How about work demands, recovery, and health? A neuroendocrine field study during and after work
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Chapter 3

A forward facilitating influence of cortisol on the catecholamines assessed during work of garbage collectors.

Abstract

Objectives In this study, the hypothesis was tested whether part of the hypothalamic-pituitary-adrenal system could have a facilitating influence on the mean adrenomedullary reactivity during a working day.

Methods This was studied on data from a field study on 115 male garbage collectors. Catecholamines and cortisol were assessed by urinary sampling during a working day and during a day off. The within-subjects baseline levels of the catecholamines, personal factors, physical workload, and work characteristics were controlled for in the analyses.

Results The results showed that there is reason to assume a ‘forward facilitating influence’ between the two aforementioned systems: the morning cortisol excretion rate explained a reasonable amount of the mean catecholamines’ excretion rates during a working day. The morning cortisol level explained more variance in adrenaline than in noradrenaline, and for both catecholamines, the influence of cortisol was more pronounced than the influence of psychosocial stress factors like autonomy and job demands.

Conclusions The morning level of cortisol proved to be a more powerful predictor of reactivity in adrenaline than in noradrenaline during work. The association between the pituitary adrenocortical system and the adrenomedullary system could therefore be a ‘forward facilitating influence’. It is recommended for future research to focus on cortisol as predictor of neuroendocrine reactivity and to find out if this predictive power is expandable to work induced health complaints.

Key terms: Adrenaline; Cortisol; Noradrenaline; Psychosocial factors; Stress; Work characteristics; Workload

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Introduction

One out of four workers feels stressed by work, and one out of every five workers experiences work-related fatigue (Euro Review 1997). In the Netherlands, work-related chronical fatigue with additional health complaints is the reason for a yearly sickness absence averaging three months in a reasonable proportion of the working population (Engers & Muller 1994). Lack of autonomy (control) appears to be a work-related psychosocial stress factor. Perceived stress increases when high job demands occur in interaction with low control on the job (Karasek & Theorell 1990). Bodily reactions from work stress include increased activity levels in most subsystems.

Psychophysiological measurements play an important role in the examination of the interaction between work, stress, and health (e.g. Frankenhaeuser et al. 1989, Lundberg 1995, Gaillard & Wientjes 1996). In studies on work stress, the neuroendocrine parameters mostly used in monitoring human reactions to different activities are adrenaline, noradrenaline, and cortisol. It is well known that anticipatory orientation towards a stressor of personal relevance is among the most important stimulants of the hypothalamus-pituitary-adrenal (HPA) axis (Hellhammer et al. 1996). A low degree of perceived control, for example, will prolong the normal habituation of the stress response (Kirschbaum et al. 1996). Interindividual differences of HPA activity have been observed for cortisol levels, both at rest (baseline) and during work. Especially the morning baseline values were found to vary with chronic or traumatic stress, and to be associated with genetic and personality traits (Hellhammer et al. 1996). Additional neuroendocrine responses to stressors are reactions of the sympathetic adrenomedullary system. The catecholamine levels during work are indicators of general arousal as a functional adaptation in mental (adrenaline) and physical (noradrenaline) working situations to which the subject is exposed. The ratio between adrenaline and noradrenaline excretion can be used as a representation of the nature of the workload (Gaillard 1996). During the first hours after work, spillover of catecholamine reactivity is often present, which indicates incomplete recovery from occupationally exerted efforts. Increases in adrenomedullary activity, assessed by plasma adrenaline levels, often correlate more closely with increases in pituitary-adrenocortical activity, represented by plasma levels of corticotropin (ACTH), than with increases in sympathoneural activity, as indicated by plasma noradrenaline levels (Goldstein 1995).
Associations between cortisol excretion and the sympathetic adrenomedullary system in humans are often proposed, but the relationship is not always clear (Goldstein 1995, Korunka et al. 1996). A line of reasoning could be followed, in which these associations are thought to be the modifying factor of the vicious circle in developing chronic fatigue complaints. The cortisol morning baseline values vary with chronic or traumatic stress level, and these circadian peak values run in front of the natural raising of catecholamine levels. This means that it could be possible that the cortisol peak value influences the mean excretion rates in catecholamines, and that spillover effects in catecholamines could serve as additional stressor causing the cortisol baseline to be heightened the following day. Thus, a ‘forward facilitating influence’ is hypothesised here, where the early morning peak level of cortisol is thought to have a facilitating influence on the mean excretion rate of adrenaline during the day. It is further hypothesised that the morning excretion level of cortisol has a greater predictive power for the mean excretion rate of adrenaline than for noradrenaline, because adrenaline reflects mental workload.

The purpose of this study, therefore, was to investigate the facilitating influence of cortisol on adrenomedullary reactivity. This influence was tested on data from a field study among garbage collectors. The baseline levels of the catecholamines, personal factors, physical workload, and work characteristics were controlled for.

Subjects and methods

Design and population
A cross-sectional design with repeated measurements was used. The subjects were examined in the laboratory (for the assessment of body weight, body height, and the maximum heart rate (HR$_{\text{max}}$)). The subjects were examined in their natural (work) environment for the neuroendocrine measurements during work and in the off-work situation, and the assessment of the heart rate (HR) during work. The study population consisted of 115 male garbage collectors working throughout The Netherlands for 29 different companies. They were randomly selected and informed about the followed procedures. Inclusion criteria were 1) collecting garbage at least four days/week according to the same method, and 2) one year experience minimally. The mean age of the collectors was 37 years (sd 8.7; range 22-57). Their mean weight was 82 kg (sd 14.9; range 57-128), and height was 1.78
m (sd 7.6; range 1.54-1.95). Their mean body mass index (BMI) was 26.1 kg/m$^2$ (sd 4.1; range 19.6-40.4).

**Work related variables**

Each garbage collector completed a questionnaire concerning working conditions. Dutch versions of scales concerning job demands and autonomy were included (Karasek & Theorell 1990). The scale sum scores were transformed into Z scores.

**Physical workload**

The HR$_{\text{max}}$ was determined in the laboratory using a maximal treadmill test (described in Frings-Dresen et al. 1995). In the natural work environment, the HR (b/min) was continuously recorded and averaged every 15 s (Sport tester PE 3000, Polar Electro, Finland) during the whole working day to get an indication of the relative workload of the activities during the day. Firstly, for each subject the mean HR (b/min) on the working day was calculated. Hereafter, the percentage of the maximum HR (\%HR$_{\text{max}}$) was calculated by dividing the mean HR of the working day by the HR$_{\text{max}}$ and multiplying this outcome with 100. The mean HR during the working day was 105 b/min (sd 12.0; range 79-132), and the mean \%HR$_{\text{max}}$ during the working day was 57 \% (sd 6.8; range 43-75).

**Catecholamines and cortisol measurements**

**Procedure.** Excretion rates of catecholamines and cortisol were assessed during a working day and a rest day (a Sunday). The subjects were asked to collect all urine during these days and to provide samples (1) around 07 00 h, (2) around lunch break (11 00 h), (3) around end of work time (15 30 h), (4) around 20 00 h, and (5) before going to bed. Times of all urinations were recorded during the two days. Analyses were performed on sample 2, 3, and 4. Sample 2 and 3 reflected the hours of work in the morning and afternoon respectively. Sample 4 reflected the first recovery hours after work.

**Analysis.** The subjects were asked to urinate in a jar that contained 0.7 g of citric acid. Firstly, the volume of each urine sample was assessed. Secondly, 40 ml from each sample was kept, of which 20 ml was acidified with 0.1 ml 10 M HCl for catecholamine analyses. These 20 ml samples were kept frozen (-20°C) until analysis. The urinary catecholamine concentrations were determined by HPLC with fluorescence detection (Boos et al. 1987). The urinary cortisol concentrations were determined by the Amersham Amerlite Cortisol assay, which uses a competitive immunoassay technique, based on enhanced luminescence (Amersham Inc. 1973).
Data analysis and statistics
Firstly, the urinary concentrations (ng/ml) were multiplied by the volume of the corresponding urine sample. This amount was divided by the period of time (min) between the urination of this sample and the previous urination time, to obtain the mean excretion rate (ng/min) for an exact period of time. Secondly, a repeated measures analysis of variance (MANOVA; F test correcting with Mauchly's test for sphericity) was performed for each day to test whether there were diurnal differences. To evaluate the reactivity of the catecholamines and cortisol, the mean urinary excretion rates for the working day and the rest day (baseline) were calculated for adrenaline and noradrenaline. In all analyses differences were accepted as significant at p<0.05. To test our hypothesis, hierarchical multiple linear regression analyses were carried out for both the catecholamines, with the mean excretion rate on the working day as the dependent variable. The mean excretion rates of the catecholamines on the rest day and the morning levels of cortisol on the working day were entered into the model in the first step as independent variables. The variables age, BMI and %HR\textsubscript{max} were entered into the model in the second step. In the third step, the variables concerning job demands and autonomy were entered into the model. To be able to control for collinearity, tolerance levels were checked in the models of the third step.

Results

Catecholamines and cortisol
For adrenaline and cortisol, circadian rhythmicity was notable on both days (p<0.05 for both days). For noradrenaline, the working day showed circadian rhythmicity (p<0.01), but no circadian rhythm was found on the rest day. Table 1 shows the mean (sd) excretion rates of adrenaline, noradrenaline, and cortisol for each day. The overall mean excretion rates of adrenaline and noradrenaline on the working day were significantly higher than on the rest day (p<0.01). For cortisol, no differences were found between the working day and the rest day.
Table 1. Overall mean (sd) excretion rate of Adrenaline, Noradrenaline, and Cortisol per day (ng/min) in garbage collectors (n=115).

<table>
<thead>
<tr>
<th></th>
<th>Working day mean (sd)</th>
<th>Rest day mean (sd)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenaline</td>
<td>12.40 (5.49)</td>
<td>7.86 (4.02)</td>
</tr>
<tr>
<td>Noradrenaline</td>
<td>65.76 (20.75)</td>
<td>42.92 (13.50)</td>
</tr>
<tr>
<td>Cortisol</td>
<td>107.64 (44.22)</td>
<td>107.72 (42.07)</td>
</tr>
</tbody>
</table>

In table 2 and 3 the results are presented of the hierarchical multiple regression analyses. Table 2 shows that in the first step 46% of the variance in the mean adrenaline excretion rate on the working day was explained by the morning level of cortisol, and the baseline value of adrenaline. At the following stage, a marginally significant increase in $R^2$ ($p=0.06$) occurred when the variables age, BMI, and %HR$_{max}$ were entered into the regression model. The variable %HR$_{max}$ contributed significantly. The third step showed a significant increase in $R^2$ ($p=0.03$) when the variables job demands and autonomy were entered. Only autonomy contributed significantly ($p<0.05$) in explaining variance in the mean adrenaline excretion rate on the working day. Tolerance figures were above 0.82 for all independent variables.
Table 2. Step-wise multiple regression with Adrenaline excretion rate on the work day of garbage collectors as dependent variable and Adrenaline excretion rate on the rest day, Morning level of Cortisol, Age, Percentage of the maximum Heart Rate (%HR\text{max}), Body Mass Index (BMI), Work demands, and Autonomy as independent variables (n=115).

<table>
<thead>
<tr>
<th>Step One</th>
<th>Step Two</th>
<th>Step Three</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Standard.*</td>
<td>p-value</td>
</tr>
<tr>
<td></td>
<td>regress. coeff.</td>
<td>of t-test</td>
</tr>
<tr>
<td>Rest day adrenaline</td>
<td>0.38</td>
<td>0.00</td>
</tr>
<tr>
<td>Morning level cortisol</td>
<td>0.51</td>
<td>0.00</td>
</tr>
<tr>
<td>Age</td>
<td>-0.11</td>
<td>0.15</td>
</tr>
<tr>
<td>%HR\text{max}</td>
<td>0.16</td>
<td>0.03</td>
</tr>
<tr>
<td>BMI</td>
<td>0.13</td>
<td>0.08</td>
</tr>
<tr>
<td>Work demands</td>
<td></td>
<td>0.03</td>
</tr>
<tr>
<td>Autonomy</td>
<td></td>
<td>0.18</td>
</tr>
<tr>
<td>$R^2$</td>
<td>0.46</td>
<td></td>
</tr>
<tr>
<td>Significance of change*</td>
<td>0.06</td>
<td></td>
</tr>
<tr>
<td>$F$ of regression equation</td>
<td>48.55</td>
<td></td>
</tr>
<tr>
<td>Significance of $F^*$</td>
<td>0.00</td>
<td></td>
</tr>
</tbody>
</table>

* = standardised regression coefficient (beta)
+= p-values
Durbin-Watson test = 1.97

Table 3 shows the outcomes of the hierarchical multiple regression analysis, in which the excretion rate of noradrenaline was used as dependent variable. The morning value of cortisol and the base line value of noradrenaline accounted together for 19% of explained variance in the mean noradrenaline excretion rate on the working day. A significant increase in $R^2$ occurred by the second step when the variables age, BMI, and %HR\text{max} were entered into the regression model (from 0.19 to 0.31, $p=0.00$). In the third step no significant contributions in explained variance occurred with the entering of the variables job demands and autonomy. Tolerance figures were above 0.81 for all independent variables.
Table 3. Step-wise multiple regression with Noradrenaline excretion rate on the working day of garbage collectors as dependent variable and Noradrenaline excretion rate on the rest day, Morning level of Cortisol, Age, Percentage of the maximum Heart Rate (%HR$_{max}$), Body Mass Index (BMI), Work demands, and Autonomy as independent variables (n=115).

<table>
<thead>
<tr>
<th></th>
<th>Step One</th>
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<th>Step Two</th>
<th></th>
<th>Step Three</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Rest day noradrenaline</td>
<td>0.33</td>
<td>0.00</td>
<td>0.23</td>
<td>0.01</td>
<td>0.23</td>
<td>0.01</td>
</tr>
<tr>
<td>Morning level cortisol</td>
<td>0.21</td>
<td>0.02</td>
<td>0.17</td>
<td>0.05</td>
<td>0.17</td>
<td>0.05</td>
</tr>
<tr>
<td>Age</td>
<td>-0.02</td>
<td>0.79</td>
<td>-0.02</td>
<td>0.85</td>
<td></td>
<td></td>
</tr>
<tr>
<td>%HR$_{max}$</td>
<td>0.31</td>
<td>0.00</td>
<td>0.32</td>
<td>0.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>0.19</td>
<td>0.03</td>
<td>0.19</td>
<td>0.04</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Work demands</td>
<td>0.04</td>
<td>0.63</td>
<td>0.01</td>
<td>0.91</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Autonomy</td>
<td>0.04</td>
<td>0.63</td>
<td>0.01</td>
<td>0.91</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

R$^2$ | 0.19 | 0.31 | 0.31 |
Significance of change* | 0.00 | 0.87 |
F of regression equation | 13.32 | 9.85 | 6.97 |
Significance of F* | 0.00 | 0.00 | 0.00 |

*= standardized regression coefficient (beta)
* = p-values
Durbin-Watson test = 2.045

Discussion

The neuroendocrine reactivity during a working day and a rest day, work characteristics, as well as physical workload were assessed in a field study on 115 Dutch garbage collectors.

Like in other field studies (e.g. Frankenhaeuser et al. 1989, Aronsson & Johansson 1987, Fibiger et al. 1986, Lim et al. 1987, Härenstamm & Theorell 1988, Evans & Carrère 1991, Van der Beek et al. 1995, Sluiter et al. 1998), the measurement of catecholamines took place via urine in order to get an overall view of the reactivity over large time periods. Cortisol has been measured more often in saliva (e.g. Houtman 1991, Jin 1992, Motohashi 1992, Fox 1993 & 1995, French et al. 1994, Burton et al. 1996). Investigating cortisol by urine sampling is preferred when an
overall picture of cortisol reactivity is the purpose of study. In urine, the excretion rate is measured over an exact period of time between two urinations.

The absolute mean values of adrenaline and noradrenaline during the working day and during the rest day were the same as found in a comparable field study on 32 lorry drivers (Van der Beek et al. 1995). Most field studies, in which comparable neuroendocrine assessments have been undertaken, contained far fewer subjects because of the time-consuming character and costs of this kind of research. The resting day was assessed as baseline. To get a more precise picture of recovery from work, it is recognised that it would have been more desirable to assess a consecutive day off between the working day and the resting day as well.

The work of garbage collectors is characterised by physical exertions and low control over the sequence of task performance. The laboratory measurements of the $\text{HR}_{\text{max}}$ by means of a maximal treadmill test made it possible to get an appropriate indication of the individual relative physical workload of the activities during the day by calculating the percentage of the maximum heart rate ($\%\text{HR}_{\text{max}}$). The physical nature of the job was confirmed by the significantly explained variance in noradrenaline reactivity by the $\%\text{HR}_{\text{max}}$ and BMI. This last finding was also found by Van der Beek et al. (1995). The excretion rate of noradrenaline is known to be a better indicator of physical than of psychological load. In addition, it is said that plasma and urinary noradrenaline may not be used as indicators of sympathetic effects of psychological activation (Ursin & Knardahl 1985). Both the significant influence of $\%\text{HR}_{\text{max}}$ and BMI on the mean noradrenaline excretion rate, and the finding that work characteristics had more impact on adrenaline than noradrenaline, confirmed the existing knowledge (Kuiper et al. 1998).

Possibly due to the similarity in work demands of the garbage collectors, and the therefore minor variation in scale scores, no influence of job demands on the catecholamines excretion rates was found. More contrast was found in the scale scores on autonomy. The level of autonomy alone is also known to influence experienced work stress (Karasek & Theorell 1990). This was confirmed in this study as this psychosocial work factor was found to be related to the adrenaline excretion rate during work. As adrenaline reactivity has often proved to represent mental workload, this outcome seems appropriate. Theoretically, the outcomes of the analyses could have been influenced by the fact that job demands and job control were not entered before the third step. However, the tolerance figures did not indicate multi-collinearity.
In this study, the hypothesis was tested whether the morning level of cortisol could have a facilitating influence on the mean adrenomedullary reactivity during a working day. Although the exact underlying mechanism remains unclear, the predictive power of the morning level of cortisol on the variance in adrenomedullary reactivity during a working day was confirmed. Together with the baseline values of the catecholamines, the morning level of cortisol on the working day explained 46% and 19% of the variance in reactivity in adrenaline and noradrenaline respectively. Because corticotropin excretion showed to be strongly related to cortisol excretion, this study confirmed the closer association between pituitary-adrenocortical activity with adrenomedullary activity compared to sympathoneural activity as was described by Goldstein (1995). The ‘forward facilitating hypothesis’ that was found in this study could have interesting implications when comparing fundamental animal and human brain research with field studies of this kind. In a review, Buijs (1996) described the possibility that, next to melatonin, the corticosterone peak serve to synchronise the activity of the suprachiasmatic nucleus (SCN) when constant dark conditions are present. Normally, the SCN controls the daily peak in plasma corticosterone and corticotropin. Earlier, Buijs et al. (1997) hypothesised that a circadian profile in transmitter secretion from SCN terminals is responsible for the 24-h rhythms in hormonal and behavioural patterns. Furthermore, cell atrophy was recently found in the SCN of passed away essential hypertension patients (Buijs, preliminary results). Hypothetically, this could cause a disturbance in SCN function and therefore in the daily peak of corticosterone. Hypertension has proven to be one of the possible long-term results of chronic work stress (e.g. Karasek & Theorell 1990). The findings of this study, therefore, could confirm that people with high peak levels of cortisol, and therefore higher mean adrenomedullary reactivity during the working day are more at risk in developing hypertension overtime.

Conclusions
The morning level of cortisol proved to be a more powerful predictor of reactivity in adrenaline than in noradrenaline during work. The association between the pituitary adrenocortical system and the adrenomedullary system could therefore be a ‘forward facilitating influence’. The level of autonomy contributed significantly in explaining adrenaline reactivity, but not noradrenaline reactivity. It is recommended for future research to focus on cortisol as predictor of neuroendocrine reactivity and to find out if this predictive power is expandable to work induced health complaints.
Acknowledgements

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