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Exhaustion and endocrine functioning in clinical burnout: An in-depth study using the experience sampling method

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Abstract

The current study investigates the relationship between HPA-axis functioning and burnout symptoms by employing an electronic symptom diary. This diary method circumvents the retrospection bias induced by symptom questionnaires and allows to study relationships within-in addition to between-subjects.

Forty two clinically burned-out participants completed the exhaustion subscale of the Maslach burnout inventory and kept an electronic diary for 2 weeks to assess momentary exhaustion and daily recovery through sleep. On 3 consecutive weekdays within the diary period, saliva was sampled to determine the cortisol awakening response (CAR), levels of dehydroepiandrosterone-sulphate (DHEAS) on the first 2 weekdays, and to conduct the dexamethasone suppression test (DST) on the third weekday.

We found significant relationships between endocrine values and general momentary symptom severity as assessed with the diary, but not with the retrospective questionnaire-assessed burnout symptoms. Simultaneous assessments of endocrine values and burnout symptoms assessed with the diary after awakening rendered significant associations between persons, and a trend within persons. More severe burnout symptoms were consistently associated with a lower level and smaller increase of CAR, higher DHEAS levels, smaller cortisol/DHEAS ratios and a stronger suppression after DST.

Burnout symptoms were significantly related to endocrine functioning in clinical burnout under the best possible conditions of symptom measurement. This adds support to the view that severity of burnout symptoms is associated with HPA-axis functioning.
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Keywords: Burnout; Cortisol; Exhaustion; Experience sampling method; Electronic diary; DHEAS

1. Introduction

Burnout is a syndrome of severe energy depletion, dysfunctional attitudes towards the job and a lack of professional efficacy due to chronic stress at work (Maslach et al., 2001). The severity of exhaustion, its resistance to change and its insusceptibility to rest suggest a physiological deregulation in burnout (Melamed et al., 2006). Since the Hypothalamus Pituitary Adrenal axis (HPA-axis) is the central stress-physiological system for the long term adaptation of an organism to stress (Cook, 2002; Sapolsky et al., 2000), and burnout is supposed to be the result of chronic work stress, most studies on the physiology of burnout have focused on this physiological system (Raison and Miller, 2003). Heim et al. suggested a state of hypocortisolism to be associated with stress-related bodily disorders. The fatigue symptoms of burnout (i.e. exhaustion) resemble the severe fatigue in chronic fatigue syndrome (CFS). CFS is, if anything, characterized by a slight hypofunctioning of the HPA-axis, i.e. lower cortisol levels and an increased feedback sensitivity (Cleare, 2003; Heim et al., 2000; Parker et al., 2001). Although the HPA-axis has been associated with stress (Sapolsky et al., 2000), depression (Holsboer, 2001), and fatigue (Cleare, 2003), between group studies on burnout have produced inconsistent results. In relatively healthy employees with mild burnout symptoms who are still working (mild burnout), both elevated cortisol levels during the day (Melamed et al., 1999) and lower

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levels after awakening (Pruessner et al., 1999) have been found as compared to healthy controls. In more strongly affected individuals on sickness absence or in clinically diagnosed burned-out cases both lower (Mommersteeg et al., 2006a) and higher (De Vente et al., 2003; Grossi et al., 2005) salivary cortisol levels after awakening have been found as compared to healthy controls, but an absence of cortisol deviations has also been reported (Mommersteeg et al., 2006b).

A less common way to examine the association between burnout and HPA-axis functioning is looking at relationships between symptom severity and endocrine measures within a group of affected persons. The few studies performed, however did not find any significant relationships between severity of burnout symptoms and cortisol levels. A study among 48 employees rendered non significant correlations between evening salivary cortisol and scores on a burnout questionnaire (Galantino et al., 2005). In clinical burnout samples no relationships were found between a burnout questionnaire and the cortisol awakening response, the day-curve and dexamethasone-suppressed cortisol levels (Mommersteeg et al., 2006a,b).

The common way to measure symptoms in burnout research, as in all aforementioned studies, is retrospectively by questionnaires. Participants are asked to remember and integrate recent experiences of symptoms and make the best possible estimate of the general severity of their symptoms. Unfortunately, questionnaires produce retrospection bias, which restricts the accuracy of the symptom assessments (Bolger et al., 2003; Fahrenberg et al., 2001; Houtveen and Oei, in press; Hufford et al., 2001; Robinson and Clore, 2002). Rating the past rather than the present induces, for example, the tendency to report more negative emotions and to stay nearer to the scale midpoint (Fahrenberg et al., 2001). Moreover, retrospective assessments are strongly influenced by peak experiences, current state and personal semantic memories (Fahrenberg et al., 2001; Hufford et al., 2001; Robinson and Clore, 2002). A more accurate way to assess symptom severity is to measure symptoms right at the moment they are experienced. When aggregating these momentary assessments over several moments and days, a more reliable estimate of general symptom severity is acquired in comparison to retrospective questionnaires over the same time period. For this purpose, electronic diary methods like the experience sampling method (ESM; Csikszentmihalyi and Larson, 1987) have been developed (Bolger et al., 2003). The present study seeks to improve the methodology to investigate relationships between HPA-axis function and symptoms in clinical burnout by employing ESM.

The aggregated value of ESM symptom assessments offers an estimate of the general severity of complaints during, for example, 2 weeks (i.e. like retrospective questionnaires do). But ESM allows us to relate cortisol to symptom levels right at the moment of cortisol sampling as well, in our case: the moment after awakening. Cortisol levels show intra-individual variations between days, and therefore it is common practice to sample cortisol across several days to increase the reliability of between-subject comparisons (Pruessner et al., 1997).

However, within-person variations of cortisol levels across days may reflect meaningful situational effects, and aggregating momentary assessments means ignoring these effects and loosing important information (Hruschka et al., 2005). Studies using ambulatory measurement of both physiological and psychological measures have revealed that there may be a relationship between fluctuations of variables *within* an individual. For example, there is ample evidence showing that state negative affect is positively associated within individuals with cortisol levels sampled at the same moment (Hanson et al., 2000; Van Eck and Nicolson, 1994; Van Eck et al., 1996a,b; Smyth et al., 1998; Adam, 2006). In other words, cortisol levels are higher when an individual experiences more negative affect, and lower when the same individual experiences less negative affect in proportion to his own mean levels of cortisol and negative affect. Momentary within-subject relationships may be found irrespective of between-subject relationships. Therefore negative results of between-subject relationships of cortisol and exhaustion, even at the same moment, may wrongfully lead to the conclusion that no relationship exists between cortisol and symptoms. Since exhaustion and poor recovery through sleep fluctuate within individuals (Sonnenschein et al., in press-a,b), and cortisol shows intra-individual variability, it may be that these fluctuations cohere. As far as we know, the current study is the first to differentiate between- and within-person relationships of same moment assessments of exhaustion and cortisol in clinical burnout.

Burnout has been defined as a three-dimensional syndrome, that becomes apparent at work through exhaustion, cynicism towards work and reduced professional efficacy (Maslach et al., 2001). Since our sample consisted of participants on sick leave due to burnout symptoms, we focused our study on exhaustion, which persists as a daily experience once on sick leave (for example, see Mommersteeg et al., 2006a). Exhaustion has long been recognized as burnouts core symptom, but we are aware that burnout can not be reduced to mere exhaustion (Maslach et al., 2001). Closely related to exhaustion experience itself, is our earlier observation that daily fatigue in burned-out individuals does not respond to sleep, as in healthy individuals (Sonnenschein et al., in press-b). Therefore, we will relate cortisol functioning to poor recovery through sleep in addition to straightforward symptom reports of exhaustion.

HPA-axis functioning can be investigated through several parameters. In the current study we therefore considered the following three parameters. First, the cortisol awakening response (CAR), the immediate rise of cortisol levels within 30 min after awakening (both level and increase). Second, dehydroepiandrosterone-sulphate (DHEAS), an adrenal hormone released in response to ACTH. DHEAS levels are hypothesized to deviate in stress-related syndromes (Kroboth et al., 1999; Wolf and Kirschbaum, 1999). DHEAS differs from cortisol in that it shows actions opposite to the regulatory effects of cortisol (Chen and Parker, 2004). Therefore the cortisol/DHEAS-ratio was assessed as well. And last, we considered the feedback sensitivity of the HPA-axis by conducting the dexamethasone suppression test (DST; De

Kloet et al., 1998). The synthetic glucocorticoid dexamethasone that participants take, mimics the negative feedback effect of cortisol. After a low dose of dexamethasone (0.5 mg), the cortisol level is reduced, but not completely, allowing the detection of subtle individual differences in feedback function.

Summarizing, we investigate the association between energy depletion in clinical burnout and indicators of HPA-axis functioning in a reliable and in-depth way through ESM symptom assessments. Preparatory to the research issue 1 the difference between ESM and retrospective questionnaire assessment of burnout symptoms will be demonstrated by examining the relations between both methods (*preparatory issue a*). Subsequently we will examine whether the general severity of exhaustion and recovery through sleep are associated with the CAR, DHEAS and DST in clinical burnout by using a retrospective questionnaire (*research issue 1a*) and by using 2-week aggregated diary assessments (*research issue 1b*). Preparatory to research issue 2 we will demonstrate that burnout symptoms and cortisol levels fluctuate within clinically burned-out individuals (*preparatory issue b*). Lastly, we examine whether same moment assessment of exhaustion and recovery through sleep (i.e. after awakening) are associated with morning cortisol levels between persons (*research issue 2a*) and within persons (*research issue 2b*).

2. Methods

2.1. Participants

Burned-out employees on sick leave were recruited from new enrollments of Dutch centers of expertise in burnout treatment and from the Internet. Two hundred and ninety-three individuals responded to the call, of whom 209 (71%) were actually willing to participate and returned the screening checklist. Individuals were eligible for participation when they met the following inclusion criteria: (1) severe burnout complaints according to validated cut-off points from the Dutch Maslach burnout inventory—general survey (MBI-GS; exhaustion ≥ 2.20, and either cynicism ≥ 2.00 or personal accomplishment ≤ 3.67 (Schaufeli and Van Dierendonck, 2000) and the Checklist Individual Strength (CIS; total score ≥ 76; Bültmann et al., 2000), (2) extended absence and enrollment in professional care due to burnout symptoms, and (3) fulfilling the criteria for ICD-10 work-related neurasthenia (WHO, 1993), which has been proposed as the psychiatric equivalent of clinical burnout (Schaufeli et al., 2001). We allowed secondary psychological disorders to co occur with burnout. A semi-structured clinical interview (Hoogduin et al., 1999), conducted by a senior psychologist or by junior psychologists under supervision, and the symptom checklist-90-R (SCL-90-R, general severity Index <214; Arrindell and Ettema, 2002) were used to assess work-related neurasthenia and secondary co-morbid psychiatric disorders, and to exclude primary psychiatric disorders. We excluded individuals who suffered from primary psychiatric disorders, individuals who used antidepressants or anxiolytics, or if pregnant. Finally, 47 respondents (22%) met the inclusion criteria. Unfortunately, three participants (6.4%) retreated from the project during the first week of assessment, one produced unreliable data due to serious neglect of the instructions, and for one participant the data were erased due to technical problems.

The final sample consisted of 42 clinically burned-out individuals, 24 women and 18 men, on average 42.7 years old (S.D. = 8.3) and highly educated (52.4% held a college or university degree). All participants were on sick leave ($M = 14.3$ weeks, S.D. = 14.1) and experienced complaints longer than 6 months ($M = 26.1$ weeks, S.D. = 22.8). Sixteen participants (38.1%) suffered from co-morbid psychiatric disorders, mainly from depressive disorder ($n = 9$), which was accompanied in three cases by an anxiety disorder and in one case by somatization disorder. Other co-morbidities were anxiety disorder ($n = 6$) and chronic pain disorder ($n = 1$).

2.2. Measures

2.2.1. Questionnaire

Exhaustion was measured using the exhaustion subscale of the Dutch version of the Maslach burnout inventory—general survey (MBI-GS or in Dutch UBOS; Schaufeli and Van Dierendonck, 2000). High scores on this subscale are indicative for burnout, and the score can range from 0 = never to 6 = every day. The internal consistency of the subscale was high (Cronbach's $\alpha = .95$).

2.2.2. Electronic diary (ESM)

The electronic diary was programmed into a PalmOne™ personal digital assistant computer (PDA) using Pendragon software (Corporation, 1998) and a separate program that generated randomized alarms (Houtveen, 2002). During 14 days, participants kept the electronic diary every morning after waking up (morning diary), before going to bed (evening diary) and on average at five random time points per day (alarm-controlled diary). An alarm was programmed to occur randomly within 2.5 h time units during the entire waking day, and prompted participants to fill in the alarm-controlled diary. The diary items appeared one by one, and the items could be answered through tapping the soft-touch screen of the PDA with a stylus. Compliance was high, since 82% of all alarms was answered by a diary entry, and 94% of the morning diaries and 93% of the evening diaries were completed. The study yielded a total of 2276 alarm-controlled diaries ($M = 56$, range 26–73), 557 morning diaries ($M = 13$, range 0–16) and 552 evening diaries ($M = 13$, range 0–15). Burned-out participants appreciated the method well, and no reactivity effects were detected, i.e. changes in ratings of symptoms over time due to the method of diary keeping itself. More detailed information on the feasibility of ESM in clinical burnout, and information on the method itself is described elsewhere (Sonnenschein et al., 2006a).

Variables under study were measured according to ESM premises: with singular diary items that measure states instead of constructs, mimic an internal dialogue, and are short and easy to comprehend (Delespaul, 1995). *Exhaustion* was measured by the statement 'Right now I feel exhausted', based on the MBI-emotional exhaustion item 'I feel mentally exhausted from my work' (factor loading of .75; Schaufeli and Van Dierendonck, 2000). We generalized the exhaustion item since individuals were on extended sick leave, and simplified it according to ESM premises. Answers were given on a seven point scale anchored 1 = not at all to 7 = very much. *Recovery through sleep* was calculated as the difference between fatigue intensity before going to sleep and when waking up the following morning. The item 'Right now I am tired', was formulated to measure fatigue intensity, based on the high loading item 'I feel fatigued' of the CIS-subscale 'Subjective Fatigue' (factor loading of .75; Vercoulen and Bleijenberg, 1999).

2.2.3. Endocrine parameters

To assess the cortisol awakening response (CAR) participants collected saliva on 2 consecutive weekdays upon awakening (0 min), and 15 and 30 min after awakening, by soaking a cotton role with saliva and saving it in a plastic tube (Sarstedt, Etten-Leur, The Netherlands). Participants collected saliva within the 2-week period of diary measurement and started with cortisol sampling on average on the sixth day of the 2-week period (S.D. = 3.6 days). They were instructed not to brush their teeth, eat or drink coffee from awakening until the last saliva sample. Dehydroepiandrosterone-sulphate (DHEAS) was assessed on the same days as CAR measurement. Participants collected an extra saliva sample via passive drool (Shirtcliff et al., 2001), immediately after taking the last saliva sample (30 min after awakening). CAR level (ground) and CAR increase (slope) were examined separately. To conduct the dexamethasone suppression test (DST), participants took an oral dose of dexamethasone (0.5 mg, PO) at 22:30 in the evening on the second day of saliva collection for CAR assessment, and a reminder was programmed in the electronic evening diary. On the third morning, again three saliva samples were collected (0, 15 and 30 min) to determine the dexamethasone-suppressed cortisol levels. During the collection period all cortisol samples were kept at 4 °C. After non-cooled transport, the samples were stored at −20 °C at the research centre. The cortisol samples were analyzed using a chemiluminescence assay (LIA), as described elsewhere (http://www.ibl-hamburg.com). The salivary DHEAS measurements

Table 1
Means (S.D.) of burnout symptoms and endocrine measures in clinical burnout ($n = 42$)

Variables	Questionnaire[a]	Diary (ESM)[a]			
		2-week aggregate	Day 1	Day 2	Day 3
Burnout symptoms					
Exhaustion	4.71 (1.02)	3.41 (.91)	3.38 (1.50)	3.41 (1.42)	3.26 (1.80)
Recovery		1.19 (1.06)	0.95 (1.84)	1.06 (1.95)	1.33 (1.45)

Variables	Sampling moment (minutes after awakening)	Diary (ESM)[a]			
		Aggregate (day 1 and 2)	Day 1	Day 2	Day 3 DST
Endocrine measures					
Cortisol (nmol/l)	0	15.09 (5.91)	15.30 (7.51)	14.87 (7.24)	0.94 (1.01)
	15	19.76 (7.31)	21.07 (9.62)	18.57 (7.52)	1.04 (1.74)
	30	21.57 (8.33)	22.51 (9.32)	20.66 (9.89)	1.55 (2.59)
DHEAS (ng/ml)	30	3.25 (2.79)	2.85 (2.79)	3.26 (2.91)	–
Cortisol/DHEAS ratio		15.39 (21.56)	15.06 (20.37)	14.41 (19.81)	–

Note. The ESM assessments of days 1–3 concern the three consecutive cortisol sampling days, and represent the values of exhaustion in that particular morning diary and recovery that morning (i.e. fatigue in that morning diary subtracted from fatigue in the preceding evening diary). Cortisol measurements on the third day were influenced by dexamethasone intake, i.e. the dexamethasone suppression test (DST).

[a] Method.

were done with a kit from Diagnostic Systems Laboratories (DSL) (http://www.dslabs.com/). The intra- and interassay variability was less than 10%.

2.3. Procedure

An information brochure about the research project, a screening questionnaire (including scales of the MBI-GS, CIS, and SCL-90-R) and an informed-consent form were sent to potential participants, either on paper or via e-mail. When meeting the inclusion criteria on the questionnaires, a clinical interview was conducted. After inclusion, a 1-h instruction at home was given to explain the use of the electronic diary, as well as the collection of saliva. Participants kept the diary for 2 weeks and collected saliva on 3 consecutive weekdays within the 2-week diary period. Within 2 days after instruction, participants were inquired by phone about their first experiences and potential problems. Telephone assistance was made available during the entire recording period. The assessment period was concluded with a debriefing interview and the collection of the PDA and saliva samples. The study was approved by the Medical Ethics Review Committee of Utrecht University Medical Centre.

2.4. Statistical analysis

Two-week-aggregates of diary assessments were obtained by calculating the mean of all available records per individual. The cortisol/DHEAS ratio was calculated by dividing the mean of the three cortisol samples after awakening by the DHEAS level. We used the log 10 transformation of DHEAS levels and cortisol/DHEAS ratios in analyses because of the skewed distribution of values. To examine *preparatory issue a* and *preparatory issue b* we calculated Pearson PM correlations using SPSS 12.0. Next, we examined associations between burnout symptoms and endocrine measures (*research issues 1a, 1b, 2a and 2b*) with multilevel regression modelling using MlwiN 2.02. Multilevel regression modelling is recommended for within-subject analyses because it accounts for within-subject dependencies of data points, and can discern on which level (i.e. subject, day or sample level) variance is explained by the independent variable (Hruschka et al., 2005). This method is comparable to multiple regression analysis in that its intercept and slope parameters are analogous to the unstandardized coefficients in a regular regression analysis. The multilevel regression equations can be found in Appendix A. In all cortisol analyses we controlled for the influence of time of measurement (0, 15 or 30 min after awakening).

Additional analyses were performed with exclusion of negative CARs, to rule out the effect of non-compliance (Kudielka et al., 2003). A negative CAR may indicate that the participant did not sample cortisol directly after awakening, and therefore 'missed' the CAR. We did not perform this additional

analysis for the DST, since DST suppresses the CAR itself. In total 21.4% of the CARs showed a negative slope either on day 1 or day 2. All analyses were rerun with the exclusion of individuals with co-morbid psychopathology. Depressive symptoms are thought to be related to a hyperactive HPA-axis, with overall higher levels and a reduced sensitivity for dexamethasone (Parker et al., 2003). Despite recent findings of an absence of fatigue and depression effects on cortisol function in burnout (Mommersteeg et al., 2006b), we performed these analyses to rule out that associations were due to co-morbid psychopathology instead of burnout. Sixteen persons suffered from co-morbid psychopathology, mainly mood and anxiety disorders.

3. Results

Table 1 presents descriptive data on symptoms and endocrine values in the clinical burnout sample.

3.1. Correlation between retrospective questionnaire and diary measurement of exhaustion (preparatory issue a)

To identify to what extent ESM assesses symptoms in a different way than questionnaires do, we established the relationship between exhaustion severity as measured by a questionnaire, the MBI–exhaustion scale, and the individual mean level of exhaustion as assessed during 2 weeks of ESM diary recording. Questionnaire and ESM assessments of exhaustion were moderately related ($r = .46$, $p = .07$[1]). The questionnaires were filled out 4 days before the diary recording period (S.D. = 11.7). To control for the time lag between questionnaire and diary assessments we calculated a partial correlation (partialling out time lag) and found similar results ($r = .49$, $p = .05$). Thus as expected, only a moderate relationship was found between questionnaire and ESM assessment of exhaustion.

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[1] This correlation was calculated solely on participants on partial sick leave who had partially resumed work ($n = 17$), due to low validity of the MBI-exhaustion scale in employees on full sick leave (Sonnenschein et al., in press-a).

Table 2a
Associations (β) between endocrine measures and general symptom severity in clinical burnout

Endocrine measure	Symptom assessment				
	Assessment information on endocrine measures		General symptom severity		
	Day[a]	Min after awakening[a]	Questionnaire[a]	Diary[a,b] (ESM)	
			Exhaustion (β)	Exhaustion (β)	Recovery (β)
CAR level	1, 2	0, 15, 30	.06	−.14	.27[*]
CAR increase	1, 2	0, 15, 30	−.13	−.33	.13
DHEAS[c]	1, 2	30	−.01	.26[+]	−.09
Cortisol/DHEAS ratio[c]	1, 2	30	.09	−.26[+]	.16
DST CAR level	3	0, 15, 30	.01	−.26[+]	−.15
DST CAR increase	3	0, 15, 30	.17	−.69[**]	−.16

[+] $p < .10$; [*] $p < .05$; [**] $p < .01$; the significance of effects was determined with the Wald test: Z = estimate/standard error of estimate, where Z is referred to the standard normal distribution.

[a] Burnout symptom.

[b] Two-week aggregated score.

[c] DHEAS values and the cortisol/DHEAS ratio were log 10 transformed.

Table 2b
Associations (β) of endocrine measures and same-moment symptom assessments in clinical burnout

Endocrine measure	Symptom assessment					
	Assessment information on endocrine measures		Same-moment symptom assessments			
	Day[a]	Min after awakening[a]	BP[b]		WP[b,c]	
			Exhaustion (β)	Recovery (β)	Exhaustion (β)	Recovery (β)
CAR level	1, 2	0, 15, 30	−.27[*]	.38[***]	−.14[+]	−.10
CAR increase	1, 2	0, 15, 30	−.37[*]	−.13	−.10[+]	−.03
DHEAS[d]	1, 2	30	.25	−.04	−.10	.01
Cortisol/DHEAS ratio[d]	1, 2	30	−.39[**]	.27[+]	.01	−.07
DST CAR level	3	0, 15, 30	−.04	.08	–	–
DST CAR increase	3	0, 15, 30	−.18	−.20	–	–

[+] $p < .10$; [*] $p < .05$; [**] $p < .01$; [***] $p < .001$; the significance of effects was determined with the Wald test: Z = estimate/standard error of estimate, where Z is referred to the standard normal distribution.

[a] Burnout symptom.

[b] BP, between person variability of the symptom; WP, within person variability of the symptom.

[c] The dexamethasone suppression test (DST) was only performed once. Therefore, no within-person associations were calculated for DST CAR level and DST CAR increase.

[d] DHEAS values and the cortisol/DHEAS ratio were log 10 transformed.

3.2. Associations between symptoms and endocrine values

Tables 2a and 2b show the strength of the relationship between burnout symptoms and endocrine measures expressed in standardized β-coefficients calculated with multilevel regression analyses. The β-coefficients express the ability of burnout symptoms to statistically predict the HPA-axis parameters. We accounted for the confounding influence of time of awakening, depressive mood, sleep quality, BMI, smoking, oral conceptive usage, age, gender and partial or full sick leave. We additionally ran every analysis excluding (a) negative CARs (with the exception of the cortisol values after intake of dexamethasone, day 3) and (b) without participants that suffered from co-morbid psychopathology.

3.2.1. The questionnaire and cortisol parameters (research issue 1a)

We found no significant associations between questionnaire assessment of exhaustion, the MBI-exhaustion scale, and

endocrine measures (Table 2a). Additional analyses, subsequently excluding samples without a CAR increase and participants that suffered from co-morbid psychopathology, did not change these results.

3.2.2. General symptom severity assessed with ESM and cortisol parameters (research issue 1b)

Second, we examined the associations of HPA-axis parameters with 2-week aggregated scores of burnout symptom assessments with the diary. We found two significant associations and three trends shown in Table 2a: higher exhaustion levels were associated with a decreased level of cortisol after intake of dexamethasone (DST CAR level), a smaller rise after dexamethasone intake (DST CAR increase), and higher levels of DHEAS as well as lower cortisol/DHEAS ratios. Burned-out individuals who were characterized by generally poor recovery through sleep showed lower cortisol levels after awakening (CAR level). The amount of explained variance of these findings varied between 3 and 16%, with the

Table 3
Intercorrelations of assessments across days

Category	Variable	Days		
		1–2, *r*	2–3, *r*	1–3, *r*
Burnout symptoms (*n* ranges from 35 to 42)	Exhaustion	.38[*]	.40[*]	.64[**]
	Recovery	.22	.49[**]	.05

Category		Variable		
Endocrine measures (*n* ranges from 38 to 42)		Cortisol 0 min		.30
		Cortisol 15 min		.45[*]
		Cortisol 30 min		.53[**]
		DHEAS		.26
		Cortisol/DHEAS ratio		.49[**]

Note. Days 1–3 concern the three consecutive cortisol sampling days. The burnout symptoms are assessed in the morning diary. No correlations are calculated for the third day, since this sample was influenced by the dexamethasone suppression test (DST). [*]$p < .05$; [**]$p < .01$.

exception of exhaustion that explained 30% of the variance in CAR increase after dexamethasone intake (DST CAR increase).

After excluding samples without a CAR increase for the assessments on days 1 and 2, the association between the aggregated value of poor recovery through sleep and a lower CAR level remained ($\beta = .27$, $p < .05$). When excluding participants that suffered from co-morbid psychopathology no associations remained significant, even the strong association between exhaustion and DST CAR increase.

3.2.3. Fluctuations of symptoms and endocrine measures across days (preparatory issue b)

The three morning assessments of exhaustion were intercorrelated moderately (Table 3). The three morning assessments of recovery through sleep did either not correlate or correlated moderately, as did the two morning assessments of cortisol and DHEAS. Since relationships between measurements are moderate, symptoms and endocrine measures seem to fluctuate between days within individuals.

3.2.4. Same moment assessment, between person associations (research issue 2a)

We analyzed the associations of cortisol and DHEAS with the *individual 2-day average* level of same-moment exhaustion and recovery through sleep (between person association or BP). BP-exhaustion was significantly associated with a lower level of cortisol (CAR level) and with a smaller cortisol/DHEAS ratio (Table 2b). BP-recovery was as well significantly associated with a lower CAR level and a trend appeared for a smaller cortisol/DHEAS ratio. In addition, BP-exhaustion was associated with a smaller CAR increase. The amount of explained variance of the significant results varied between 4 and 12%.

Higher BP-exhaustion and poorer BP-recovery remained significantly associated with lower CAR levels when excluding samples without a CAR increase ($\beta = -.25$, $p < .05$; $\beta = .33$, $p < .05$) and individuals with co-morbid psychopathology ($\beta = -.18$, $p < .10$; $\beta = .32$, $p < .05$). The cortisol/DHEAS ratio only remained significantly related to BP-exhaustion when excluding samples without a CAR increase ($\beta = -.31$, $p < .10$), but not after exclusion of co morbidity). The smaller

CAR increase remained associated with higher BP-exhaustion when excluding co-morbid psychopathology ($\beta = -.49$, $p < .10$).

3.2.5. Same moment assessment, within person associations (research issue 2b)

A trend appeared for the association of within-person fluctuations of symptoms (WP) across days (days 1 and 2) with endocrine, as shown in Table 2b: a lower CAR level and smaller CAR increase were observed on days with higher exhaustion levels after awakening (WP-exhaustion). The amount of explained variance varied between 2 and 7%.

When excluding samples without a CAR increase none of the associations remained and without co-morbid psychopathology only one association remained, i.e. higher levels of WP-exhaustion were still significantly associated to a smaller CAR increase ($\beta = -.15$, $p < .05$).

4. Discussion

We conducted an in-depth study on relationships between HPA-axis functioning and burnout symptoms in clinically burned-out individuals. Instead of retrospective questionnaires, we used an electronic diary according to the experience sampling method to assess momentary burnout symptoms, and thereby improved symptom assessments.

In a clinically burned-out sample we found no associations between general severity of exhaustion assessed with a retrospective questionnaire and endocrine values (*research issue 1a*), but we did find associations of endocrine values with ESM assessments of general severity of exhaustion and poor recovery through sleep (*research issue 1b*). Burned-out individuals with a higher general severity of exhaustion and poor recovery through sleep in the diary displayed lower cortisol levels, higher DHEAS levels, and consequently a smaller cortisol/DHEAS ratio, as well as a stronger suppression of cortisol after DST. All of these findings consistently indicate a hypoactive HPA-axis. Our findings confirm prior research that did not find any significant relationships between retrospective burnout questionnaires and the cortisol awakening response, the day-curve, dexamethasone-suppressed cortisol levels

(Mommersteeg et al., 2006a,b) and evening cortisol levels (Galantino et al., 2005). However, we did find associations between general severity of momentary symptoms assessed with the diary. Moreover, we showed that the diary taps other information than the questionnaire, i.e. the moderate relationship between both assessment methods (*preparatory issue a*). Moderate correlations between retrospective and momentary assessments are commonly found, and mainly attributed to the cognitive processes used in retrospective assessments that distort truthful reporting (Peters et al., 2000; Stone et al., 2004). Therefore, the difference between previous questionnaire research and the current findings using ESM should probably be attributed to the more reliable way of assessing general symptom severity with ESM.

Our presumption that burnout symptoms and endocrine values fluctuate within individuals across days was confirmed (*preparatory issue b*). Endocrine values were significantly associated with same-moment assessments of burnout symptoms between individuals (research issues 2a) and a trend was found within individuals (research issues 2b). In other words, burned-out individuals with *generally* higher exhaustion and poorer recovery through sleep in the morning (BP) showed lower levels and smaller increases of cortisol values after awakening, and a smaller cortisol/DHEAS level accordingly (between-subject association). Independent of the *general* level of symptoms after awakening, days with higher symptom severity (WP) were associated (a trend) with lower CAR levels and slopes and lower CAR levels after dexamethasone intake compared to days with lower symptom severity (within-subject association). Though the latter became non-significant after excluding subjects (but see comment below). These findings are signs of a hypofunctioning of the HPA-axis between and probably also within individuals. To our knowledge, the current study is the first to show that within-person relationships seem to correspond with between-subject relationships of exhaustion and cortisol in clinical burnout.

The between-subject associations of endocrine values with the average morning levels of symptoms were more robust than associations with the general severity of symptoms and within-subject associations. Most significant associations remained for between-subject association of same-moment assessments when excluding negative CARs or co-morbid psychopathology. But most significant associations or trends disappeared for general severity of symptoms and for the within-person level of same-moment assessments. On the whole, the additional analyses excluding co-morbid psychopathology have probably been too conservative (i.e., a low statistical power), since the already small *N* dropped from 42 to 26. The additional analyses excluding samples without a CAR increase suffer the same problem, although to a lesser extent. Besides, higher exhaustion was consistently associated with a lower CAR increase, and therefore, excluding samples without a CAR increase implied excluding samples and/or individuals with higher exhaustion levels. It might be, but seems unlikely, that burned-out individuals with higher exhaustion are less compliant than burned-out individuals with lower exhaustion. In contrast, the remaining associations of high exhaustion/poor recovery with a lower CAR level after exclusion of negative CAR samples indicate that excluding samples with a negative CAR might have been too conservative as well.

We showed that in a group of burnout patients there is some (between and within) association between severity of symptoms of exhaustion and non recovering sleep on the one hand and HPA hypofunctioning on the other. In the light of these observations one would predict also to find this tendency when comparing a group of clinical burnouts with a healthy control group. Surprisingly the literature is inconsistent in this respect. Several studies in CFS showed that a lack of energy is associated with a hypofunctioning of the HPA-axis (Cleare, 2003; Jerjes et al., 2005; Parker et al., 2001; Roberts et al., 2004; Scott and Dinan, 1998). Though inconsistencies in these studies were reported as well (Gaab et al., 2002; Jerjes et al., 2006; Young et al., 1998). A between group diary study of burned-out and healthy individuals would reveal whether the earlier inconsistent findings are due to a too rough measurement of symptoms by questionnaires.

The within-subjects trend found in the relationships between exhaustion and endocrine measures is in the same direction as the observed between-subject relationships. Although the within-subject relationships seem less important and can be best considered as preliminary since we assessed only 2 days, they indicate a direct relationship between HPA-axis functioning and exhaustion, irrespective of general level of exhaustion. It might as well be that this observation holds in other populations that are not characterized by severe exhaustion. For example, low wakeup cortisol in older adults predicted higher levels of fatigue later that day (Adam et al., 2006).

This study has several limitations. First, our sample size was limited to 42 participants and 2 days of CAR and DHEAS measurement and 1 dexamethasone suppression test. This might have particularly influenced the analyses in which participants were excluded, based on the flat CAR curves and the exclusion of the participants with co-morbid psychopathology. The moderate correlation between questionnaire and diary assessment of exhaustion might be partially explained by the time lag between questionnaire and diary assessment, although no direct confounding influence of time lag on the association was found. As questionnaires usually refer to describing a previous period, an additional retrospective questionnaire at the end of the sampling period is recommended for future studies.

The new and in-depth findings of the current study ask for a more elaborate replication, in particular with an extension of cortisol sampling days. Moreover, using a diary study might clarify the inconsistent findings often found in between group studies. In general, electronic diary measurement of symptoms is an important contribution to health-related research. The method has the power to shed new light on inconsistent findings from previous retrospective studies, or to substantiate these with sound proof. The current results advocate same-moment assessments when examining symptom-cortisol associations, instead of general symptom severity.

To conclude, the current study adds support to the view that the severity of burnout symptoms is associated with HPA-axis functioning.

Appendix A. Multilevel regression equations

Dependent variables	Equation	Level of R^a
Research issue 1 (Table 2a)		
CAR level	$\text{Cortisol}_{ijk} = \text{intercept}_{ijk} + \text{time}_{ijk} + \underline{\beta\text{symptom}_i}$	Subject
CAR increase[b]	$\text{Cortisol}_{ijk} = \text{intercept}_{ijk} + \text{random time}_{ijk} + \text{symptom}_i + \underline{\beta\text{time} \times \text{symptom}_{ijk}}$	Random part subject variance
DHEAS	$\log \text{DHEAS}_{ij} = \text{intercept}_{ij} + \underline{\beta\text{symptom}_i}$	Subject
Cortisol/DHEAS ratio	$\log \text{CDratio}_{ij} = \text{intercept}_{ij} + \underline{\beta\text{symptom}_i}$	Subject
CAR dex level	$\text{Cortisol}_{ik} = \text{intercept}_{ik} + \text{time}_{ik} + \underline{\beta\text{symptom}_i}$	Subject
CAR dex increase[b]	$\text{Cortisol}_{ik} = \text{intercept}_{ik} + \text{random time}_{ik} + \text{symptom}_i + \underline{\beta\text{time} \times \text{symptom}_{ik}}$	Random part subject variance

Dependent variables	Equation	Level of R^a (BP/WP)
Research issue 2[a] (Table 2b)		
CAR level	$\text{Cortisol}_{ijk} = \text{intercept}_{ijk} + \text{time}_{ijk} + \underline{\beta\text{BP-symptom}_i} + \underline{\beta\text{WP-symptom}_{ij}}$	Subject/day
CAR increase[b]	$\text{Cortisol}_{ijk} = \text{intercept}_{ijk} + \text{random time}_{ijk} + \text{BP-symptom}_i + \text{WP-symptom}_{ij}$ $+ \underline{\beta\text{time} \times (\text{BP-symptom})_{ik}} + \underline{\beta\text{time} \times (\text{WP-symptom})_{ijk}}$	Random part subject variance/random part day variance
DHEAS	$\log \text{DHEAS}_{ij} = \text{intercept}_{ij} + \underline{\beta\text{BP-symptom}_i} + \underline{\beta\text{WP-symptom}_{ij}}$	Subject/day
Cortisol/DHEAS ratio	$\log \text{CDratio}_{ij} = \text{intercept}_{ij} + \underline{\beta\text{BP-symptom}_i} + \beta\text{WP-symptom}_{ij}$	Subject/day
CAR dex level	$\text{Cortisol}_{ik} = \text{intercept}_{ik} + \text{time}_{ik} + \underline{\beta\text{BP-symptom}_i}$	Subject
CAR dex increase[b]	$\text{Cortisol}_{ik} = \text{intercept}_{ik} + \text{random time}_{ik} + \text{BP-symptom} + \underline{\beta\text{time} \times (\text{BP-symptom})_{ik}}$	Random part subject variance

Note. Underscored is the explaining variable; i = subject level, j = day level, k = moment level. For the sake of clarity we did not add confounders to the formula of the appendix and left out the β's that were not reported in Tables 2a and 2b. The equations of Research issue 1 were tested for three different independent variables (symptom): (1) MBI-exhaustion score (research issue 1a); (2) 2-week aggregated diary score of exhaustion (research issue 1b); (3) 2-week aggregated diary score of recovery through sleep (research issue 1b). Research issues 2a and 2b were tested in one equation. The equations were tested for two different independent variables (symptom): (1) exhaustion in the morning; (2) recovery through sleep in the morning.

[a] Between- and within-variability were tested according to the method of Schwartz and Stone (1998).

[b] 'Random time' means that the equation allowed each individual to have his/her own regression coefficient for time (CAR slope). The explaining variable time × symptom is a cross-level interaction term and tries to statistically explain why individuals have different slopes.

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