Scand J Work Environ Health 2006;32(5):333-337

<https://doi.org/10.5271/sjweh.1028>

Issue date: 31 Oct 2006

**Burnout and functioning of the
hypothalamus-pituitary-axis—there are no simple answers**

by [Sonnentag S](#)

Affiliation: University of Konstanz, Department of Psychology, Work and Organizational Psychology, PO Box D 42, DE-78457 Konstanz, Germany. sabine.sonnentag@uni-konstanz.de

Refers to the following text of the Journal: [2006;32\(5\):339-348](#)

Key terms: [burnout](#); [editorial](#); [function](#);
[hypothalamus-pituitary-adrenal axis](#)

This article in PubMed: www.ncbi.nlm.nih.gov/pubmed/17091200

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Burnout and functioning of the hypothalamus-pituitary-adrenal axis—there are no simple answers

In this issue of the *Scandinavian Journal of Work, Environment & Health*, Langelaan, Bakker, Schaufeli, van Rhenen & van Doornen (1) report findings from an interesting study on burnout and cortisol that will probably keep readers thinking about it—not because the authors describe spectacular relationships, but because—overall—they did not find such relationships.

Langelaan et al compared burned-out, engaged, and healthy managers with respect to the functioning of the hypothalamus-pituitary-adrenal (HPA) axis, the central system that regulates a person's adaptation to stress. As the experience of stressors (2, 3) and health problems (4, 5) are associated with elevated cortisol levels and other indicators of HPA-axis dysregulation, it is a rather straightforward endeavor to examine whether people experiencing burnout show dysregulations of the HPA axis. In contrast to what many might expect, Langelaan et al did not find any differences between burned-out and healthy control managers with respect to various indicators of HPA-axis functioning (cortisol awakening response, salivary dehydroepiandrosterone-sulfate, the dexamethasone suppression test). Only highly engaged managers (ie, managers scoring extremely low for burnout) exhibited a stronger cortisol suppression in response to the dexamethasone suppression test.

The lack of any significant difference in HPA-axis functioning between burned-out and healthy persons might be surprising at first, but this finding fits rather well into the larger picture emerging from a range of other studies. When comparing cortisol measures of persons high versus those low with respect to burnout, some studies support lower morning levels in burned-out persons, others indicate higher baseline cortisol levels or other evidence of a dysregulation of the HPA axis, and a number of studies did not find any differences. [For overviews, see the reports of Kudielka et al (6) and Melamed et al (7).]

When facing a study with largely nonsignificant findings, one should address the following two core questions: (i) Why did the researchers find no significant differences? and (ii) What can we learn from the study?

Why did the researchers find no significant differences?

The first reason why researchers often do not find differences in HPA-axis functioning between burned-out and healthy persons is related to the complexity of the processes of the HPA axis and the associated problems of measuring its functioning. Cortisol levels are influenced by a range of factors such as gender, pregnancy, and menstrual cycle phase (in women), as well as by smoking, specific medications, and physical activity (8–10). Measures of the cortisol awakening response are highly dependent on the exact time of saliva collection and awakening time (11). Therefore, well-decided exclusion criteria and a well-developed and controlled study protocol are essential for collecting reliable cortisol measures.

Overall, Langelaan et al applied a well-controlled procedure that can rule out many of the potential reasons for not finding significant differences. For example, by including only men in their study, they avoided many of the problems researchers face when including both men and women in studies on cortisol (12). In addition, they ran additional analyses by excluding participants who did not comply with the timing requests of the study protocol—without finding different results.

Thus, although problems due to confounding variables and other nuisances can never be ruled out completely [eg, it would have been preferable to have more sampling days (13)], it would be too simple to attribute Langelaan et al's findings to a poorly developed study protocol.

The second reason why Langelaan et al—among other researchers—did not find differences between burned-out managers and healthy controls is related to issues associated with the samples included in the analyses. First of all, there is the question of defining cut-off scores for differentiating between burned-out and healthy persons. Although it may be tempting to use a median split—as done in some earlier studies—for dividing study participants into high versus low burnout subgroups, such an approach might obscure any existing differences. Langelaan et al followed a less arbitrary approach and used well-defined cut-off scores for creating the high-burnout versus low-burnout subgroups. This procedure reduced the risk of people without burnout actually being assigned to the high-burnout subgroup and vice versa.

Second, small sample sizes and associated problems with statistical power are a cause of concern in many studies sampling cortisol. In some studies, a restriction of range in the core variables may also be a problem. However, a study using a larger sample of 74 clinically diagnosed burnout persons and comparing these persons with 35 healthy controls did not find significant differences in the cortisol awakening response and other indicators of HPA-axis functioning either (14).

A third possible reason why Langelaan et al did not find differences in the cortisol measures, particularly the cortisol awakening response between burned-out managers and healthy control managers is related to the participants' work and life situation. Langelaan et al's burned-out participants were (still) integrated in the employment process. This sample characteristic implies that the burnout symptoms may have been relatively mild ("healthy worker effect") and that the daily routine of these burned-out managers did not differ largely from that of the control participants. However, symptom severity is maybe not the crucial explaining factor for the authors not finding differences in the cortisol awakening response, as the burned-out managers had scores above previously validated cut-off scores. Moreover, other researchers who compared clinically diagnosed burnout patients with healthy controls did not find any differences either (14), for a male subsample (12).

The interpretation that maintaining a relatively regular daily routine accounted partially for the nonsignificant findings seems more plausible. Empirical evidence from studies with healthy persons indicates that the cortisol awakening response differs between workdays and weekends (15, 16) and, therefore, suggests that the cortisol awakening response partially reflects an anticipation of the demands of a specific weekday. The difference in the cortisol awakening response between workdays and weekends was also found in Langelaan et al's study, the finding indicating that, also in burned-out persons, the HPA axis works differently on workdays as opposed to weekends. The workday scores for the cortisol awakening response may be indicative of an anticipation of this day's demands. Thus the findings may imply that, also among burned-out employees, the anticipated demands of a manager's workday "override" the tendency of burned-out persons to show a low cortisol awakening response, as found in some earlier studies (17, 18).

A fourth reason for finding no differences between burned-out and healthy persons may be due to processes associated with hypocortisolism. Heim, Ehler, & Hellhammer have described how initial hyperactivity of the HPA axis may develop into hypoactivity as a response to chronic stress (19). Such hypoactivity of the HPA axis has been observed in the chronic fatigue syndrome and after chronic stress and trauma. It may be that people who are developing burnout first respond with an increase in HPA-axis activity—but, as stressors continue to be present and the persons in question do not expect that they can successfully cope any longer, HPA-axis activity may be reduced (6). Applied to Langelaan et al's findings, this interpretation may imply that part of the burned-out sample was still in a state of

hypercortisolism, whereas another part had already experienced hypocortisolism—so that in the total sample, on the average, no HPA-axis abnormalities were detected.

Taken together, although the first and second explanations cannot be ruled out completely, it seems plausible that the daily work routine of the burned-out participants, as well as processes associated with hypocortisolism, has contributed to the findings of Langelaan et al.

What can we learn from the study?

Although Langelaan et al's core findings do not correspond with what they had expected, their study is important for further developing our knowledge of the relationship between burnout and cortisol. Along with others (14, 20), Langelaan et al demonstrated that impairments of psychological well-being are not necessarily related to easily detectable dysregulations of the HPA axis. Experimental research on responses to acute stressors has shown that cortisol responses do not parallel subjective stress reactions (2). Similarly, it should not be taken for granted that chronic subjective stress indicators are uniformly reflected by cortisol measures (7, 17). For example, a recent intervention study found a reduction in self-reported burnout scores *and* a reduction in indicators of HPA-axis functioning—but the improvements in the two measurement domains were not related (18).

Interestingly, Langelaan et al found that engaged managers—that is, managers with extremely low scores on burnout—showed stronger cortisol suppression in response to the dexamethasone suppression test than less engaged managers. This finding, which surely calls for replication, may indicate that high work engagement not only has psychological or even economic advantages (21, 22), but also some physiological benefits. Alternatively, it may be that a well-functioning HPA axis “enables” people to experience greater work engagement.

For advancing knowledge on the relationship between burnout and dysregulations of HPA-axis functioning, we need to focus on two—intertwined—strategies. The first implies adherence to a reliable measurement procedure for HPA-axis indicators and other variables. The second refers to the development of more elaborate models of the relationship between burnout and HPA-axis functioning.

For progress to be made in research on the relationship between burnout and HPA-axis functioning, a well-developed and controlled measurement procedure is a “must”. Such an approach must address potentially confounding and moderating variables (6, 14), with respect to both stable personal characteristics and more situation-specific or state-like variables (8–11). A well-defined study protocol also implies the sampling of cortisol over several days before the measures are aggregated (13). Moreover, researchers may even question the use of the measures commonly used in today's studies. For example, Mommersteeg et al (14) recently suggested that the procedure of “just taking saliva samples or a low-dose dexamethasone suppression test might not be sensitive enough to reveal subtle dysregulations in the HPA-axis [p 223]”.

In terms of improving measurement approaches, one might also reconsider burnout measures. Although the Maslach Burnout Inventory-General Survey is widely used and is maybe the best instrument available (23), its use does not imply that the inventory is the best instrument ever possible and that it is sensitive enough to detect small variations in burnout that are relevant to the functioning of the HPA axis.

In addition, the findings of Langelaan et al suggest that, as long as burned-out persons keep up a daily routine and go to work on a regular basis, their cortisol scores mirror those of healthy persons—both on workdays and on weekends. Thus the anticipation of the workday may exert a similar influence on the cortisol awakening response of burned-out and healthy persons. With respect to measurement protocols in future studies, these interpretations imply that it is particularly important to report the (anticipated) stress level and (anticipated) activities on the days of data collection. Thus far, most

studies have reported whether burnout was clinically diagnosed or not and whether burned-out participants were on sick leave or not—but not whether they worked on the specific days and what they experienced on and expected for these specific days. Given our knowledge of the strong effects of specific acute stressors (2, 24), it is crucial that more attention be paid to acute stress perceptions and anticipation also when cortisol is measured as an indicator of more chronic processes.

Similarly, more attention should be given to the selection of control participants and to the assessment of their daily routines and their actual behavior during days of data collection. Particularly, choosing convenience samples of control participants without knowing their specific daily routines and giving them discretion about the specific weekdays (Monday through Friday) on which to provide the saliva samples may mask differences between burned-out and control persons.

As a second strategy to increase our understanding of HPA-axis functioning in burned-out persons, more effort in theory development is needed. Probably the phenomenon of hypocortisolism (19) will play a core role in such a theory (7). To interpret contradictory findings from empirical research on HPA-axis functioning in burned-out persons, Kudielka and her co-workers (25) proposed that people in the early stages of the burnout process may show signs of hypercortisolism that later develops into hypocortisolism (6). It will be particularly important and challenging to identify the factors that contribute to the change from hypercortisolism into hypocortisolism in burned-out persons (25). From a more empirical perspective, it may be promising to examine individual cortisol profiles (26) to contrast persons showing hypercortisolism versus those with hypocortisolism and then examine the variables associated with hypercortisolism versus hypocortisolism. In addition, a lack of habituation may play a role in the HPA-axis functioning of burned-out or exhausted persons (27).

Any theoretical approach that intends to account for dysregulations of the HPA axis in association with burnout must adopt a process perspective. Burnout in itself is a process developing over longer periods of time, the process implying that the HPA axis may not function uniformly in persons experiencing early stages of burnout and in persons suffering from more severe and chronic forms of burnout. Thus merely comparing burned-out persons with those not experiencing burnout without paying more attention to the time course of burnout—a difficult topic in itself (28)—might not contribute much to our knowledge. More specifically, it was proposed that experiences relevant for the HPA axis, such as a lack of perceived control, negative social evaluation, and shame (2), may be important as burnout develops—but may lose their relevance later in the burnout process (14).

Such a process perspective also implies that researchers should pay more attention to potential reciprocal processes. Thus theoretical models should not only explain why and how burnout influences the HPA axis, but also how the HPA-axis functioning may influence burnout symptoms (7).

Overall, our knowledge on the interrelationships between burnout and HPA-axis functioning is still very limited. For making progress in this research area, we need both further refinement of research methodology and advancement in terms of theory development.

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Sabine Sonnentag

University of Konstanz

Department of Psychology, Work and Organizational Psychology

PO Box D 42

DE-78457 Konstanz Germany

[E-mail: sabine.sonnentag@uni-konstanz.de]