Journal of Psychosomatic Research 78 (2015) 445–451

Contents lists available at ScienceDirect

Journal of Psychosomatic Research

Burnout and cortisol: Evidence for a lower cortisol awakening response in both clinical and non-clinical burnout

Bart G. Oosterholt [a,b,*], Joseph H.R. Maes [b], Dimitri Van der Linden [c], Marc J.P.M. Verbraak [a,d], Michiel A.J. Kompier [a]

[a] Behavioural Science Institute, Radboud University Nijmegen, Nijmegen, the Netherlands
[b] Donders Institute for Brain, Cognition and Behaviour, Radboud University Nijmegen, Nijmegen, the Netherlands
[c] Institute of Psychology, Erasmus University, Rotterdam, the Netherlands
[d] HSK Group, Arnhem, the Netherlands

ARTICLE INFO

Article history:
Received 14 August 2014
Received in revised form 22 October 2014
Accepted 4 November 2014

Keywords:
Emotional exhaustion
Fatigue
Work stress
Salivary cortisol
CAR
HPA axis

ABSTRACT

Objective: Although the relationship between burnout and cortisol levels has been examined in previous studies, the results are mixed. By adopting a design in which we attempted to overcome important limitations of earlier research, the purpose of the present study was to improve the understanding of the biological underpinnings of burnout and to further the knowledge about the relationship between burnout and cortisol.
Methods: A clinical burnout patient group ($n = 32$), a non-clinical burnout group ($n = 29$), and a healthy control group ($n = 30$) were compared on burnout symptoms, physical and psychological complaints, and on cortisol levels. In order to examine a broad range of cortisol indices, including different measures of the cortisol awakening response (CAR) and several day-curve measures, salivary cortisol was collected six times a day during two consecutive non-workdays.
Results: As expected, the clinical burnout group reported more burnout symptoms, and physical and psychological complaints than the non-clinical burnout group, which in turn reported more burnout symptoms and physical and psychological complaints than the healthy control group. With regard to cortisol levels, we found that until 30 min after awakening, the CAR of both the clinical and the non-clinical burnout group was lower compared with the healthy control group. Furthermore, there was some evidence that the decline of cortisol during the day was smaller in the non-clinical burnout group than in the healthy control group.
Conclusion: The results of the present study provide support for lowered cortisol in both clinical and non-clinical burnout.

Introduction

Burnout is a work-related chronic stress syndrome characterized by exhaustion, cynicism (a distant attitude towards the job), and feelings of reduced professional efficacy [1]. Since burnout is generally the result of a prolonged period of stress, it is often hypothesized that the hypothalamic–pituitary–adrenal axis (HPA axis), a part of the neuroendocrine system involved in the regulation of reactions to stress, may be disturbed in individuals with burnout (e.g., [2–5]). As the major output of the HPA axis is the stress hormone cortisol, cortisol levels are believed to differ in individuals with burnout relative to the levels in healthy individuals. Specifically, whereas acute stress leads to increased cortisol levels, a general notion is that chronic stress, which is usually the case in burnout, can lead to a 'breakdown of the HPA axis' resulting in decreased cortisol levels (e.g., [6–8]).

The results of previous studies on the relationship between burnout and cortisol, however, do not always fit with this line of reasoning. Although, for example, Sonnenschein et al. [9] and Marchand et al. [10] indeed found burnout to be related to reduced levels of cortisol, Melamed et al. [4] and De Vente et al. [5], on the other hand, found evidence for elevated levels of cortisol. In addition, some studies (e.g., [11,12]) failed to find any cortisol deviations in burnout. For a more comprehensive review of the literature, see Danhof-Pont et al. [13].

Several factors may underlie these mixed findings, such as heterogeneity in the assessment of cortisol, potential confounding variables which were not controlled for and the relatively small sample size in some of the previous studies. Yet perhaps the most important and fundamental factor might be the large variety of operationalizations of burnout that are used in earlier research. That is, in some studies, the burnout group comprised clinically diagnosed burnout patients [14,15], whereas in other studies (e.g., [10,16]), the burnout group consisted of healthy undiagnosed individuals who were solely selected

* Corresponding author at: Behavioural Science Institute, Radboud University Nijmegen, P.O. Box 9104, 6500 HE, Nijmegen, the Netherlands. Tel.: +31 24 3615729; fax: +31 24 3612639.
E-mail address: b.oosterholt@psych.ru.nl (B.G. Oosterholt).

http://dx.doi.org/10.1016/j.jpsychores.2014.11.003
0022-3999/

on the basis of a high score on a burnout questionnaire (i.e., reporting symptoms of a burnout). In addition to the latter, the type of burnout questionnaire which was used for this purpose also varied (e.g., compare [4,17]). Also, the criteria used for diagnosing a clinical burnout are not always clear (e.g., [18,19]) and differ between studies (compare e.g., [3, 20]). Furthermore, in a large number of studies in which a clinical burnout sample was examined, no information was provided about the time between the diagnosis of burnout and participation in the study, or the time between diagnosis and participation was relatively long (e.g., [5,21]). This may be problematic because treatment or maturation effects might have interfered. A final and key aspect with regard to the diagnosis of clinical burnout is the comorbidity of other mental disorders. Specifically, although there is substantial evidence indicating that, for example, mood and anxiety disorders have an effect on cortisol (i.e., elevated cortisol levels; e.g., [22,23]), in former research, burnout patients with comorbid mental disorders were not always excluded, and/or the effects of comorbidity were not always controlled for (e.g., [18,19]). In these studies, the observed cortisol levels in burnout patients may possibly have been influenced by mental disorders other than burnout. Finally, a factor potentially affecting the validity of the observed cortisol levels in previous studies is the day on which the cortisol samples were collected. Research has shown that cortisol levels are generally higher on workdays than on days off work (e.g., [24–26]). Yet in almost all previous studies on the relationship between burnout and cortisol, the cortisol sampling procedure took place during workdays. This may have affected the results of those studies in which the burnout group consisted of clinical burnout patients who were (largely) not working (i.e., on sick leave) and in which the control group comprised healthy participants who were working during the sampling procedure.

The purpose of the present study was to further examine cortisol levels in burnout with a design that enabled us to overcome these limitations of former research. To this end, we carefully selected a group of recently clinically diagnosed burnout patients without comorbid mental disorders, to rule out the effect of other psychopathologies. In addition, we included a non-clinical burnout group consisting of employees who reported to have burnout symptoms, but who were not clinically diagnosed as burnout patients and were not seeking help for these symptoms. Cortisol levels of both groups were compared with a matched control group consisting of healthy employees. In order to examine a full range of cortisol indices, including different measures of the cortisol awakening response (CAR) and multiple day-curve measures, salivary cortisol was sampled six times a day during two-consecutive non-workdays. As noted above, we chose to collect cortisol on non-workdays to make sure that the sampling conditions were equal between the three different employee groups.

In sum, the aim of the present study was to determine how both clinical burnout and non-clinical burnout are related to cortisol levels.

Methods

Participants

The sample was part of a larger longitudinal research project, in which both cortisol levels and cognitive performance in burnout were studied (see also [27]). In total, 91 employees participated in the present study. Thirty-two had received a clinical burnout diagnosis (the clinical burnout group), 29 reported burnout symptoms but were neither diagnosed as burnout patients nor seeking help for these symptoms (the non-clinical burnout group) and 30 were healthy individuals (the control group). Initially, the clinical burnout group and the non-clinical burnout group consisted of 33 and 30 participants, respectively. However, one participant was excluded from each of these groups due to non-compliance with the cortisol sampling instructions. One participant did not fill out the diary (see Procedure), and one did not sample on two consecutive non-workdays. The three groups were matched on several demographical characteristics (see Table 1 for more detailed information) and consisted of employees with various occupational backgrounds. All participants were financially compensated for their participation.

The participants in the clinical burnout group were patients from HSK Group, a large mental healthcare organization in the Netherlands. Patients were selected on the basis of their burnout diagnosis as established by a team of two or three professional clinical psychologists. A burnout diagnosis was based on an intake procedure in which a structured clinical interview was used containing the Dutch translation [28] of the MINI International Neuropsychiatric Interview 5.0.0 (M.I.N.I.; [29]) and the Assessment of DSM-IV Personality Disorders (ADP-IV; [30]). Since burnout is not officially included in the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR; [31]), in the Netherlands, a burnout diagnosis is usually based on the DSM-IV-TR criteria for diagnosing an undifferentiated somatoform disorder with the addition that the cause of the symptoms must be work related. This method was also used in the present study. As an additional tool to validate the burnout diagnosis, patients filled out the Utrecht Burnout Scale (UBOS; [32]; see Measures section for more information). Patients were excluded if they fulfilled the DSM-VI criteria for any other axis I or II disorder, as assessed with the M.I.N.I. and the ADP-IV, respectively. Approximately 40% of the eligible burnout patients agreed to participate in the study after being contacted by telephone. Of the 32 participating patients, 12 were on sick leave due to their burnout, 15 continued working but worked fewer hours than prior to their burnout diagnosis and 5 remained working the same number of hours as before their diagnosis.

The participants in the non-clinical burnout group and the control group were recruited via local advertisements and social networking. Potential participants filled out a screening questionnaire in which several demographical characteristics (used to match the different groups; see Table 1), the exhaustion subscale of the UBOS and (history of) psychiatric disorders were assessed. Individuals with an average score on the exhaustion subscale of the UBOS equal to or higher than the cutoff point of 2.20 [32] were allocated to the non-clinical burnout group and those with scores below the cutoff point to the control group. Individuals with a current psychiatric disorder or with a past history of burnout were excluded.

Materials

Utrechtse Burnout Scale

Burnout symptoms were assessed with the UBOS [32], which is the Dutch adaptation of the Maslach Burnout Inventory (MBI; [33]). The version for general professions (UBOS-A; [32]) was used, which contains 15 questions that can be answered on a 7-point Likert scale (0 = “never”, 6 = “every day”). The questionnaire consists of an exhaustion, a cynicism and a professional efficacy subscale. Cronbach's alphas of the subscales were, respectively, .95, .87 and .78.

Symptom Checklist-90-Revised

General physical and psychological complaints were assessed with the Dutch adaptation [34] of the Symptom Checklist-90-Revised (SCL-90-R; [35]). The questionnaire contains 90 items divided into nine subscales: eight measuring primary symptom dimensions, and one measuring more general symptoms. Each item can be answered on a 5-point Likert scale (1 = “not at all”, 5 = “extremely”). The sum of all items results in a psychoneuroticism score, which is the equivalent of the Global Severity Index in the English version. Cronbach's alpha of this questionnaire was .98.

Cortisol

Salivary cortisol was collected on two consecutive non-workdays. On both of these days, participants individually collected six saliva samples: at awakening, 30 min after awakening, 60 min after awakening, at 12:00 h, 17:00 h and 22:00 h. On average, the patients in the burnout

Table 1
Demographical characteristics

	Clinical burnout		Non-clinical burnout		Control		
	M	*SD*	*M*	*SD*	*M*	*SD*	*p*
Age	42.41	10.68	36.90	12.64	38.93	11.23	.17[1]
Work hours per week[a]*	36.02	6.85	33.12	6.45	31.07	8.54	.03[1]
	n	%	*n*	%	*n*	%	*p*
Sex							.57[2]
Men	17	53.13	12	41.38	16	53.33	
Women	15	46.88	17	58.62	14	46.67	
Level of education[b]							.88[2]
1	0	.00	0	.00	0	.00	
2	3	9.38	2	6.90	2	6.67	
3	11	34.38	11	37.93	8	26.67	
4	18	56.25	16	55.17	20	66.67	
Irregular working hours							.69[2]
Yes	10	31.25	12	41.38	10	33.33	
No	22	68.75	17	58.62	20	66.77	
Tobacco use							.61[2]
Yes	7	21.88	4	13.79	7	23.33	
No	25	78.13	25	86.21	23	76.67	
Medication[c]							
Psychotropic drugs	3	9.38	1	3.45	0	.00	.26[2]
Somatic drugs	5	15.63	3	10.35	2	6.67	.54[2]
Corticosteroids and antihistamines	2	6.25	5	17.24	2	6.67	.29[2]
Contraceptives	6	18.75	6	20.69	4	13.33	.74[2]
Herbal drugs	0	.00	1	3.45	1	3.33	.54[2]
None	19	59.38	15	51.72	23	76.67	.13[2]

[a] Participants' contractual working hours per week.
[b] Level of education was measured in terms of highest level of education completed, ranging from 1 to 4, primary school to university degree, respectively.
[c] Since some participants used more than one type of medication, the sum of the *n* and the % of the different types of medication is larger than the total *n* of a particular group and 100%, respectively.
[1] Based on ANOVA.
[2] Based on Pearson's chi-square test.
* The clinical burnout group differed significantly from the control group ($p = .01$).

group collected the saliva samples within one month after they were diagnosed with burnout (range 7–65 days).

Different, well-validated and commonly used measures of both the CAR and the cortisol during the day were used as indices of participants' cortisol level (e.g., [36]). The area under the curve with respect to ground (AUC_G) was computed for the CAR (as a measure of total cortisol secretion after awakening; CAR AUC_G) as well as for the day (as a measure of total cortisol secretion during the day; day AUC_G). In addition, the AUC_G of the CAR was calculated in two ways: based on awakening until 30 min after awakening (CAR AUC_G 30), and based on awakening until 60 min after awakening (CAR AUC_G 60). For the computation of the AUC_G measures, the time-dependent formula was used as described in detail by Pruessner, Kirschbaum [37]. Furthermore, the slope of the CAR (i.e., the increase of cortisol after awakening; CAR slope) and the slope of the day (decline of cortisol during the day; day slope) were computed. The CAR slope was calculated as the difference in cortisol between the second sample of the day (30 min after awakening) and the first sample of the day (at awakening). The day slope was computed as the difference between the last sample of the day (at 22:00 h) and the first sample of the day (at awakening). Prior to the calculation of the different cortisol outcome measures, all samples were individually checked for abnormal values. This resulted in the exclusion of one extremely high evening value (36.19 nmol/l; see e.g., [38]) from a participant in the non-clinical burnout group. Furthermore, only the cortisol values of the samples that were collected at 0–5 min after awakening (first sample), at 25–35 min after the first sample (second sample), at 25–35 min after the second sample (third sample), within 31 min prior to or after 12:00 h (fourth sample), within 61 min prior to or after 17:00 h (fifth sample) and within 91 min prior to or after 22:00 h (sixth sample), were used for the calculation of the different cortisol outcome variables. Of the total of 1092 cortisol samples, 165 samples (15.11 %) were excluded from the analyses: eight were missing (.73 %), one was an invalid high value (see above; .09 %) and 156 were collected outside the set time-limits (14.29 %). For each of the six cortisol samples, the correlation between the two days was significant and ranged between .23 and .67 (as measured with Pearson's *r*). The cortisol outcome measures were calculated separately for each of the two days first. If values of both days were available the scores were averaged. Otherwise, the value of a single day was used.

Procedure

After participants were recruited, the dates were set for the two consecutive non-workdays saliva collection, and an appointment was made for filling out the questionnaires. Prior to the saliva collection, participants received detailed instructions on how to collect the samples. Specifically, they were instructed to clean their lips (if necessary) and to not brush their teeth before sampling, and to refrain from eating or drinking (except water) within 45 min before collecting a sample. Furthermore, information about variables that are generally assumed to affect cortisol levels, such as time of awakening, exact time of sampling, intake of medication, caffeine and alcohol consumption, smoking and physical activity [36], was registered in the form of a diary. The participants collected the saliva samples in 2 ml Eppendorf tubes and kept the samples in a refrigerator or freezer until they returned them. Returned samples were stored in a freezer at –20 °C until analyzed. The saliva samples were analyzed in duplo at the Biochemical Laboratory of the University of Trier in Germany by a time-resolved immunoassay with fluorescence detection (DELFIA method), as described in detail by Dressendörfer, Kirschbaum [39]. All participants gave informed consent, and the study was approved by the Ethical Committee of the Faculty of Social Sciences at the Radboud University Nijmegen in the Netherlands.

Table 2
Group means and standard deviations, and the results of the statistical analysis of the UBOS and SCL-90-R

	Clinical burnout		Non-clinical burnout		Control						
	M	*SD*	*M*	*SD*	*M*	*SD*	Effect	df_2	*F*	*p*	η^2
UBOS											
Exhaustion*	4.64	.96	2.72	.85	1.07	.51	Group	88	155.91	.00	.78
Cynicism*	3.41	1.18	1.72	1.07	.79	.62	Group	88	56.24	.00	.56
Personal efficacy**	3.56	.99	4.20	.70	4.59	.64	Group	88	13.46	.00	.23
SCL-90-R*	185.47	46.51	132.36	33.90	106.87	14.30	Group	88	41.91	.00	.49

* All groups differed significantly from each other.
** The clinical burnout group differed significantly from both the control group and the non-clinical burnout group (the non-clinical burnout group differed marginally significant from the control group ($p = .061$)).

Statistical analyses

Both the questionnaires and cortisol data were analyzed with a one-way univariate ANOVA, with group (clinical burnout vs. non-clinical burnout vs. control) as a between-subject factor. For all outcome measures, within-group outliers were replaced with the group mean + or − three standard deviations. After replacing the outliers (6 in total), inspection of the data revealed that the scores of the outcome measures were approximately normally distributed. All tests of statistical significance were based on two-tailed tests using an alpha level of .05. When a statistically significant overall group effect was obtained, pair-wise group comparisons were made using Fisher's protected least significant different (FPLSD) post hoc tests. Partial eta-squared (η^2) was calculated as an effect size estimate. All statistical analyses were performed with SPSS for Microsoft Windows, version 20.0 (SPSS, Inc., Chicago, IL).

Results

Demographical characteristics

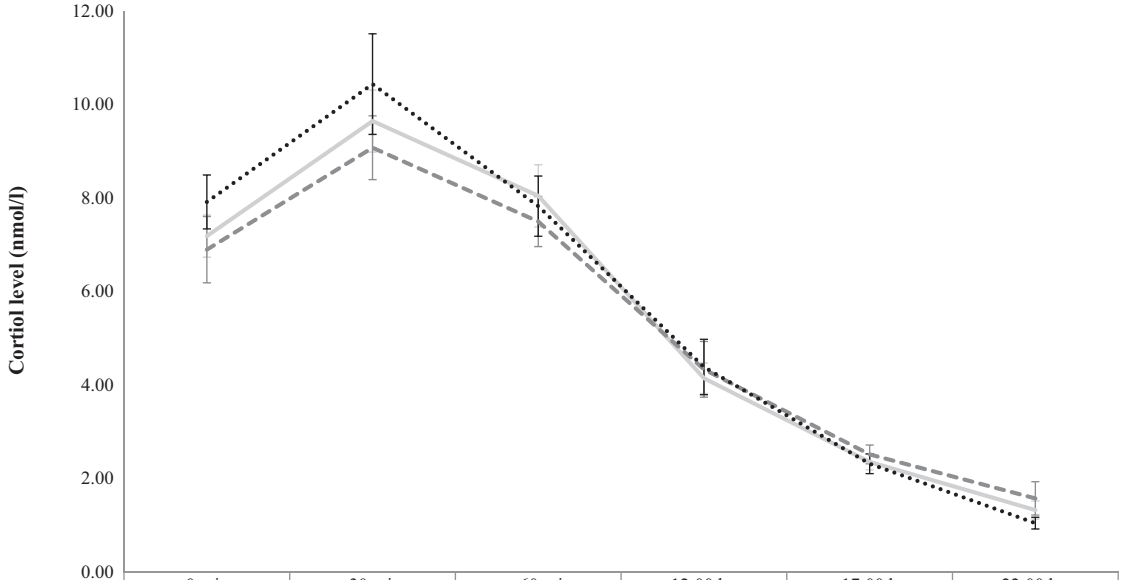
The demographical characteristics of the three groups are displayed in Table 1. The results of the analyses of the demographical characteristics revealed that the groups did not significantly differ on age, sex, level of education, working irregular working hours, tobacco use, and intake of medication.

UBOS and SCL-90-R

For all subscales, the analysis of the UBOS scores yielded a significant overall main effect of group (see Table 2 for the statistics). Post hoc tests revealed that, except for a marginally significant difference ($p = .061$) between the non-clinical burnout group and the control group on the professional efficacy scale, the three groups differed significantly from each other on all subscales (p's < .01). On all subscales, the scores of the non-clinical burnout group were in between those of the clinical burnout group and those of the control group. The results of the analyses of the SCL-90-R scores showed a significant overall main effect of group. Post hoc tests indicated that the individuals with clinical burnout reported significantly more physical and psychological complaints than both the individuals in the non-clinical burnout group and the individuals in the control group did (p's < .001). Furthermore, the non-clinical burnout group scored significantly higher on physical and psychological complaints than the control group did ($p = .006$).

Cortisol

Fig. 1 shows, for each of the groups, the raw means and standard errors of the cortisol levels on the different time points at the two consecutive non-work days. Analysis of the CAR AUC_G 30 revealed a significant overall main effect for group (see Table 3 for the statistics). Post hoc tests indicated that 30 min after awakening, the CAR of both the clinical burnout group ($p = .030$) and the non-clinical burnout group ($p = .020$) was significantly smaller compared with the CAR of the control group. ANOVA of the day slope revealed a marginally significant overall main effect for Group. A post hoc test showed that individuals with a non-clinical burnout had a significantly smaller decline of cortisol during the day than the healthy controls ($p = .027$). No significant differences were found between the groups for the other cortisol outcome measures.



	0 min	30 min	60 min	12:00 hrs	17:00 hrs	22:00 hrs
Clinical burnout	7.19	9.65	8.05	4.15	2.36	1.33
Non-clinical burnout	6.90	9.08	7.50	4.34	2.52	1.58
Control	7.92	10.44	7.83	4.39	2.32	1.05

Fig. 1. Raw group means and standard errors of the mean cortisol level on the two consecutive non-work days for each sampling time. On average, the participants woke up at 08:18 h (there were no significant differences between the three groups).

Table 3
Group means and standard deviations, and the results of the statistical analysis of the cortisol levels

	Clinical burnout		Non-clinical burnout		Control						
	M	*SD*	*M*	*SD*	*M*	*SD*	Effect	df_2	*F*	*p*	η^2
CAR AUC_G 30*	244.23	64.68	237.01	96.44	299.29	108.01	Group	73	3.49	.04	.09
CAR AUC_G 60	508.81	143.43	475.98	194.84	578.87	209.85	Group	65	1.77	.18	.05
CAR slope	2.26	3.62	1.76	3.86	3.71	7.70	Group	73	.87	.43	.02
Day AUC_G	3137.91	914.45	2812.80	667.22	2978.12	1216.76	Group	50	.55	.58	.02
Day slope	-6.05	2.73	-5.36	3.56	-7.35	2.65	Group	70	2.65	.08	.07

Note. All cortisol values are in nmol/l.
* Both the clinical burnout group and the non-clinical burnout group differed significantly from the control group, with respectively $p = .030$ and $p = .020$).

Confounding variable analysis

All cortisol outcome measures were re-analyzed with analyses of covariance to control for the following potential confounding variables: use of medication (for each type of medication separately), smoking, alcohol and caffeine intake, physical activity (all coded as dichotomous variables: no/yes), time of awakening, sleep duration, sleep quality (1–10), sex and age (all variables were self-reported). Controlling for these variables did not substantially change the results of the primary analyses and led to identical conclusions (more detailed information can be obtained from the first author upon request).

Discussion

Although cortisol levels in burnout have been examined in previous studies, the results of these studies are inconsistent. By using a design overcoming relevant limitations of previous research, the aim of the present study was to get more insight in the biological underpinnings of burnout, through the investigation of the relationship between burnout and cortisol.

With regard to the results of the self-reports, we found that, as expected, patients in the clinical burnout group experienced significantly more burnout symptoms (UBOS) compared to individuals in the non-clinical burnout group, who in turn reported significantly more burnout symptoms compared with the healthy controls. This same pattern of results was obtained for self-reported physical and psychological complaints (SCL-90-R).

Regarding the observed cortisol levels, we found that 30 min after awakening, and compared with the healthy control group, both the clinical and non-clinical burnout group displayed a significantly lower CAR (CAR AUC_G 30). These findings are in line with those of previous studies of Mommersteeg et al. [3] and Sonnenschein et al. [9], and those of Marchand et al. [10] and Moya-Albiol et al. [40], in which clinical burnout and non-clinical burnout, respectively, were also found to be related with a smaller CAR 30 min after awakening. Although there are no other studies that specifically assessed the CAR 30 min after awakening in a non-clinical burnout sample, there is however also previous research showing clinical burnout to be unrelated to any cortisol deviation [15] as well as related to higher cortisol [5] with respect to this measure. Besides the effects of the CAR, we found some evidence for the slope of the day (day slope) to be significantly smaller in the non-clinical (but not in the clinical) burnout group compared with the healthy control group (with the omnibus test being marginally significant), indicating that this former group had a flattened cortisol pattern during the day. There are no comparable previous studies in which this measure was assessed.

As regards our results of the CAR 60 min after awakening (CAR AUC_G 60), we found no differences between the three groups. Nor did we identify any differences in the slope of the CAR (CAR slope) and the total secretion of cortisol during the day (day AUG_G). These findings both fit the results of previous studies (e.g., [12,15,17,25,41]) and are in contrast with earlier research (e.g., [5,20]).

The results of the present study remained unchanged after statistically correcting for potential confounders, such as use of medication, health behaviors and sleep indicators. For example, from the literature (e.g., [42]), it is known that individuals with burnout tend to report higher levels of sleep complaints. Although also in this study burnout individuals reported a worse sleep quality (1–10 report mark; clinical burnout: 6.47; non-clinical burnout: 7.38; healthy controls: 7.93), this difference in sleep quality did not play a role in explaining the deviation in morning cortisol levels (i.e., CAR AUC_G 30).

As already mentioned briefly, a possible explanation for why in some previous studies (both studies with a non-clinical and clinical burnout sample), null results or increased cortisol levels in burnout were found might be due to comorbid depression and/or anxiety, disorders proven to be related to elevated cortisol levels (e.g., [22,23]). However, it should be noted that comorbidity not always explains variance in the observed cortisol levels in burnout (e.g., [43]). Another explanation for the null results found in some earlier clinical burnout research may well be that patients in previous studies already had been in therapy for a longer period, or that the time interval between diagnosis and cortisol sampling was larger than was the case in the present study (for both possibilities, often no information is provided in previous research to exclude these possibilities). Mommersteeg et al. [3], for example, found that cortisol levels were lower in patients with burnout than in healthy controls directly after diagnosis, but these differences disappeared during a period of psychotherapy. In other words, during treatment (or just in the course of), it might be that the HPA axis recovers from an initial breakdown and that cortisol levels return back to normal. A similar explanation could also account for null results in some previous non-clinical burnout studies. That is, if in these studies the period of time between the assessment of burnout symptoms and the collection of cortisol was relatively long (again, information which is often not provided) maturation effects may occur, which could be responsible for the observed null effects.

The present study showed clinical and non-clinical burnout individuals to have a similar attenuated cortisol pattern shortly after awakening. This finding provides evidence for lowered cortisol in both of these 'different types' of burnout. It is an interesting, but at present hard to answer, question as to what is the clinical relevance of this lower cortisol pattern shortly after waking up. Hopefully, future high-quality studies will make it clear whether these cortisol results can be replicated and paint a more detailed picture as to what these mean for future health and well-being. Furthermore, it is important to emphasize that, although we treated clinical and non-clinical burnout as two different types of burnout, there may be some overlap between these two groups, which is also reflected in the more or less similar cortisol profile in both of these burnout groups.

The fact that we found some evidence for the slope of the day to be smaller in the non-clinical burnout group only was based on not only a low cortisol level in the morning directly after awakening but also on a relatively high cortisol level in the evening in this group. Although, at first sight, this high (but insignificant) cortisol level in the evening may indicate evidence for a hyperactive HPA axis, the combination with low cortisol in the morning makes the overall slope flatter. Such a flattened slope is considered to reflect a failure to activate the HPA axis after awakening and to a failure to deactivate it in the evening, indicating a hypoactive HPA axis (e.g., [7,44,45]). In addition, a high cortisol level in the evening is regarded to reflect poor recovery from stress, which in turn, may be regarded as a major risk factor for developing a more severe (clinical) burnout.

Strengths and limitations

An asset of the present research is that we studied cortisol levels in both a clinical and non-clinical burnout sample, arguably reflecting two different types of burnout. Furthermore, the clinical burnout patients' high-quality burnout diagnosis as assessed by a team of professional clinical psychologists using a semi-structured interview, and our clearly described selection criteria, can be considered as a strong feature. In addition to our clinical burnout diagnosis, we only included patients without comorbidity, such as, for example, mood and anxiety disorders, which enabled us a relatively pure examination of burnout in relation to cortisol. Our extensive cortisol collection and the fact that we collected cortisol on non-workdays, instead of during workdays (for reasons described earlier), is another strength of the study. Moreover, we only included cortisol samples that were collected within strict time-limits, which contributes to the validity of the cortisol results.

Despite these strengths, the study has limitations as well. For example, although we included relatively large groups, we lost power due to excluding cortisol samples which were not collected within our strict time limits, or for which no sampling time was reported. Nevertheless, we were still able to find differences between the groups, although perhaps we would have found even more effects if more participants had sampled within our time-limits and if more of them had reported the time of sampling. In this framework, in future studies, it might be worthwhile to enhance compliance by, for example, using electronic devices that remind participants to sample at the correct times and/or using motion-sensors to verify participants' reported sampling times whenever participants forget to report the time they sampled. Furthermore, the present data are limited by the cross-sectional design of the study, which makes it hard to draw causal inferences. Longitudinal studies might address this issue of causality, and could furthermore provide information about whether these effects are temporary (e.g., can be reversed through therapy) or not.

Conclusion

Both burnout groups displayed a similar lower CAR 30 min after awakening compared with the healthy control group. Furthermore, we found some evidence indicating that the non-clinical burnout group had a flattened cortisol pattern during the day. These results suggest that both clinical and non-clinical burnout are related to lowered cortisol and reflect a hypoactive HPA axis in both of these different types of burnout.

Competing interest statement

The authors have no competing interests to report.

Acknowledgements

We are thankful for the support of Moniek Veltman in setting up the study. Furthermore, we are indebted to Carla Ziebertz, Lennert Paasman, Hanna Lanz, Lauke Bos, Sanneke Peters and the personnel of HSK Group for assisting with the data collection. Last, we would like to express our gratitude to all the participants who took part in this study, in particular, to those of the clinical burnout group.

References

[1] Maslach C, Schaufeli WB, Leiter MP. Job burnout. Annu Rev Psychol 2001;52:397–422.
[2] Pruessner JC, Hellhammer DH, Kirschbaum C. Burnout, perceived stress, and cortisol responses to awakening. Psychosom Med 1999;61:197–204.
[3] Mommersteeg PMC, Keijsers GPJ, Heijnen CJ, Verbraak MJPM, van Doornen LJP. Cortisol deviations in people with burnout before and after psychotherapy: a pilot study. Health Psychol 2006;25:243–8.
[4] Melamed S, Ugarten U, Shirom A, Kahana L, Lerman Y, Froom P. Chronic burnout, somatic arousal and elevated salivary cortisol levels. J Psychosom Res 1999;46:591–8.
[5] De Vente W, Olff M, Van Amsterdam JGC, Kamphuis JH, Emmelkamp PMG. Physiological differences between burnout patients and healthy controls: blood pressure, heart rate, and cortisol responses. Occup Environ Med 2003;60:54–61.
[6] McEwen BS. Protective and damaging effects of stress mediators. New Engl J Med 1998;338:171–9.
[7] Fries E, Hesse J, Hellhammer J, Hellhammer DH. A new view on hypocortisolism. Psychoneuroendocrinology 2005;30:1010–6.
[8] Gunnar MR, Vazquez DM. Low cortisol and a flattening of expected daytime rhythm: potential indices of risk in human development. Dev Psychopathol 2001;13:515–38.
[9] Sonnenschein M, Mommersteeg PMC, Houtveen JH, Sorbi MJ, Schaufeli WB, Van Doornen LJP. Exhaustion and endocrine functioning in clinical burnout: an in-depth study using the experience sampling method. Biol Psychol 2007;75:176–84.
[10] Marchand A, Juster RP, Durand P, Lupien SJ. Burnout symptom sub-types and cortisol profiles: what's burning most? Psychoneuroendocrinology 2014;40:27–36.
[11] Grossi G, Perski A, Evengård B, Blomkvist V, Orth-Gomér K. Physiological correlates of burnout among women. J Psychosom Res 2003;55:309–16.
[12] Mommersteeg PMC, Heijnen CJ, Verbraak MJPM, Van Doornen LJP. Clinical burnout is not reflected in the cortisol awakening response, the day-curve or the response to a low-dose dexamethasone suppression test. Psychoneuroendocrinology 2006;31:216–25.
[13] Danhof-Pont MB, Van Veen T, Zitman FG. Biomarkers in burnout: a systematic review. J Psychosom Res 2011;70:505–24.
[14] Österberg K, Karlson B, Hansen ÅM. Cognitive performance in patients with burnout, in relation to diurnal salivary cortisol. Stress 2009;12:70–81.
[15] Mommersteeg PMC, Heijnen CJ, Kavelaars A, van Doornen LJP. Immune and endocrine function in burnout syndrome. Psychosom Med 2006;68:879–86.
[16] Moya-Albiol L, Serrano MA, Salvador A. Burnout as an important factor in the psychophysiological responses to a work day in teachers. Stress Health 2010;26:382–93.
[17] Bellingrath S, Weigl T, Kudielka BM. Cortisol dysregulation in school teachers in relation to burnout, vital exhaustion, and effort-reward-imbalance. Biol Psychol 2008;78:104–13.
[18] Sandstrom A, Peterson J, Sandstrom E, Lundberg M, Nystrom I-LR, Nyberg L, et al. Cognitive deficits in relation to personality type and hypothalamic–pituitary–adrenal (HPA) axis dysfunction in women with stress-related exhaustion. Scand J Psychol 2011;52:71–82.
[19] Moch SL, Panz VR, Joffe BI, Havlik I, Moch JD. Longitudinal changes in pituitary-adrenal hormones in South African women with burnout. Endocrine 2003;21:267–72.
[20] Grossi G, Perski A, Ekstedt M, Johansson T, Lindström M, Holm K. The morning salivary cortisol response in burnout. J Psychosom Res 2005;59:103–11.
[21] Sertoz OO, Binbay IT, Koylu E, Noyan A, Yildirim E, Mete HE. The role of BDNF and HPA axis in the neurobiology of burnout syndrome. Prog Neuropsychopharmacol 2008;32:1459–65.
[22] Abelson JL, Khan S, Liberzon I, Young EA. HPA axis activity in patients with panic disorder: review and synthesis of four studies. Depress Anxiety 2007;24:66–76.
[23] Herbert J. Cortisol and depression: three questions for psychiatry. Psychol Med 2013;43:449–69.
[24] Kunz-Ebrecht SR, Kirschbaum C, Marmot M, Steptoe A. Differences in cortisol awakening response on work days and weekends in women and men from the Whitehall II cohort. Psychoneuroendocrinology 2004;29:516–28.
[25] Langelaan S, Bakker AB, Schaufeli WB, Van Rhenen W, Van Doornen LJ. Do burned-out and work-engaged employees differ in the functioning of the hypothalamic–pituitary–adrenal axis? Scand J Work Environ Health 2006;32:339–48.
[26] Schlotz W, Hellhammer J, Schulz P, Stone AA. Perceived work overload and chronic worrying predict weekend-weekday differences in the cortisol awakening response. Psychosom Med 2004;66:207–14.
[27] Oosterholt BG, Maes JH, Van der Linden D, Verbraak MJPM, Kompier MAJ. Cognitive performance in both clinical and non-clinical burnout. Stress 2014;17:400–9.
[28] Overbeek T, Schruers K, Griez E. MINI. Mini International Neuropsychiatric Interview. Dutch version 5.0.0. DSM-IV. Maastricht, the Netherlands: University of Maastricht; 1999.
[29] Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, et al. The Mini-International Neuropsychiatric Interview (MINI): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J Clin Psychiatry 1998;59:22–33.
[30] Schotte C, De Doncker D. ADP-IV Vragenlijst. Edegem, Belgium: Universitair Ziekenhuis Antwerpen; 1994.
[31] American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed., text revision ed. Washington, DC: Author; 2000.
[32] Schaufeli WB, Van Dierendonck D. UBOS. Utrechtse Burnout Schaal. Handleiding Lisse, the Netherlands: Swets & Zeitlinger; 2000.
[33] Maslach C, Jackson SE, Leiter MP. Maslach Burnout Inventory. 3rd ed. Palo Alto, CA: Consulting Psychologists Press; 1996.
[34] Arrindell WA, Ettema JHM. SCL-90. Handleiding bij een multidimensionele psychopathologie-indicator. Lisse, the Netherlands: Swets & Zeitlinger; 2003.
[35] Derogatis LR. SCL-90-R. Administration, scoring and procedures manual-I for the R(evised) version. Baltimore: Johns Hopkins University School of Medicine, Clinical Psychometrics Research Unit; 1977.
[36] Nicolson NA. Measurement of cortisol. In: Luecken LJ, Gallo LC, editors. Handbook of physiological research methods in health psychology. Los Angeles, CA: Sage; 2008.
[37] Pruessner JC, Kirschbaum C, Meinlschmid G, Hellhammer DH. Two formulas for computation of the area under the curve represent measures of total hormone concentration versus time-dependent change. Psychoneuroendocrinology 2003;28:916–31.

[38] Nicolson N, Storms C, Ponds R, Sulon J. Salivary cortisol levels and stress reactivity in human aging. J Gerontol Med Sci 1997;52:68–75.
[39] Dressendörfer RA, Kirschbaum C, Rohde W, Stahl F, Strasburger CJ. Synthesis of a cortisol-biotin conjugate and evaluation as a tracer in an immunoassay for salivary cortisol measurement. J Steroid Biochem Mol Biol 1992;43:683–92.
[40] Moya-Albiol L, Serrano MA, Salvador A. Job satisfaction and cortisol awakening response in teachers scoring high and low on burnout. Span J Psychol 2010;13:629–36.
[41] Ekstedt M, Akerstedt T, Soderstrom M. Microarousals during sleep are associated with increased levels of lipids, cortisol, and blood pressure. Psychosom Med 2004; 66:925–31.
[42] Armon G, Shirom A, Shapira I, Melamed S. On the nature of burnout-insomnia relationships: a prospective study of employed adults. J Psychosom Res 2008;65:5–12.
[43] Sjörs A, Ljung T, Jonsdottir IH. Long-term follow-up of cortisol awakening response in patients treated for stress-related exhaustion. Br Med J Open 2012;2.
[44] Heim C, Ehlert U, Hellhammer DH. The potential role of hypocortisolism in the pathophysiology of stress-related bodily disorders. Psychoneuroendocrinology 2000;25: 1–35.
[45] Dmitrieva NO, Almeida DM, Dmitrieva J, Loken E, Pieper CF. A day-centered approach to modeling cortisol: diurnal cortisol profiles and their associations among U.S. adults. Psychoneuroendocrinology 2013;38:2354–65.