Individual differences in shift work tolerance
Lammers-van der Holst, H.M.

Citation for published version (APA):

General rights
It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations
If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: http://uba.uva.nl/en/contact, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.
“A good laugh and long sleep are the best cures in the doctor’s book”

Irish Proverb
Chapter 5

Individual differences in the cortisol awakening response during the first two years of shift work: a longitudinal study in novice police officers

Abstract
Cortisol acts as a critical biological intermediary through which chronic stressors like shift work impact upon multiple physiological, neuro-endocrine and hormonal functions. Therefore, the cortisol awakening response (CAR) is suggested as a prime index of shift work tolerance. Repeated assessments of the CAR in a group of 25 young novice police officers showed that in the interval between about four and 14 months after transitioning from regular day work to rotating shift work, mean values began to rise from baseline to significantly higher levels at about 14 months after they commenced shift work. Visual inspection of the individual trends revealed that a subgroup of 10 subjects followed a monotonically rising trend, whereas another 14 subjects, after an initial rise from about four to 14 months, reverted to a smaller, baseline level cortisol response at about 20 months after the start of shift work. If the initial increase in the cortisol response marks the development of a chronic stress response, the subsequent reversal to baseline levels in the subgroup of 14 participants might be indicative of a process of recovery, possibly the development of shift work tolerance.

**Introduction**

Shift work is a key feature of our contemporary 24/7 society, employing several successive work teams to sustain round-the-clock operations (Tucker & Folkard, 2012). However, numerous studies present results that imply, if not indicate, that the long-term experience of frequently shifting the periods of sleep and wakefulness poses a serious threat to the shift worker’s physical, mental and psychosocial health (Knutsson, 2003; Matheson et al., 2014; Morris et al., 2012b; Puttonen et al., 2010; Rajaratnam et al., 2013; Wang et al., 2011).

One of the major issues related to the adverse consequences of shift work concerns the impact of inter-individual differences. The most recent review, covering the period 1998 – 2009 (Saksvik et al., 2011), identified a total of 60 studies on inter-individual differences in shift work (in-) tolerance. This comprehensive review shows that most studies, in keeping with the definition as originally formulated by Reinberg and coworkers in 1979 (Reinberg et al., 1979), operationalized ‘tolerance’ in terms of subjective or objective measures of some aspect(-s) of health (only 1 study included ‘stress’ as outcome variable). Across studies, a rich diversity of indices of tolerance is found, ranging from subjective ratings of health, quality of sleep, fatigue, satisfaction with work schedule, and work-family conflict to objective measures of sleep, neurocognitive performance, obesity and mortality, thereby presenting a puzzling view on the concept of tolerance.

In an effort to avoid any ambiguity in the interpretation of the results, the present study favored an alternative output variable, a key variable that is more upstream in the cascade from shift work as stressor to multiple affected body tissues, i.e. cortisol. The most commonly studied physiological system that responds to stress is the HPA (hypothalamic-pituitary-adrenocortical) axis. Through this neuro-endocrine response system, a broad array of physical and psychosocial stressors increase the release of cortisol, thereby exposing multiple bodily tissues to elevated concentrations of this hormone. If sustained, this process is thought to lead to tissue damage and subsequent physiological disruption and dysregulation of biological systems, causing complex effects in brain structures like the hippocampus and amygdala, hypertension, immunosuppression, metabolic syndrome, cardiovascular disease, and many other health problems. Thus, cortisol acts as a critical biological intermediary through which chronic stressors like shift work impact upon
multiple physiological, neuro-endocrine and hormonal functions (see reviews by Clow et al., 2010; Fries et al., 2009; Miller et al., 2007).

Differences in these functions and their interactions are thought to underlie inter-individual variability in stress tolerance, also known as resilience (Feder et al., 2009). In the present, longitudinal study, inter-individual differences in shift work tolerance were measured by repeated assessments of morning cortisol in saliva (cortisol awakening response, CAR) in novice police officers in the course of their first two years of working in rotating shifts. The CAR, first established by Pruessner et al. (1997) and recently reviewed by Elder et al. (2014), refers to the phasic increase in cortisol levels observed immediately following awakening (Clow et al., 2004; Steptoe, 2007). The CAR is a distinct aspect of the cortisol profile as driven by the circadian control of the HPA axis, and is considered a genuine response to awakening, gearing up the body for the impending activity phase by increasing the amount of available energy (Elder et al., 2014; Kalsbeek et al., 2012). The CAR is considered a reliable marker of HPA activity and has been shown to exhibit a relatively high intra-individual stability across two consecutive days (Wüst et al., 2000). Evidence indicates that the CAR is positively related to work stress, adverse prior day experiences and anticipation of forthcoming challenges (Chida & Steptoe, 2009; Clow et al., 2010; Elder et al., 2014; Fries et al., 2009), suggesting the CAR as a prime index of shift work tolerance.

**Methods**

**Participants**

In this longitudinal study, 46 novice police officers (32 males, 14 females; ages 20–46 years, mean age 27) from two parallel classes of the Dutch police force academy volunteered to participate. At the start of the study, the police officers were near the end of their four-year training period. They reported to be in good health, had no psychiatric records, did not use medication and did not have any prior shift work experience. All subjects gave written informed consent. The study was approved by the Ethical Committee of the University of Amsterdam, and was conducted in accordance with international ethical standards (Portaluppi et al., 2010). A total of 25 subjects (16 males, 9 females; ages
20-44 years, mean age 28) completed the whole protocol of the longitudinal study successfully and were included in the data analyses. Reasons for attrition included reluctance to continue (N = 9) and incomplete records (N = 12).

**Study protocol**

Participants were tracked over a period of two years, during which they were tested four times. Baseline measurements (B) were taken while subjects were at the police academy and worked daytime (08:00-16:00). During three follow-up sessions (T1, T2, T3) the subjects worked full time in rotating shift work, with the exception of one class (11 subjects) that followed an eight-weeks daytime schedule in the interval between T1 and T2. During the initial period of four months, the novice police officers were closely supervised. The first, second and third follow-up sessions took place at respectively 15 ± 5 (mean ± SD; range 8-27) weeks (about 4 months), 55 ± 5 (range 44-65) weeks (about 14 months) and 82 ± 5 (range 75-93) weeks (about 20 months) after commencing shift work.

During shift work, the typical work schedule included three eight-hour shifts: morning shift (07:00–15:00), evening shift (15:00–23:00), and night shift (23:00–07:00), rotating in forward direction. Inter-session intervals did not differ in the numbers of night-shifts. Extended shifts (≥ 9 hours) occurred in 41% of all recorded workdays. Other roster specifications could not be calculated reliably, due to the high degree of ad hoc scheduling that is characteristic of field working police officers.

**Cortisol measures**

At baseline, saliva samples were collected during a period of day work (i.e. training at the academy). During the follow-ups, samples were taken during days of the morning shifts, hoping that the times of awakening would not differ substantially. As shown in Table 1, our hopes were fulfilled, since the times of awakening did not differ significantly between the measurement points. Saliva samples were collected immediately after awakening and again after approximately 30 and 60 minutes. As recommended by recent reviewers (Clow et al., 2010; Elder et al., 2014), the CAR was calculated as the mean post awakening increase in cortisol, MnInc (mean of cortisol values at 30 and 60 minutes after awakening minus cortisol value at awakening) (Wüst et al., 2000).
Saliva was collected using non-coated salivettes™ (Sarstedt, Nümbrecht, Germany). Participants were asked to refrain from smoking, eating, drinking or brushing their teeth for 15 minutes before each sample, to avoid contamination of saliva samples (Pruessner et al., 1997). At the designated times, the dental roll was placed in the mouth, under the tongue or between cheek and teeth for approximately two minutes, allowing saturation of the roll. Afterwards participants were instructed to store the saliva samples in the refrigerator. The salivettes were centrifuged (10 min, 2500 rpm) and stored at -20 °C in the laboratory within 24 hours after sampling. The concentration of cortisol was assayed by ELISA (DSL, Etten-Leur, the Netherlands). Sensitivity of assay was 1 ng/ml.

**Subjective measures**

The 20-item CIS questionnaire (Checklist Individual Strength), validated in working populations (Beurskens et al., 2000; Vercoulen et al., 1999) assesses four aspects of fatigue, i.e. Tiredness (8 items, e.g. “I feel tired”), Concentration (5 items, e.g. “I find it difficult to remain focused on one task”), Motivation (4 items, e.g. “I feel no desire to do anything”) and Physical Activity (3 items, e.g. “I don’t do much during the day”). For each item, the subjects rated (7-point scale) their approval/disapproval with the particular phrase, considering the past two weeks. The total score (Fatigue, range 7-140) was also calculated. Reliability of the questionnaire is high (Cronbach’s α = .90) (Vercoulen et al., 1994).

**Statistical analyses**

CAR values were analyzed with repeated-measures analysis of covariance (ANCOVA), with Session (B, T1, T2, T3) as independent factor and Class (2 levels) as covariate, and followed by post-hoc Bonferroni-adjusted comparisons if a statistically significant main effect was present. The time course of the CAR values was assessed on the basis of polynomial contrasts. Significance levels were determined after Huynh-Feldt correction.
Results

Overall trend

Mean values of cortisol, subjective fatigue and time of awakening are presented in Table 1. For the MnInc values, ANCOVA showed a significant Session effect ($F_{2,57} = 4.88$, $p < 0.01$), with significant quadratic and cubic trends ($p$-values $< 0.05$), see Figure 1. Post-hoc pairwise comparisons showed statistically significant differences between both the B and T1 sessions vs the T2 session ($p$-values $< 0.01$).

For subjective fatigue and time of awakening no significant differences were observed.

Table 1. Mean (± SD) values of the CAR (cortisol awakening response, calculated as MnInc), the CIS (Checklist Individual Strength) Fatigue score and time of awakening (N = 25).

<table>
<thead>
<tr>
<th></th>
<th>B</th>
<th>T1</th>
<th>T2</th>
<th>T3</th>
<th>Pairwise comparisons*</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAR</td>
<td>3.31 ± 2.9</td>
<td>4.11 ± 4.1</td>
<td>10.26 ± 8.07</td>
<td>7.24 ± 9.9</td>
<td>B &lt; T2; T1 &lt; T2</td>
</tr>
<tr>
<td>Fatigue</td>
<td>61.08 ± 24.4</td>
<td>58.28 ± 27.0</td>
<td>58.79 ± 21.7</td>
<td>53.64 ± 21.2</td>
<td>n.s.</td>
</tr>
<tr>
<td>Time of awakening</td>
<td>06:32 ± 0:30</td>
<td>06:10 ± 1:48</td>
<td>06:22 ± 1:36</td>
<td>05:59 ± 1:12</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

* $p < 0.01$.

Individual trends

Apart from the overall trend of the successive mean cortisol values, Table 1 and Figure 1 show a marked increase in their dispersion (in particular for T2 and T3 vs B and T1), suggesting the potential influence of inter-individual differences. Visual inspection of the individual trends confirmed that individuals could be differentiated into two subgroups. Ten subjects (5 females, overall mean age: 26 years) followed a monotonically rising trend (dubbed ‘non-adapters’), whereas 14 subjects (4 females, overall mean age: 27 years)
showed a trend reversal after T2 (‘adapters’; see Figure 2). For this subgroup analysis, one male subject was excluded because of his inconsistent trend. Repeated-measures ANCOVA with Subgroup (2) as between-subjects factor, Session (4) as within-subjects factor and Class as covariate showed a significant Session effect ($F_{3,63} = 5.96, p < 0.01$) and a significant Subgroup x Session interaction ($F_{3,63} = 9.39, p < 0.001$). Post-hoc tests clarified that baseline and T1 values did not differ significantly between the two subgroups, whereas the T2 values ($t_{22} = -2.45, p < 0.05$) as well as the T3 values ($t_{22} = 3.77, p < 0.01$) differed significantly between the subgroups. In addition, paired-sample t-tests corroborated the impression given by Figure 2, i.e. that the T3 values for the non-adapters differed significantly from their B values ($t_{9} = -5.75, p < 0.001$), whereas the T3 values for the adapters did not differ from their B values ($t_{13} = 0.57, p > 0.50$). ANCOVA’s of the overall CIS Fatigue score and the scores on the scales Tiredness, Concentration, Motivation, and Physical Activity did not show any statistically significant effect.

Figure 1. Mean (± SEM) cortisol awakening response (MnInc) values for the baseline (B, day work) and 3 follow-up (T1-T3, shift work) sessions.
Discussion

Repeated assessments of the CAR in a group of 25 young novice police officers showed that in the interval between about four and 14 months after transitioning from regular day work to rotating shift work, mean values began to rise from baseline to higher levels at about 14 months after they commenced shift work. Visual inspection of the individual trends revealed that a subgroup of 10 subjects followed a monotonically rising trend, whereas another 14 subjects, after an initial rise from about four to 14 months, reverted to a smaller, baseline level cortisol response at about 20 months after the start of shift work. If the initial increase in the cortisol response marks the development of a chronic stress response, the subsequent reversal to baseline levels in the subgroup of 14 participants might be indicative of a process of recovery, possibly the development of shift work tolerance.

Shift work is well known to result in a dysregulation of the circadian timing system, involving the circadian output to the HPA axis and its role in the transmission of circadian...
Individual differences in the cortisol awakening response during first two years of shift work

information throughout the body (Kalsbeek et al., 2012). In addition, shift work provokes a range of sleep disturbances (Åkerstedt, 2003), all of which have also been associated with modifications of the cortisol response (Elder et al., 2014). As a consequence, shift work most probably has an effect on the CAR through its effect upon the circadian system, its effect upon the quality of sleep and its impact as stressor.

During the initial months, the demands of a new job including shift work seemed not to tax the stress system, as suggested by the absence of any difference in the baseline vs 4-month cortisol values. Only after this initial period, cortisol increased significantly. This trend resembles the ‘sleeper effect model’ as described by Frese and Zapf (1988; cited in Bradley, 2007), stating that job stressors may have little initial impact and may begin to cause problems only after a lengthy period of exposure. Bradley (2007), drawing on Karasek’s (1979) ‘job demands - control - support’ model, points out that, in general, the job environment of novice workers is substantially different from that of experienced workers. In the initial stages of employment, when the new-starter is closely supervised and coached in dealing with unfamiliar and perhaps unanticipated job stressors (as was certainly true for the police officers of the present study), there is a condition of high social support and high sense of job control, moderating (buffering) the stress-inducing effects of new job demands. In addition, for the present study this buffering effect is likely to have benefited from the young age of the participants, as reported in many previous studies (Saksvik et al., 2011). Thus, the delayed cortisol response may be interpreted as a consequence of the delayed introduction of the full-blown, unmasked set of demands of the new shift work job.

In the same vein, the difference in CAR trends observed in the present study may be attributed to inter-individual differences in getting a grip on the new job demands. Apparently, the majority of novice police officers learned new strategies to cope with the job demands and/or had a genetic background or phenotype favoring resilience (De Kloet et al., 2005; Karatsoreos & McEwen, 2013), and as a consequence, the impact on the HPA axis that existed earlier dissipated over time. Thus, these participants appeared to have habituated (Grissom & Bhatnagar, 2009) to the conditions of their new job, whereas the other subgroup of participants probably did not, as suggested by their still increasing cortisol levels. These results match those of earlier studies (see reviews by Chida &
Steptoe, 2009; Elder et al., 2014), demonstrating that the levels of perceived workload and lack of control are positively related to the magnitude of the CAR. The study by Brant and colleagues (2010) comes closest to ours, showing that in a sample of novice doctors, greater CARs were observed at the beginning of a clinical rotation, characterized by greater uncertainty and perceived lack of control, as compared with the end of the rotation, 3-4 months later (Brant et al., 2010). Another similarity between the two studies relates to the constancy of self-report measures across the successive time-points, suggesting no perceived change in well-being on a subjective level. Alternatively, responses could have been affected by social desirability and the particular occupational culture (the police culture is often described as ‘macho’), that might have acted to suppress admissions of stress-related or emotional problems (Kop & Euwema, 2001).

Besides strengths (longitudinal design, assessment of subjective and objective stress responses), this study also has limitations. All participants started simultaneously with a regular job and shift work. The inclusion of a control group working only day shifts would have allowed differentiating between the impacts of these two stressors. Unfortunately, organizational limitations prevented this. Through internships during their formal training at the police academy, however, participants were quite knowledgeable of the organizational and substantive aspects of their new job. Thus, it is speculated that the major impact of their transition to a regular job could be attributed to shift work.

The time span of this longitudinal study was restricted to an average of 20 months after the regular job start, mainly due to time limits set by the police organization as well as the grant provider. It cannot be ruled out that the distinction between the two subgroups does not follow from a distinction between ‘adapters’ vs ‘non-adapters’, but rather a distinction between fast vs slow adapters. It certainly would be worthwhile pursuing the long-term development of the resilience of shift workers, in association with known covariates like age, health, family condition and organizational changes.

The present study has calculated the CAR as the mean post awakening increase in cortisol (MnInc), as recommended in a recent review (Elder et al., 2014). This review also notes that the CAR is sensitive to the effects of methodological factors, particularly those pertaining to the timing of samples. The sampling resolution as applied in the present study was rather low, i.e. at the moment of awakening and 30 and 60 minutes later. Thus, it is
conceivable that for some subjects the peak value of their CAR was missed, considering that peaking can be expected to occur 30 - 45 minutes post-awakening (Clow et al., 2004; Fries et al., 2009). It is unlikely, however, that this error component was systematically associated with the repeated-measurement factor of the present study.

Finally, it is possible, or most probable, that an alternative selection of subjective variables would have led to a different perspective on the covariation between cortisol and subjective variables. Reviewing the relevant literature, Hellhammer and colleagues (2009) have noted that not only neuro-endocrine factors account for the limited association between cortisol and subjective-psychological stress responses, but also factors related to the assessment of perceived stress by self-report methods. So, in order to capture the multidimensional concept of (in-)tolerance for shift work, future studies preferably adopt multivariate measurements, subjective as well as objective.