In Individuals Following Aneurysmal Subarachnoid Haemorrhage, Hair Cortisol Concentrations Are Higher and More Strongly Associated with Psychological Functioning and Sleep Complaints than in Healthy Controls

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Abstract
Background: Following an aneurysmal subarachnoid haemorrhage (aSAH), many patients report persistent deficits in psychological functioning, characterised by high levels of stress and symptoms of depression, low life satisfaction, along with poor sleep. Such deficits have been associated with altered saliva and serum cortisol levels due to a dysregulation of hypothalamic-pituitary-adrenal axis activity (HPA-AA). However, hair cortisol concentrations (HCCs) have not been assessed in this population, although this method allows a long-term insight into cortisol values. Therefore, the objective of this study was to compare HCCs in aSAH patients and healthy controls and to examine how HCCs are associated with perceived stress, psychological functioning, and sleep complaints. ***Methods:*** In this cross-sectional study, data on depressive symptoms, hypochondriacal beliefs, life satisfaction, and sleep complaints were gathered in 15 aSAH patients and 17 healthy controls. HCCs of the previous 3 months were assessed. ***Results:*** aSAH patients had significantly higher HCCs than healthy controls. In aSAH patients, higher HCCs were significantly associated with increased depressive symptoms, hypochondriacal beliefs, lower life satisfaction, and increased sleep complaints. Such significant associations were not found in healthy controls. ***Conclusions:*** Our findings indicate that a dysregulation of HPA-AA is associated with some of the long-term impairments in psychological functioning and sleep in aSAH survivors. While the direction of association remained unclear, a dysregulated HPA-AA may be causally linked with the maintenance of poor psychological functioning and poor sleep. The overall findings should be considered in the planning of long-term treatment aimed at improving psychological functioning and sleep in aSAH patients.

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Introduction

Aneurysmal subarachnoid haemorrhage (aSAH) is characterised by the rupture of a cerebral artery and consequent bleeding into the area surrounding the brain known as the subarachnoid space [1]. Although this form of stroke has a high morbidity and mortality, in past decades improvements in neurosurgery and emergency treatment algorithms have increased the survival rate to 65% [2]. However, a large proportion of survivors continues to suffer from physical and psychological deficits following the initial recovery period [3]. The aSAH itself, combined with the frequently persistent deficits experienced in the aftermath, results in a severely impaired quality of life of aSAH survivors years after ictus [4].

As regards the psychological functioning, aSAH survivors reported increased anxiety levels [5], probably associated with the fear of recurrent haemorrhage [6]. Compared to healthy controls, aSAH patients also experienced more frequent depressive symptoms [7], increased fatigue [8], and a poorer sleep quality [7]. Symptoms of depression, fatigue, and poor sleep persisted up to 4 years after ictus [9], which explained why quality of life also remained low many months after surgery [10].

Besides the anxiety of a next stroke, one explanation for the persistently impaired psychological functioning in aSAH survivors might be the possibility of a dysregulation of hypothalamic-pituitary-adrenal axis activity (HPA-AA) after aSAH [11], with cortisol as main outcome marker. While a downregulation of the adrenocorticotropic hormone (ACTH), the precursor of cortisol, has been repeatedly shown, findings on the cortisol levels are less consistent.

With regard to ACTH, an underactivity of the HPA-AA has been documented in aSAH survivors: Tanriverdi et al. [12] reported ACTH deficiencies in 23% of aSAH patients in the acute phase, and 14% 12 months after ictus. Moreover, in a large register study with 417 aSAH patients the prevalence of hypopituitarism in the chronic phase (at least 5 months after the event) by laboratory values, physician diagnoses, and stimulation tests, was 35, 36, and 70%, respectively, with decreased ACTH levels being the most frequent endocrine dysfunction in this group of patients [13]. Finally, similar results were reported in a meta-analysis with 19 studies and 1,137 aSAH patients, yielding hypopituitarism in 47% of patients in the chronic phase [14].

As regards the cortisol secretion assessed in blood and saliva, prior research has provided mixed results. For instance, Karaca et al. [15] found that serum basal cortisol levels were significantly elevated 3 years after aSAH. However, Brand et al. [7] found no statistically significant differences between aSAH patients (5–9 months after ictus) and healthy controls with regard to the salivary cortisol awakening response (CAR), neither for the area under the curve with respect to increase (AUCi; representing the increase in cortisol secretion in relation to the first of the postwaking measurements) nor with respect to ground (AUCg; representing overall cortisol output). Furthermore, the CAR was neither related to patients' psychological functioning nor to their subjective or objective sleep. By contrast, Gerber et al. [16] observed that compared to healthy controls, aSAH patients (mean = 44 months after ictus) had significantly higher salivary CAR as measured by the AUCi. However, aSAH patients also had descriptively lower overall cortisol output values, represented by the AUCg. Gerber et al. concluded that a disconnection between the AUCi and AUCg values was plausible, as the values represented differing aspects of HPA-AA (reactivity vs. total output) [16].

In summary, previous research suggested that the HPA-AA was indeed affected in aSAH patients. However, given the inconsistencies in the available literature, it remains unclear whether aSAH patients have lower or higher basal cortisol levels than healthy controls, and how exactly cortisol levels are related to other health outcomes. In part, the inconsistencies found in prior research can be attributed to the fact that salivary and plasma cortisol levels represent single time point assessments and only reveal acute circulating cortisol levels or mean cortisol secreted over a relatively short period of time. Moreover, salivary and plasma cortisol are easily affected by temporary or transient disturbances in psychosocial stress on the day of measurement, subject to diurnal variations and affected by any food intake, smoking and physical activity that takes place shortly before sampling. By contrast, hair cortisol measurement has the potential to overcome these methodological difficulties associated with the assessment of long-term cortisol levels [17, 18]. For instance, Stalder et al. [19] showed that hair cortisol concentrations (HCCs) have a high intra-individual stability, with correlations of repeated assessments between 2 months and 1 year ranging between 0.68 and 0.79. Therefore, hair cortisol assessments have become an increasingly accepted approach in endocrinology and biopsychology during the last few years [18].

To date, hair cortisol as a biomarker of HPA-AA has not been studied in aSAH patients. Therefore, the goal of the present study was twofold: first, to compare for the first time HCCs in aSAH patients and healthy controls;

second, to examine how HCCs are associated with perceived stress, psychological functioning, and sleep complaints, domains in which aSAH patients have frequently reported deficits, separately for aSAH patients and healthy controls.

The following 2 hypotheses were formulated. Following Dettenborn et al. [20] and Van Uum et al. [21], our first hypothesis was that higher HCCs would be associated with poorer psychological functioning (including depressive symptoms, hypochondria, and life satisfaction). Second, although Maurer et al. [22] were unable to find significant associations between hair cortisol and objective sleep parameters in young children, we assumed that higher HCCs would be associated with poorer quality of sleep in aSAH survivors, because poor sleep and depressive symptoms are strongly correlated in aSAH patients [16, 23].

Methods

Participants

The sample comprised 32 participants (22 women, 10 men; mean age = 57.4 years, SD = 10.7; mean BMI = 26.2, SD = 3.7). Fifteen participants (11 women, 4 men; mean age = 57.2 years, SD = 8.9) were patients with aSAH and following neurosurgical or endovascular intervention. One patient had received coiling, and 14 underwent clipping. No patient presented with additional untreated aneurysms. The mean Glasgow Outcome Score was 4.33 (SD = 0.6), indicating an ability to live independently but with some deficits. Five had a Fisher grade of 4, another 5 had a grade of 3, and 1 of 2. These data were not available for 4 patients. Five had a Hunt and Hess grade of 4, then 5 had a grade of 3, and 2 of 2. This information was not available for 3 patients. The mean time spent in intensive care was 8.3 days (SD = 2.8). The mean time after intervention was 44 months (SD = 28.9; range 3–72 months, median = 60 months, 25th percentile: 9 months, 75th percentile: 69 months).

The second group consisted of 17 healthy controls (11 women, 6 men; mean age = 59.8 years, SD = 10.8). To reduce bias, healthy controls were matched for age and sex. Accordingly, the 2 groups did not differ with regard to age, $F(1, 31) = 0.01$, $p = 0.946$, $\eta^2 = 0.000$, sex, $\chi^2(1, 31) = 0.28$, $p = 0.599$, $\Phi = 0.092$, and BMI, $F(1, 31) = 2.75$, $p = 0.108$, $\eta^2 = 0.084$. Use of medication tended to be more frequent among aSAH patients ($n = 12$; 80%) than healthy controls ($n = 3$; 25%), $\chi^2(1, 31) = 3.69$, $p = 0.055$, $\Phi = 0.322$. However, none of the participants indicated that they used corticosteroid medication.

Study Design and Procedure

The design of this study was cross-sectional. Patients were eligible if they were treated for aSAH at the Department of Neurosurgery at the University Hospital Basel, Switzerland, and were recruited during the consultation hours. Healthy controls were recruited via online advertisements on local news websites. Those willing to participate in the study provided informed consent and were assured confidentiality of their responses prior to the data assessment. Approval for the study was obtained from the local ethical committee (EKNZ, approval No. 61/12). The study was conducted in accordance with the ethical principles described in the 1964 Declaration of Helsinki. Power analysis was used to establish the minimal sample size to find large correlations ($r = 0.50–0.60$). Using G*Power Software 3 (alpha error = 0.05, power = 0.80), between 13 ($r = 0.60$) and 21 ($r = 0.50$) aSAH patients and healthy controls were needed.

All data assessments took place at the participants' homes between April 2012 and April 2013 and were carried out by a trained research assistant. Previously, data from this study had been published indicating that aSAH patients reported poorer subjective sleep and more sleep-related dysfunctional cognitions and hypochondriacal beliefs than healthy controls [16]. However, data on hair cortisol have not been published elsewhere.

Instruments

Depressive Symptoms

The Beck Depression Inventory was used to assess the severity of depressive symptoms [24]. It consists of 21 items scaled from 0 to 3 including a range of affective, behavioural, cognitive, and somatic symptoms that are indicative of unipolar depression (e.g., "I am so unhappy/sad that I can't stand it"). Possible scores ranged from 0 to 63 with higher scores indicating more depressive symptoms.

Hypochondriacal Beliefs

The 14-item Whiteley Index was used to assess hypochondriacal beliefs (e.g., "Are you bothered by many aches and pains?") [25]. Answers were "yes" (=1) or "no" (=0), with higher sum scores reflecting a greater inclination to overestimate bodily sensations and pain.

Satisfaction with Life

The 5-item Satisfaction with Life Scale was used to obtain an overall judgement of respondents' satisfaction with life [26]. Answers are given on a 7-point Likert-type scale (e.g., "In most ways, my life is close to my ideal"). The items were summed to generate a composite score.

Sleep Complaints

The 7-item Insomnia Severity Index was administered to assess participants' subjective sleep complaints [27]. The items refer in part to the DSM-IV criteria for insomnia by measuring difficulty in falling asleep, difficulties maintaining sleep, early morning awakening, increased daytime sleepiness, low daytime performance, low satisfaction with sleep, and worrying about sleep. Possible answers range from 0 (not at all) to 4 (very much), with higher sum scores reflecting higher insomnia.

Hair Cortisol

HCC was assessed using samples of hair, approximately 3 mm in diameter, which are cut close to the scalp of the study participants. The 3 cm of hair closest to the scalp are tested for cortisol concentration and provide a value encompassing the previous 3 months. In some cases, participants with particularly short hair do not provide sufficient material for analysis; this was the case with 3 participants from the control group, who were subsequently excluded from the analyses. The samples were analysed at the bio-

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Table 1. Descriptive statistics of all study variables

	Mean ± SD	α (items)	Range		Skew	Kurtosis
			potential	actual		
Hair cortisol concentration, nmol/L	3.28±1.80	–	0+	0.74–10.38	1.80	2.99
Depressive symptoms (BDI)	6.47±5.48	0.87 (21)	0–63	0–26	1.56	3.83
Hypochondriacal beliefs (WI)	3.13±3.93	0.78 (14)	0–56	0–19	2.68	8.35
Satisfaction with life (SWLS)	26.59±7.00	0.93 (5)	5–35	5–35	–1.41	1.95
Sleep complaints (ISI)	5.91±4.50	0.83 (7)	0–28	0–17	0.90	0.07

α = Cronbach's alpha. n = 32. BDI, Beck Depression Inventory; WI, Whiteley Index; SWLS, Satisfaction with Life Scale; ISI, Insomnia Severity Index.

chemical laboratory of the University of Dresden, Germany, as described in the protocol by Kirschbaum et al. [28]. To summarise, each individual hair sample is washed twice with 2.5 mL of isopropanol for 3 min, dried over a 12-h period, and then powdered in a Retsch ball mill at 30.0 Hz, for a period of 5 min; 25 mg of the powdered hair is then transferred into a 2-mL cryovial. Then 1.5 mL of pure methanol is added to the vial, which is rotated slowly for 45 min, in order for steroids to be extracted. The sample is then centrifuged at 10,000 r.p.m. for a period of 3 min (relative centrifugal force = 10,080 g). One millilitre of clear supernatant is placed in a new vial, and the methanol is evaporated using a steady stream of nitrogen (60°C) until the sample is dry; 0.4 mL of commercially available phosphate buffer (IBL-International, Hamburg, Germany) containing 0.1% bovine serum albumin, at a pH of 7.1, is added to the vial, which is then vortexed for 15 s. Cortisol is determined by analysing 80 μL of the reconstituted sample by a commercially available immunoassay (CLIA, IBL-International, Hamburg, Germany). In accordance with the study of Skoluda et al. [29], the minimal amount of powdered hair used in this study was 25 mg, instead of 50 mg in the protocol of Kirschbaum et al. [28]. Intra- and interassay coefficients of variance were below 10% in the present study.

Statistical Analyses

None of the participants had missing values. Differences in HCCs, psychological functioning, and sleep between aSAH patients and healthy controls were examined with univariate analyses of variances (ANOVAs). Differences between aSAH patients and healthy controls with regard to stress, psychological functioning, and sleep have been described elsewhere [16]. Bivariate associations between hair cortisol levels, stress, psychological functioning, and sleep were examined via Pearson's product moment correlations, separately for aSAH patients and healthy controls. Following Cohen [30], effect sizes for ANOVAs (partial η^2) were considered as follows: small = 0.01 > η^2 < 0.059, medium = 0.06 > η^2 < 0.139, or large = η^2 ≥ 0.14. Cohen's criteria were also used to interpret correlations (e.g., small: 0.10–0.30; medium: 0.30–0.50; large: >0.50) [30]. The level of probability was set at p < 0.05 across all analyses. All statistics were performed with SPSS® 22.0 (IBM Corporation, Armonk, NY, USA) for Apple MacIntosh®.

Results

Descriptive Statistics

The descriptive statistics for the total sample are presented in Table 1. Table 1 also shows that the internal consistencies for all indicators related to psychological functioning and subjective sleep were adequate.

Differences in Hair Cortisol, Psychological Functioning, and Sleep between aSAH Patients and Healthy Controls

HCCs were significantly higher in aSAH patients compared to healthy controls, $F(1, 28)$ = 5.04, p < 0.05, η^2 = 0.157 (aSAH: mean = 4.24 nmol/L, SD = 2.91; healthy controls: mean = 2.39 nmol/L, SD = 1.26). Moreover, aSAH patients perceived more depressive symptoms than healthy controls, $F(1, 28)$ = 4.75, p < 0.05, η^2 = 0.149 (aSAH: mean = 8.50, SD = 6.65; healthy controls: mean = 4.27, SD = 3.41), reported higher hypochondriacal beliefs, $F(1, 28)$ = 6.72, p < 0.05, η^2 = 0.199 (aSAH: mean = 4.00, SD = 3.44; healthy controls: mean = 1.60, SD = 0.99), and exhibited more sleep complaints, $F(1, 28)$ = 10.04, p < 0.01, η^2 = 0.271 (aSAH: mean = 8.64, SD = 5.15; healthy controls: mean = 3.93, SD = 2.49). No significant group differences were found with regard to satisfaction with life, $F(1, 28)$ = 1.60, p = 0.22, η^2 = 0.056 (aSAH: mean = 24.93, SD = 8.16; healthy controls: mean = 28.27, SD = 5.96).

Correlations between Hair Cortisol and Psychological Functioning

In aSAH patients, higher HCCs were significantly associated with increased depressive symptoms, hypochondriacal beliefs, and with lower life satisfaction (Table 2). The scatterplot shown in Figure 1 suggests that the statis-

Table 2. Correlations between hair cortisol and psychological variables, separately for aSAH patients and healthy controls

		1	2	3	4	5
1	Hair cortisol concentration, nmol/L	–	–0.40	–0.13	–0.10	–0.26
2	Hypochondriacal beliefs (WI)	0.62*	–	0.20	0.07	0.40
3	Depressive symptoms (BDI)	0.56*	0.74***	–	–0.39	0.27
4	Satisfaction with life (SWLS)	–0.65*	–0.65**	–0.72**	–	–0.29
5	Sleep complaints (ISI)	0.54*	0.18	0.56*	–0.26	–

Above the diagonal: healthy controls ($n = 17$). Below the diagonal: aSAH patients ($n = 15$). *** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$. For abbreviations, see Table 1.
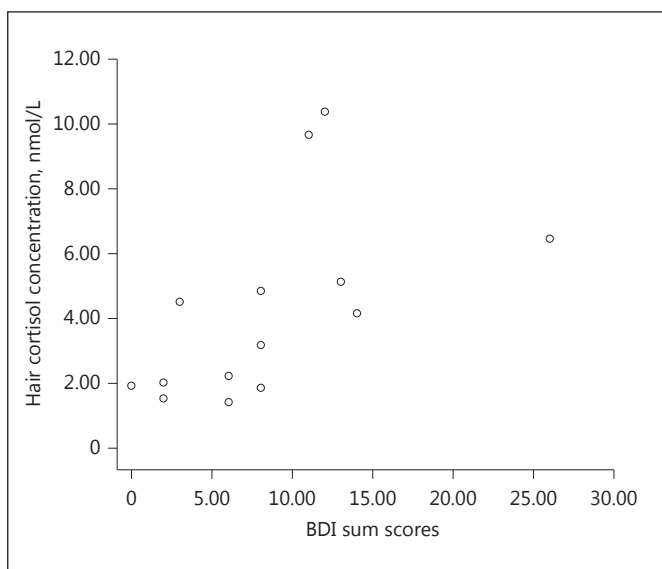

Fig. 1. Scatterplot illustrating the bivariate relationship between hair cortisol concentrations and depressive symptoms in aSAH patients.

tically significant correlation between patients' HCCs and their depressive symptoms was not due to the impact of a single outlier. Similar patterns of results were found for all other indicators of psychological functioning.

In healthy controls, none of the correlations were significant. Descriptively, however, higher HCCs tended to be associated with fewer psychological symptoms ($r = –0.08$ to $–0.40$, p = ns).

Correlations between Hair Cortisol and Sleep

In aSAH patients, higher HCCs were significantly associated with increased sleep complaints (Table 2). In

contrast, in healthy controls, no significant associations existed between participants' HCCs and their subjective sleep. However, descriptively, higher HCCs were associated with fewer subjective sleep complaints ($r = –0.26$, p = ns).

Discussion

The key findings of the present study are that aSAH patients had higher hair cortisol levels than healthy controls. Moreover, in the aSAH group, statistically significant associations existed between increased HCCs and impaired psychological functioning and sleep, while such associations were not observed in healthy controls. In many respects, this study explored unknown territory. To the best of our knowledge, no research has been published so far on hair cortisol levels in aSAH patients compared to healthy controls, and few studies have assessed the degree to which high hair cortisol levels are associated with stress and psychological functioning in clinical and non-clinical populations. Thus, the present study expands upon the current literature in an important way, in that we were able to show that patients with aSAH reported poorer subjectively assessed psychological functioning and more sleep complaints [16], which at the physiological level were reflected by statistically significantly higher HCCs. Higher HCCs, in turn, are believed to reflect a chronic upregulation of HPA-AA.

An underlying cause of irregularities in endocrine dysfunction in patients who have undergone aSAH and subsequent medical intervention can be damage to regions of the brain involved in HPA axis regulation [31, 32]. These irregularities have been shown to persist up to 24 months after ictus [33]. Some studies have suggested that this is

more likely following clipping, as opposed to coiling [34]; in the present study, 14 of the 15 patients had undergone clipping. For instance, damage to the hippocampus, which can be the result of clipping, can lead to alterations in cortisol secretion [35]. However, in the present study, there was no suggestion that major areas of the hypothalamic-pituitary system were damaged. Consequently, we are unable to draw conclusions about the influence of particular haemorrhage locations on HCCs.

Given the absence of previous studies, we did not formulate a specific hypothesis as to whether aSAH patients would have higher or lower HCCs compared to healthy controls. In the present study, we observed higher HCCs in the aSAH group. Accordingly, the present data are at odds with studies showing that patients with aSAH have suffered from hypopituitarism [14, 36] and tended to have a lower morning overall cortisol output [16]. However, previous studies have also shown that compared to healthy controls, aSAH patients had a higher CAR as measured by the AUCi [16]. Moreover, serum basal cortisol and ACTH levels were found to significantly increase from the first to the third years after surgical intervention [15]. Thus, the elevated HCCs might be explained by the fact that the mean time since surgery amounted to 44 months in the present study. Unfortunately, the present data do not allow a determination of the cause of the high HCCs found in aSAH patients. Thus, once these findings have been confirmed in larger samples, a next step could be to examine whether the elevated HCCs in aSAH survivors are attributable to ACTH dependent or ACTH independent sources [37]. Nevertheless, the elevated HCCs in aSAH patients are critical as increased HCCs have been shown to constitute a risk factor for cardiovascular diseases [38], diabetes mellitus [39], increased BMI and obesity [40], and the occurrence of metabolic syndrome [41]. Finally, as reported in a previous paper [16], aSAH patients reported significantly higher depressive symptoms, hypochondriacal beliefs, and sleep complaints than healthy controls.

Two hypotheses were formulated. Our first hypothesis was that higher HCCs would be associated with poorer psychological functioning, and the data did confirm this notion, though specifically in aSAH patients, but not in healthy controls. Importantly, in aSAH patients, most correlations between HCCs and psychological functioning were of strong magnitude (r_s between 0.54 and –0.65), and the inspection of the scatterplots indicated that single outliers did not affect the correlations. Moreover, the same pattern of results was found across all indicators of psychological functioning including depressive symptoms, hypochondriacal beliefs, and life satisfaction. The close link between increased HCCs and poor psychological functioning accords well with previous research showing that higher HCCs have been observed in individuals suffering from depression [20] and severe chronic pain [21]. The fact that HCCs were significantly associated with psychological functioning in aSAH patients, and not in healthy controls, accords well with a study on healthy young adults [42], in which higher HCCs were associated with lower depressive symptoms. However, our findings add to the existing literature by providing preliminary evidence that high HCC levels can be used as a biomarker for poor psychological functioning among aSAH populations. This finding is important as researchers were not able to correlate assessments of pituitary hormone dysregulation with the outcomes of aSAH patients in previous studies [36].

Our second hypothesis was that higher HCCs would be associated with more frequent sleep complaints [16, 23]. The data supported this hypothesis for aSAH patients, but not for healthy controls. While heightened activity of the HPA axis has been associated with sleep complaints [43], it has to date not been conclusively established whether HPA axis overactivity precedes sleep complaints or occurs as a result of the emotional stress of poor sleep [44].

While the present study provided novel insights into the association between HCCs, psychological functioning, and sleep in aSAH versus healthy controls, the current results must be considered in light of certain limitations. First, the relatively small sample size made it difficult to detect statistically significant correlations, and precluded separate analyses for male and female participants. Nevertheless, results showed medium to large effect sizes, which do not rely on sample sizes. Second, patients were recruited at different time points following surgery. However, ANOVAs comparing participants below versus above the median of posttreatment time revealed no influence on the existence or severity of deficits in the measured parameters or with regard to HCC (data not shown). Accordingly, the increased hair cortisol levels in aSAH patients appear to be due to the event per se and do not represent a cumulative effect over time. Third, the cross-sectional study design did not allow conclusions to be drawn regarding a possible causal relationship between HCCs, psychological functioning, and sleep. Fourth, medication intake prior to the beginning of the study was not recorded. It is therefore possible that the hair samples may have been affected by medications which influence cortisol secretion. However, as noted in

the text, participants provided detailed information about their medication intake at the moment of the data assessment. The inspection of this data revealed that no participant consumed corticosteroid medication. Moreover, the medications consumed have been analysed in light of their potential effects on the activity of the HPA axis and cortisol secretion. In the aneurysm group, 1 patient took the diabetes medication metformin. While Haugen [45] notes that metformin has been reported to affect thyroid function, this finding has not been confirmed by multiple studies and requires further investigation. Moreover, no direct effects upon cortisol secretion have been documented [46]. Additionally, 1 patient took 2 forms of antidepressant (escitalopram and mirtazapine), which both have been shown to reduce salivary cortisol [47, 48]. While purely hypothetical, as our findings show increased cortisol levels amongst aSAH patients, we feel that the intake of these medications by 1 patient is not likely to have exaggerated our results. In the control group, 1 participant took medication for high cholesterol (Crestor), and 1 took hormone replacement therapy. In the comprehensive list of medications of Granger et al. [49], which, by their mechanism of action, could influence salivary cortisol, these forms of medication are considered. However, Rosuvastatin, the active ingredient in Crestor, taken alone, has not been shown to affect plasma cortisol levels [50, 51]. Regarding the hormone replacement therapy, this was a combination of oestrogen and progesterone, which has not been shown to significantly increase plasma cortisol concentration, in comparison to oestrogen alone [52]. Fifth, we acknowledge that while we used a standardised and validated tool to assess self-reported symptoms of depression, this instrument does not correspond to a diagnostic tool to assess depression as defined in the international classification systems such as the ICD-10 [53]. Because the HPA system is usually disturbed during an acute major depressive episode [54], we were not able to control for this confounding factor of altered HPA regulation.

Conclusion

The findings indicate that a dysregulation of HPA-AA may explain some of the long-term deficits experienced by aSAH survivors. However, these findings need to be replicated in future research, and more knowledge is required as to how hair cortisol levels change over the course of time in aSAH survivors. Finally, our findings suggest that HPA axis abnormalities should be taken into account in the planning of long-term treatment in aSAH survivors.

Disclosure Statement

The authors declare that there is no conflict of interest.

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