



## Measuring Occupational Stress and HRA Axis Dysregulation among Healthy Workers by Salivary Cortisol Levels

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### Authors' contributions

*This work was carried out in collaboration between all authors. Author TCC designed the study, author EM wrote the protocol, and wrote the first draft of the manuscript. Author MM managed the literature searches. All authors read and approved the final manuscript.*

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### ABSTRACT

**Background:** Salivary cortisol is a useful biomarker in stress research, as a valid measure for HPA axis activity, whose deregulation is one of the ways that psychosocial risk factors at work, result to the creation of illness.

**Aim:** The aim of this review was to summarize current literature of salivary cortisol as measures of work stress in healthy workers, so as to investigate the association between work stress and cortisol secretion as well as to identify specific work characteristics, that affect the cortisol secretion.

**Methods:** We identified articles through PubMed using search terms related to salivary cortisol, HPA axis, work stress.

**Results:** Many studies have shown that altered level of cortisol, appears to be associated with work related stress factors. Work shift, working hours, the nature of work, organizational characteristic of work (effort reward imbalance, high demand-low control, over-commitment, conflicts between home and work demands, and workload) as well as bullying at work, socio-

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demographic characteristics, financial strain, physical risk factors and social support at work are found to affect Cortisol levels. Though the relationship between the cortisol secretion and some of the above work stressors was found to be contradictory.

**Discussion:** From the present study it is obvious that the researches present an inconsistency regarding the impact of work stressors on cortisol levels.

It has been identified that increased cortisol levels in populations reporting increased distress couldn't replicate this association. Among the reasons identified to be behind these inconsistent findings are the differences in the prevalence of potential confounders, differences in analytical approach and the duration of stressful stimulus.

**Conclusion:** The detailed knowledge about factors that play pivotal role in measures of the cortisol secretion is very important, as the biomarkers have been demonstrated that can characterize and quantify the biological impact of psychological stress. Targeted prevention policy and evidence based interventions in workplace might include the identification of sources of occupational stress and this is the first that can affect cortisol secretion.

*Keywords: Occupational; stress; cortisol; HRA axis; work stressors.*

## 1. INTRODUCTION

Stress, up to a certain point, will improve people's performance and quality of life [1]. If stress is intense, continuous, and repeated, it becomes a negative phenomenon or "Distress". The negative stress and it can lead to physical illnesses [2] (psychological disorders [3], psychopathology [4-6], low psychological well-being [7,8] unhealthy habits [9], reduced productivity [10] and problems with memory and learning [11]. It's believed that chronic stress is responsible for 90% of Psychosomatic illnesses [12].

Experimental and clinical evidence suggest that one biological system thought to be important in linking stressor exposure to disease, is the hypothalamic-pituitary adrenocortical (HPA) axis [13], and this is the reason why the role of chronic stressors in cortisol response has received considerable attention [14]. Cortisol is one of neuro-endocrine markers that make up the main products of adrenocortical activity in response to the adrenocorticotrophic hormone (ACTH) and plays an important role in establishing human responses to stressful events and appears to be a valid measure for the HPA axis activity [13,15].

Cortisol secretion shows profound circadian rhythmicity [16,17] as it is high early in the day, then decreases over the remainder of the day and evening [18]. A study suggests that although the cortisol awakening response is modulated by circadian influences, it primarily reflects phasic psychophysiological processes specific to the sleep-wake transition [18].

The rapid increase and peak in cortisol level after awakening is termed the cortisol awakening response (CAR) [19] and has received much attention as regards the investigation of chronic psychological stress [13,16,20-24]. Other components of the cortisol profile that have been investigated are the height of cortisol curve across the waking hours [25], slope of decline over the day [25,26] the level of cortisol in the evening [27-29], and the area under the curve (AUC<sub>G</sub>) [30].

Studies of the past decade have shown that saliva samples present various advantages versus blood samples [31,32], and provide a useful procedure for cortisol measurement as the salivary cortisol (Sa-Cor) reflects the free plasma cortisol [33,34]. All of the above have been confirmed in recent research [35,36].

In psychophysiology, salivary cortisol sampling is frequently used to unravel the body's response to different stressors [14], and as work stress is one type of chronic stress, physiological monitoring under the naturalistic conditions of everyday work life is a powerful tool in the investigation of psychosocial work influences on health [18].

Due to the fact that occupational stress can emerge from various aspects of work such as organizational factors at work or the nature of work itself, it would be useful to identify the specific characteristics of work environment, which can affect cortisol secretion thus leading to illness.

## 2. AIM

The aim of this review was to summarize current literature of salivary cortisol as measures of work stress in healthy workers, so as to investigate the

relationship between work stress and cortisol secretion as well as to identify specific work characteristics that affect the cortisol secretion.

### 3. METHODS

We identified articles through PubMed using search terms related to salivary cortisol, HPA axis, work stress.

### 4. RESULTS

#### 4.1 The Relationship between Work-Related Stress and Cortisol Secretion

Most studies have examined the effects of psychosocial job strain on the cortisol secretion but results are frequently inconsistent.

In many studies cortisol secretion shows responsiveness to physical and psychological stressors [17,23], with disruptions in its diurnal rhythms among people exposed to chronic stress [13,25,27].

The cortisol secretion has been found in a number of studies to be positively associated with stress [7,8] particularly in chronic [13,20,37], or acute work stress [38,39].

Another suggestion that cortisol can be affected by work-related stress derives from studies which have shown that the hypothalamic-pituitary adrenocortical axis activation was higher during workdays than at weekends, [40-44]. According to studies' findings, differences may be explained by chronic work overload and worrying[40] and cortisol was an average of 21.7% higher early in the working day in the high strain job group [20].

Adversely in other studies, the level of salivary cortisol was lower in the high-strain group than in the low-strain group and during the acute stress phase decline in cortisol levels was more prolonged and steeper [45], whereas in another study, cortisol was higher on leisure days than work days [46].

In contrast to the above studies neither psychosocial factors at work [47] or acute stress due to the examination [48], or due to clinical practicum [49] or difficulties in emotion regulation or chronic stress [50,51], had significant relationship with cortisol levels. This is in line with an investigation that has observed no differences in the daytime cortisol levels between workdays and the weekend [52]. In a study with emergency

physicians the perceived stress levels assessed with Psychosocial Questionnaire, were significantly higher than in the general population but were not associated with Cortisol levels [53].

The present review has summarized studies which had investigated work factors that seem to be sources of job-related stress and had explored their relationship with the deregulation of the HPA axis, through changes in the cortisol level. These factors have to do with either the nature or the specific conditions or organizational characteristics of the job.

#### 4.2 Work Shift

Study in fourteen subjects, (emergency care providers) showed that there was a significant time effect, with early morning cortisol levels being significantly attenuated following the 24 hour work shift [24]. On the other hand night work was associated with a 4.28% increase in cortisol secretion (in samples that were taken 3 h and 45 min after waking) [54], whereas the concentration of salivary cortisol on a dayshift was significantly lower [55].

A study among 47 bus drivers, showed higher cortisol morning-evening difference in the afternoon, versus morning shift employees [56], whereas a study among Finnish media work staff showed, that irregular shift work, severe stress, and less sleep, were independently associated with an augmented cortisol response after awakening [57].

#### 4.3 The Nature of Work

Meta-analysis reviews of 208 laboratory studies of acute psychological stressors showed that psychological stressors increased cortisol levels; however, effects varied widely across tasks. Tasks that were uncontrollable or characterized by social-evaluative threat (task performance could be negatively judged by others), elicited cortisol responses [58].

#### 4.4 Effort-reward Imbalance (Eri) At Work

According to Siegrist's work stress model, effort reward imbalance (ERI) reflects stress due to a lack of reciprocity between personal costs and gains at work, whereas over commitment (OC) is conceptualized as a personality trait mainly characterized by the inability to withdraw from work obligations.

In a study OC was significantly associated with lower salivary cortisol responses [59]. Adversely, in another study neither effort—reward imbalance nor over commitment predicted biological responses in women. The same study found more pronounced cortisol awakening responses and higher cortisol output over the working day in employed men who were over committed to their job [60] (Steptoe et al. 2004). This is in line with a study, where cortisol response to waking as well as cortisol averaged from 8 samples over the working day, were positively associated with over commitment in men.

In contrast, individuals scoring higher in effort-reward imbalance at work had both lower cortisol awakening response, and lower diurnal secretary activity [13]. ERI was also negatively and significantly associated with salivary at awakening (S0) for women and positively associated with CAR [61].

#### **4.5 High Demand Low Control at Work**

Job demand refers to the workload, and has been operationalized mainly in terms of time pressure and role conflict. Job control refers to the person's ability to control his or her work activities [62].

Interestingly, workers suffering from high demand and/or low control showed increased cortisol output over the working day [41] and especially elevated cortisol awakening response [20,40,47] Later the first clear-cut experimental evidence regarding the idea that the negative impact of high job demands on endocrinological responses was given. Endocrinological responses can be buffered by high levels of job control as high control eliminated the impact of high demands on salivary cortisol responses and high demands led to increased cortisol reactions only in the low control conditions [63]. Similarly in Alderling's study, women in low strain jobs (high control and low demand) had significantly lower saliva cortisol half an hour after awakening than women in high strain jobs (low control and high demand), active (high control and high demands) or passive jobs (low control and low demand) [64]. In addition according to a study the participants who reported higher levels of chronic work overload and worrying, showed a stronger increase and higher mean levels of cortisol after awakening on weekdays, but not on weekends [40].

#### **4.6 Objective Workload**

Study that subjective stress was recorded with each sample of cortisol and at shift end Objective workload for each shift and nursing unit was derived from the hospital's LEP Nursing Workload Management System show that the Subjective stress was significantly related to increased cortisol secretion whereas Objective workload was not [65].

#### **4.7 The Amount of Working Hours**

The salivary cortisol levels of subjects who worked less than or up to 5 days per week and graduated from the university were significantly lower at 8:00 am, compared to those who worked more days and had lower education level.

A study among 200 women in Sweden suggested, that participants with excessive overtime (more than 10 h/week) had on average about twice as high morning cortisol levels as women with moderate overtime (< 10 h/week) or normal working hours (35-40 h/week) [66]. The positive association between the number of work hours per week and cortisol concentrations during these days has been confirmed by a recent study [67]. According to the same study, work hours act as a stressor that is associated with significant variations in cortisol concentrations over working days. Non-working days may contribute to stress reduction in workers who experience longer work hours [67].

On the contrary in an experimental study, in which 16 white-collar workers undertook one work week with normal working hours (8 hours) and 1 week of overtime with 4 extra hours of regular work tasks (12 hours), it was proved that one week of overtime work with a moderate workload produced no main effects on physiological stress markers (salivary cortisol) [68].

#### **4.8 Bulling at Work**

A study that measured saliva cortisol as putative markers in individuals suffering from bulling at work, did not find significant difference between groups in cortisol levels at any time, nor in area under the curve (AUC) and cortisol awakening response (CAR) [69].

On the other hand, Hansen in his study on the associations among being subjected to bullying,

health outcomes, and physiological stress response, found that concentrations of cortisol in the saliva, were lower at awakening in bullied respondents compared with non-bullied ones [70] whereas the same association among cortisol and being bullied was found in a more recent study [71]. In the same study frequent bullying was associated with lower salivary cortisol concentrations but no such association was observed for occasional bullying [71].

#### **4.9 Conflicts between Home and Work Demands**

Individual differences in mothers' morning cortisol levels, cortisol decrease across the day and average cortisol levels were predicted among other factors, by maternal relationship functioning, home and work demands. Those variables accounted for 40% of the variance in mothers' morning cortisol values, 43% of the variance in cortisol slopes and 35% of the variability in mothers' average cortisol levels. More hours of maternal employment and a greater number of children in the household were associated with lower morning cortisol values and a less steep decline in cortisol levels across the day [25].

#### **4.10 Financial Strain**

Financial strain is usually analyzed as an indicator of chronic psychosocial adversity [18]. Elevated levels of cortisol in the evening were positively associated with financial strain in a sample of long-term unemployed women, with a near significant effect in men [27]. Steptoe in a longitudinal study hypothesized that if improved financial strain has beneficial biological consequences, it would be associated with lower blood pressure and a smaller CAR than would be recorded in people for whom financial strain had not changed or worsened. As regards its results, men who reported an improvement in financial strain had a lower CAR in comparison with those in the worse/no change group. There was no difference in women. There were no differences in the slope of cortisol decline over the day or in evening values [18].

#### **4.11 Social Support**

As regards the association of perceived social support and cortisol secretion, study showed that negative work characteristics in terms of high demands and low social support contributed

significantly to the biological stress levels in middle-aged women [37].

Study that provided data on salivary cortisol concentrations in a large (990 subjects) middle-aged community sample, find that higher perceived social support was associated with lower  $AUC_G$  and smaller slope (area under the curve ( $AUC_G$ )) [30], whereas study in sample of 257 men and women aged 30 to 64 years, steeper diurnal rhythm was related to social support [72]. According to Evans and Steptoe, (2001), work social support was not related to cortisol on work days, but on leisure days, cortisol was elevated among individuals reporting high social support [73].

#### **4.12 Physical Risk Factors at Work**

In recent years, levels of stress hormones (i.e., catecholamine and cortisol) have been used to evaluate the physiological effects of noise. Many laboratory experiments and some epidemiological studies suggest that noise may elevate the stress hormone levels [74-76].

Study to demonstrate an effect of low frequency moderate levels of noise at work on neuroendocrine activity suggested that the normal circadian decline in cortisol concentration was however significantly attenuated in subjects with high-sensitive to noise in general, when they were exposed to the noise [77].

#### **4.13 Other Organizational Risk Factors at Work**

In study that compared stress between nurses at general wards and emergency department showed that low morning salivary cortisol was negatively correlated with PSS (mental health professional stress scale) scores of organizational structure and process, and conflict with other professionals. The difference between morning and afternoon cortisol concentration in ED nurses was lower than in GW nurses. The low value of the difference correlated marginally with PSS and significantly with scores of organizational structure and process, lack of resources, and conflict with other professionals [78].

### **5. DISCUSSION**

In the present study, we investigated the relationship between work-related stress factors and cortisol secretion. From the present study it is obvious that the researches present an

inconsistency regarding the impact of work stressors on cortisol levels. While there is a substantial literature that has identified increased cortisol levels in populations reporting increased distress [13,20,37] several investigations have failed to replicate this association [47-51,55,78].

One reason behind these inconsistent findings may be the differences in the prevalence of potential confounders such as smoking habits [79], gender [80], age [81], socioeconomic position [82], sampling factors [83], sampling time [84], time of awakening [19,85,86], alcohol consumption, body mass index, and medication between study samples [64].

Additionally Vedhara et al. [87] believe that some of the factors which increase the likelihood of variance and inaccuracy in the determination of cortisol and potentially contributing to the apparent equivocal relationship between emotional distress and cortisol, is the inherent variability in cortisol levels both between and within individuals effects of time of day, medication, or food in-take and differences in analytical approach (e.g. area under the curve, single versus multiple measures, delta values etc).

Apart from the above factors that are often regarded as confounders, there are others that rarely had taken into account in research. For instance in a single case study which examined the relationship between intra-individual changes in measures of the CAR and psychosocial state variables, it was shown that a considerable amount (22%) of the intra-individual variability in the dynamic of the CAR, can be explained by taking into account both prior-day levels of sadness/happiness and anticipations about the level of obligations/no leisure for the study day [50]. This is in line with results of a study that found a positive association between the factor lonely/sad/overwhelmed the previous days and the dynamic of the CAR [29]. In addition, social relationships with parents in childhood may have lasting effects on cortisol levels well into middle and later life [88].

Although in this study, surveys addressing healthy subjects were selected, possible conditions like chronic fatigue or burnout may not be treated as a disease and as a criterion for exclusion from the sample of studies. Never the less it has been discovered that subjects with pronounced symptoms of exhaustion such as the chronic fatigue syndrome are unable to raise

their cortisol level in challenging situations and they also show very small circadian variation ("low flat curves"). These physiological processes may lie behind some of the contradictory findings [64].

The work shift appears to be one of the factors which affect the secretion of cortisol. Workers in the afternoon [56] and night work shift [54] show pronounced deviations from the daily pattern of cortisol secretion, as this appears to be increased.

The reduced levels of morning cortisol after a 24 hour work [89], can be attributed as indicative of a long-term response to chronic stress [90], since it seems that the duration of stressful stimulus plays an important role in cortisol response. Friedman et al. [91] examined how longer-term histories of social conflict covering approximately a decade relate to current diurnal cortisol rhythms and find that cortisol rhythms of individuals with higher levels of social conflict are much flatter than those of their counterparts. These effects are slightly more pronounced for those individuals with a history of social conflict over a ten year period.

So while there is systematic research on 208 laboratory studies that confirms the increase of cortisol induced by acute stress [58] a lot of studies present reduction of cortisol in chronic work stressors, like Effort- reward imbalance (ERI) at work [13], bullying at workplace [92] and financial strain [18].

Another factor that could be of importance to these contradictory findings is the definition of "awakening". Whether subjects physically rise to their feet or not has been shown to be unimportant therefore the point of "awakening" needs to be defined in a sufficiently standardized way [17].

## 6. CONCLUSION

The psychobiology of stress has received increasing attention throughout the past two decades. The hypothalamic-pituitary-adrenal (HPA) axis is a key component of the body's physiological regulatory machinery that orchestrates patterns of physiological adaptation to the stimuli and conditions we confront throughout the course of our lives.

Physiological monitoring under the naturalistic conditions of everyday life is a powerful tool in the investigation of psychosocial influences on

health [93]. A pivotal method that has emerged over recent decades is periodic cortisol sampling [18].

Despite growing evidence suggesting important associations between the cortisol secretion and some work stressors, there still remains uncertainty as the studies' findings on the role of the hypothalamo-pituitary-adrenal axis in some stressors is contradictory [16,22].

Given this unsatisfactory situation, it is important to identify potential reasons for such inconsistencies, as a crucial prerequisite in cross-sectional research is the availability of detailed knowledge about factors that play pivotal role in measures of the cortisol secretion [50].

Subjective stress, but not objective, was significantly related to increased cortisol secretion [65]. The salivary cortisol level has been associated with organizational characteristics of work, like job demands [41], low control condition [63], over commitment [60], conflicts among home and work demands [25], social support [30], organizational structure and process, lack of resources, and conflict with other professionals [78]. The question of the effect's direction in cortisol level due to the existence of effort-reward imbalance [13,60] and bullying [70] in workplace, remains.

Cortisol has also been found to be affected by job factors such shift, weekday, nature of task [58], the amount of working hours [84] as well as financial strain [27] and noise [76].

Potential confounders such as the smoking habit [79], gender [80], age [81], socioeconomic position [82] sampling factors [30], alcohol consumption, body mass index, and medication between study samples [64], prior-day levels of sadness/happiness and anticipations about the level of obligations/no leisure for the study day [50], emerge among the studies. Whether these modulating factors are considered as confounders or as important part of the information certainly depends on the research question [94].

Monitoring cortisol excretion as measure of subjective work stress may be useful among individuals who are working in occupations with a high risk of HPA axis strain [57,95].

Biomarkers can help characterize and quantify the biological impact of psychological stress [93,96], and therefore be used as a valid tool for evaluation of workplace interventions, in order to determine the targets for organizational changes in workplace [65,97-100].

## CONSENT

Not applicable.

## ETHICAL APPROVAL

Not applicable.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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