P. Balog, A. Stauder, G. Salavecz, S. Rózsa, G. Purebl, S. Ádám, Measures of stress in epidemiological research, J. Psychosom. Res., Focus on Heart Dis. 69 (2010) 211–225, https://doi.org/10.1016/j.jpsychores.2009.09.006.

[6] L. Rietschel, F. Streit, G. Zhu, K. McAloney, C. Kirschbaum, J. Frank, N.K. Hansell, M.J. Wright, J.J. McGrath, S.H. Witt, M. Rietschel, N.G. Martin, Hair cortisol and its association with psychological risk factors for psychiatric disorders: a pilot study in adolescent twins, Twin Res. Hum. Genet. 19 (2016) 438–446, https://doi.org/10.1017/thg.2016.50.

[7] V. Prado-Gascó, U. de la Barrera, S. Sancho-Castillo, J.E. de la Rubia-Ortí, I. Montoya-Castilla, Perceived stress and reference ranges of hair cortisol in healthy adolescents, PLoS One 14 (2019), e0214856, https://doi.org/10.1371/journal.pone.0214856.

[8] A.J. Oldehinkel, J. Ormel, N.M. Bosch, E.M.C. Bouma, A.M. Van Roon, J.G. M. Rosmalen, H. Riese, Stressed out? Associations between perceived and physiological stress responses in adolescents: the TRAILS study, Psychophysiology 48 (2011) 441–452, https://doi.org/10.1111/j.1469-8986.2010.01118.x.

[9] B. Vanaelst, I. Huybrechts, K. Bammann, N. Michels, T. de Vriendt, K. Vyncke, I. Sioen, L. Iacoviello, K. Günther, D. Molnar, L. Lissner, N. Rivet, J.-S. Raul, S. de Henauw, Intercorrelations between serum, salivary, and hair cortisol and child-reported estimates of stress in elementary school girls, Psychophysiology 49 (2012) 1072–1081, https://doi.org/10.1111/j.1469-8986.2012.01396.x.

[10] J. Ling, D. Xu, L.B. Robbins, J.S. Meyer, Does hair cortisol really reflect perceived stress? Findings from low-income mother-preschooler dyads, Psychoneuroendocrinology 111 (2020), 104478, https://doi.org/10.1016/j.psyneuen.2019.104478.

[11] J. Milam, R. Slaughter, G. Verma, R. McConnell, Hair cortisol, perceived stress and dispositional optimism: a pilot study among adolescents, J. Trauma Stress Disord. Treat. 3 (2014), 1000126, https://doi.org/10.4172/2324-8947.1000126.

[12] B. Vanaelst, N. Michels, T. De Vriendt, I. Huybrechts, K. Vyncke, I. Sioen, K. Bammann, N. Rivet, J.-S. Raul, D. Molnar, S. De Henauw, Cortisone in hair of elementary school girls and its relationship with childhood stress, Eur. J. Pediatr. 172 (2013) 843–846, https://doi.org/10.1007/s00431-013-1955-1.

[13] S.M. Staufenbiel, B.W.J.H. Penninx, A.T. Spijker, B.M. Elzinga, E.F.C. van Rossum, Hair cortisol, stress exposure, and mental health in humans: a systematic review, Psychoneuroendocrinology 38 (2013) 1220–1235, https://doi.org/10.1016/j.psyneuen.2012.11.015.

[14] N.A. Gray, A. Dhana, L. Van Der Vyver, J. Van Wyk, N.P. Khumalo, D.J. Stein, Determinants of hair cortisol concentration in children: a systematic review, Psychoneuroendocrinology 87 (2018) 204–214, https://doi.org/10.1016/j.psyneuen.2017.10.022.

[15] D.J. Glasscock, J.H. Andersen, M. Labriola, K. Rasmussen, C.D. Hansen, Can negative life events and coping style help explain socioeconomic differences in perceived stress among adolescents? A cross-sectional study based on the West Jutland cohort study, BMC Publ. Health 13 (2013) 532, https://doi.org/10.1186/1471-2458-13-532.

[16] U.K. Moksnes, I.E. Moljord, G.A. Espnes, D.G. Byrne, The association between stress and emotional states in adolescents: the role of gender and self-esteem, Pers. Indiv. Differ. 49 (2010) 430–435.

[17] K.M. O'Brien, E.Z. Tronick, C.L. Moore, Relationship between hair cortisol and perceived chronic stress in a diverse sample, Stress Health 29 (2013) 337–344, https://doi.org/10.1002/smi.2475.

[18] M. Singla, N.P. Jain, R. Chaudhry, Correlation of type 2 diabetes mellitus with perceived stress and family functioning, in: Diabetologie Und Stoffwechsel. Presented at the Diabetes Kongress 2018 – 53, Jahrestagung der DDG, Georg Thieme Verlag KG, 2018, p. 57, https://doi.org/10.1055/s-0038-1641815.

[19] M.A. Ferro, M.H. Boyle, The impact of chronic physical illness, maternal depressive symptoms, family functioning, and self-esteem on symptoms of anxiety and depression in children, J. Abnorm. Child Psychol. 43 (2015) 177–187, https://doi.org/10.1007/s10802-014-9893-6.

[20] J.G. Simmons, F. Azpitarte, F.D. Roost, E. Dommers, N.B. Allen, S. Havighurst, N. Haslam, Correlates of hair cortisol concentrations in disadvantaged young children, Stress Health 35 (2019) 104–111, https://doi.org/10.1002/smi.2842.

[21] M.A. Combs, W.H. Canu, J.J. Broman-Fulks, C.A. Rocheleau, D.C. Nieman, Perceived stress and ADHD symptoms in adults, J. Atten. Disord. 19 (2015) 425–434, https://doi.org/10.1177/1087054712459558.

[22] S. Steudte-Schmiedgen, S. Wichmann, T. Stalder, K. Hilbert, M. Muehlhan, U. Lueken, K. Beesdo-Baum, Hair cortisol concentrations and cortisol stress reactivity in generalized anxiety disorder, major depression and their comorbidity, J. Psychiatr. Res. 84 (2017) 184–190, https://doi.org/10.1016/j.jpsychires.2016.09.024.

[23] E. Koumantarou Malisiova, I. Mourikis, C. Darviri, N.C. Nicolaides, I.M. Zervas, C. Papageorgiou, G.P. Chrousos, Hair cortisol concentrations in mental disorders: a systematic review, Physiol. Behav. 229 (2021), 113244, https://doi.org/10.1016/j.physbeh.2020.113244.

[24] M. Gerber, N. Kalak, C. Elliot, E. Holsboer-Trachsler, U. Pühse, S. Brand, Both hair cortisol levels and perceived stress predict increased symptoms of depression: an exploratory study in young adults, NPS 68 (2013) 100–109, https://doi.org/10.1159/000351735.

[25] J.L. Ford, S.J. Boch, C.R. Browning, Hair cortisol and depressive symptoms in youth: an investigation of curvilinear relationships, Psychoneuroendocrinology 109 (2019), 104376, https://doi.org/10.1016/j.psyneuen.2019.104376.

[26] J. Straub, L.M. Klaubert, S. Schmiedgen, C. Kirschbaum, L. Goldbeck, Hair cortisol in relation to acute and post-traumatic stress symptoms in children and adolescents, Hist. Philos. Logic 30 (2017) 661–670.
[27] K. Kao, S.N. Doan, A.M. St John, J.S. Meyer, A.R. Tarullo, Salivary cortisol reactivity in preschoolers is associated with hair cortisol and behavioral problems, Stress 21 (2018) 28–35.
[28] L.O. White, M. Ising, K. von Klitzing, S. Sierau, A. Michel, A.M. Klein, A. Andreas, J. Keil, L. Quintero, B. Müller-Myhsok, M. Uhr, R. Gausche, J.T. Manly, M. J. Crowley, C. Kirschbaum, T. Stalder, Reduced hair cortisol after maltreatment mediates externalizing symptoms in middle childhood and adolescence, JCPP (J. Child Psychol. Psychiatry) 58 (2017) 998–1007, https://doi.org/10.1111/jcpp.12700.
[29] E. Kornelsen, M.C. Buchan, A. Gonzalez, M.A. Ferro, Hair cortisol concentration and mental disorder in children with chronic physical illness, Chronic Stress 3 (2019), https://doi.org/10.1177/2470547019875116, 2470547019875116.
[30] C. Buchan, S. Whitney, S.T. Leatherdale, J.G. Mielke, A. Gonzalez, M.A. Ferro, Hair cortisol and health-related quality of life in children with mental disorder, Chronic Stress 5 (2021), 24705470211047884.
[31] M.A. Ferro, E.L. Lipman, R.J. Van Lieshout, M.H. Boyle, J.W. Gorter, H. L. MacMillan, A. Gonzalez, K. Georgiades, Mental–physical multimorbidity in youth: associations with individual, family, and health service use outcomes, Child Psychiatr. Hum. Dev. 50 (2019) 400–410.
[32] S. Cohen, T. Kamarck, R. Mermelstein, A global measure of perceived stress, J. Health Soc. Behav. 24 (1983) 385–396, https://doi.org/10.2307/2136404.
[33] E.-H. Lee, Review of the psychometric evidence of the perceived stress scale, Asian Nurs. Res. 6 (2012) 121–127, https://doi.org/10.1016/j.anr.2012.08.004.
[34] J.O. Berry, W.H. Jones, The parental stress scale: initial psychometric evidence, J. Soc. Pers. Relat. 12 (1995) 463–472, https://doi.org/10.1177/0265407595123009.
[35] M. Dol, E. McDonald, M.A. Ferro, Psychometric properties of the CESD, STAI-T, and PSS among parents of children with mental illness, J. Fam. Stud. (2020) 1–17.
[36] J.J. Zelman, M.A. Ferro, The parental stress scale: psychometric properties in families of children with chronic health conditions, Fam. Relat. 67 (2018) 240–252.
[37] R.M. Radin, A.E. Mason, M.L. Laudenslager, E.S. Epel, Maternal caregivers have confluence of altered cortisol, high reward-driven eating, and worse metabolic health, PLoS One 14 (2019), e0216541, https://doi.org/10.1371/journal.pone.0216541.
[38] M.A. Ferro, A. Gonzalez, Hair cortisol concentration mediates the association between parent and child psychopathology, Psychoneuroendocrinology 114 (2020), 104613, https://doi.org/10.1016/j.psyneuen.2020.104613.
[39] L.S. Radloff, The CES-D scale: a self-report depression scale for research in the general population, Appl. Psychol. Meas. 1 (1977) 385–401.
[40] M.A. Ferro, K.N. Speechley, Factor structure and longitudinal invariance of the Center for Epidemiological Studies Depression Scale (CES-D) in adult women: application in a population-based sample of mothers of children with epilepsy, Arch. Womens Ment. Health 16 (2013) 159–166, https://doi.org/10.1007/s00737-013-0331-5.
[41] C.D. Spielberger, State-trait Anxiety Inventory for Adults, 1983.
[42] N.B. Epstein, L.M. Baldwin, D.S. Bishop, The McMaster family assessment device, J. Marital Fam. Ther. 9 (1983) 171–180.
[43] I.W. Miller, N.B. Epstein, D.S. Bishop, G.I. Keitner, The McMaster family assessment device: reliability and validity, J. Marital Fam. Ther. 11 (1985) 345–356, https://doi.org/10.1111/j.1752-0606.1985.tb00028.x.
[44] I.I. Oltean, C. Perlman, S. Meyer, M.A. Ferro, Child mental illness and mental health service use: role of family functioning (family functioning and child mental health), J. Child Fam. Stud. 29 (2020) 2602–2613.
[45] S. Canada, Canadian Community Health Survey (CCHS)—Mental Health User Guide, 2013.
[46] G.Y. Zou, A. Donner, Construction of confidence limits about effect measures: a general approach, Stat. Med. 27 (2008) 1693–1702.
[47] Z. Bursac, C.H. Gauss, D.K. Williams, D.W. Hosmer, Purposeful selection of variables in logistic regression, Source Code Biol. Med. 3 (2008) 17, https://doi.org/10.1186/1751-0473-3-17.
[48] K. Heinze, A. Lin, R.L.E.P. Reniers, S.J. Wood, Longer-term increased cortisol levels in young people with mental health problems, Psychiatr. Res. 236 (2016) 98–104, https://doi.org/10.1016/j.psychres.2015.12.025.
[49] T. Stalder, S. Steudte, N. Alexander, R. Miller, W. Gao, L. Dettenborn, C. Kirschbaum, Cortisol in hair, body mass index and stress-related measures, Biol. Psychol. 90 (2012) 218–223, https://doi.org/10.1016/j.biopsycho.2012.03.010.
[50] C. Barbosa-Leiker, M. Kostick, M. Lei, S. McPherson, V. Roper, T. Hoekstra, B. Wright, Measurement invariance of the perceived stress scale and latent mean differences across gender and time, Stress Health 29 (2013) 253–260, https://doi.org/10.1002/smi.2463.
[51] J.E. Khoury, M. Bosquet Enlow, A. Plamondon, K. Lyons-Ruth, The association between adversity and hair cortisol levels in humans: a meta-analysis, Psychoneuroendocrinology 103 (2019) 104–117, https://doi.org/10.1016/j.psyneuen.2019.01.009.
[52] N.C. Low, E. Dugas, E. O'Loughlin, D. Rodriguez, G. Contreras, M. Chaiton, J. O'Loughlin, Common stressful life events and difficulties are associated with mental health symptoms and substance use in young adolescents, BMC Psychiatr. 12 (2012) 116, https://doi.org/10.1186/1471-244X-12-116.
[53] L. Villanueva, I. Montoya-Castilla, V. Prado-Gascó, The importance of trait emotional intelligence and feelings in the prediction of perceived and biological stress in adolescents: hierarchical regressions and fsQCA models, Stress 20 (2017) 355–362, https://doi.org/10.1080/10253890.2017.1340451.
[54] J.A.A. Lavoie, K.S. Douglas, The perceived stress scale: evaluating configural, metric and scalar invariance across mental health status and gender, J. Psychopathol. Behav. Assess. 34 (2012) 48–57, https://doi.org/10.1007/s10862-011-9266-1.
[55] M.A. Ferro, K.N. Speechley, What about dads? An exploratory analysis of depressive symptoms in paternal primary caregivers of children with epilepsy, Epilepsy Behav. 23 (2012) 90–91, https://doi.org/10.1016/j.yebeh.2011.10.004.
[56] S.M. Staufenbiel, B.W.J.H. Penninx, Y.B. de Rijke, E.L.T. van den Akker, E.F.C. van Rossum, Determinants of hair cortisol and hair cortisone concentrations in adults, Psychoneuroendocrinology 60 (2015) 182–194, https://doi.org/10.1016/j.psyneuen.2015.06.011.
[57] S. Steudte-Schmiedgen, C. Kirschbaum, N. Alexander, T. Stalder, An integrative model linking traumatization, cortisol dysregulation and posttraumatic stress disorder: insight from recent hair cortisol findings, Neurosci. Biobehav. Rev. 69 (2016) 124–135, https://doi.org/10.1016/j.neubiorev.2016.07.015.
[58] R.C.A. Rippe, G. Noppe, D.A. Windhorst, H. Tiemeier, E.F.C. van Rossum, V.W. V. Jaddoe, F.C. Verhulst, M.J. Bakermans-Kranenburg, M.H. van IJzendoorn, E.L. T. van den Akker, Splitting hair for cortisol? Associations of socio-economic status, ethnicity, hair color, gender and other child characteristics with hair cortisol and cortisone, Psychoneuroendocrinology 66 (2016) 56–64, https://doi.org/10.1016/j.psyneuen.2015.12.016.
[59] H.-J. Moon, J.-G. Seo, S.-P. Park, Perceived stress and its predictors in people with epilepsy, Epilepsy Behav. 62 (2016) 47–52, https://doi.org/10.1016/j.yebeh.2016.06.038.
[60] B.E. Compas, S.S. Jaser, M.J. Dunn, E.M. Rodriguez, Coping with chronic illness in childhood and adolescence, Annu. Rev. Clin. Psychol. 8 (2012) 455–480, https://doi.org/10.1146/annurev-clinpsy-032511-143108.
[61] S. Steudte, T. Stalder, L. Dettenborn, E. Klumbies, P. Foley, K. Beesdo-Baum, C. Kirschbaum, Decreased hair cortisol concentrations in generalised anxiety disorder, Psychiatr. Res. 186 (2011) 310–314, https://doi.org/10.1016/j.psychres.2010.09.002.
[62] H. Kische, T.M. Ollmann, C. Voss, J. Hoyer, F. Rückert, L. Pieper, C. Kirschbaum, K. Beesdo-Baum, Associations of saliva cortisol and hair cortisol with generalized anxiety, social anxiety, and major depressive disorder: an epidemiological cohort study in adolescents and young adults, Psychoneuroendocrinology 126 (2021), 105167, https://doi.org/10.1016/j.psyneuen.2021.105167.
[63] H.Y. Elnazer, L.C.K. Lau, H. Amaro, D.S. Baldwin, Hair cortisol concentration in anxiety disorders: exploration of relationships with symptom severity and inflammatory markers, Acta Neuropsychiatr. 33 (2021) 104–110, https://doi.org/10.1017/neu.2020.35.