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The relationships of working conditions, recent stressors and childhood trauma with salivary cortisol levels

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Summary
Background: An etiological model has been suggested where stress leads to high cortisol levels and hypothalamic—pituitary—adrenal (HPA) axis dysregulation, resulting in somatic diseases and psychopathology. To evaluate this model we examined the association of different stressors (working conditions, recent life events and childhood trauma) with various cortisol indicators in a large cohort study.
Methods: Data are from 1995 participants of the Netherlands Study of Depression and Anxiety (NESDA). Most of the selected participants had a current or remitted anxiety and/or depressive disorder. Working conditions were assessed with self-report questionnaires, life-events and childhood trauma were assessed with interview questionnaires. Cortisol levels were measured in seven saliva samples, determining the 1-h cortisol awakening response (CAR), evening cortisol levels and cortisol suppression after a 0.5 mg dexamethasone suppression test (DST).
Results: Regression analyses — adjusted for covariates — showed two significant associations: low social support at work and high job strain were associated with more cortisol suppression after the DST. No other associations were found with any of the cortisol variables.
Conclusions: Working conditions, recent stressors and childhood trauma were not convincingly associated with cortisol levels.
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1. Introduction

Stress is thought to lead to a hyperactive hypothalamus–pituitary–adrenal (HPA) axis and, when chronic, the resulting high cortisol levels may contribute to somatic diseases and psychopathology (Sapolsky, 1998). Evidence for elevated cortisol levels are for example found among persons with obesity or ischemic heart disease (Reynolds et al., 2010), hypertension or diabetes mellitus (Schoorlemmer et al., 2009) and atherosclerosis (Eller et al., 2005; Dekker et al., 2008). In addition, hyperactivity of the HPA-axis was found among persons with depression (Vreeburg et al., 2009a) and anxiety disorders (Vreeburg et al., 2010a). A central assumption is that underlying stress exposure and experience are related to altered HPA axis activity.

To assess basal HPA-axis activity, salivary cortisol measures are often used. The cortisol awakening response (CAR) reflects the natural response of the HPA-axis on awakening (Wilhelm et al., 2007), is associated with the circadian rhythm of cortisol secretion and is considered to be regulated in anticipation of demands of the upcoming day (Fries et al., 2009). The CAR is preferable to single morning cortisol measurements since it has a greater intra-personal stability (Coste et al., 1994; Wüst et al., 2000) and is considered to be a more reliable measure for the acute reagibility of the HPA-axis (Schmidt-Reinwald et al., 1999). Evening cortisol levels reflect basal activity, whereas the dexamethasone suppression test (DST) examines the reactivity to a pharmacological challenge of the stress system.

Prior studies have examined the impact of various different types of stressors on HPA-axis functioning in adulthood. Stressors examined so far differ in their recency and timing across the lifespan (e.g. recent stressors versus stressors that occurred in early life) and in their severity (traumatic versus more normative), which make research findings not easily comparable across studies. Moreover, some studies have indicated that chronic hyperactivity of the HPA-axis in response to early chronic or traumatic stressors results in a possible adaptational pattern of decreased cortisol levels in later life. This may explain why also lower cortisol levels have been found among persons with stress-related conditions like chronic fatigue syndrome, fibromyalgia and posttraumatic stress disorder (Heim et al., 2000a; Fries et al., 2005; Miller et al., 2007; Pervanidou, 2008) and would suggest that the impact of early-life stressors (such as childhood trauma) may even be reversed as compared to recent stressors that take place in later life (such as job stressors or recent life stressors) (Gerritsen et al., 2010).

To assess the negative effects of *work stressors*, the job demand-control model is frequently used. This model assumes that job strain is the combination of high job demands with low job control, also called decision latitude. Job strain has been positively associated with morning cortisol (Steptoe et al., 2000; Alderling et al., 2006) and CAR levels (Maina et al., 2009a,b). The CAR also has been positively associated with high job demands in men and with low decision latitude in women (Maina et al., 2008). Furthermore, higher evening saliva cortisol levels were associated with high job strain (Rystedt et al., 2008). In contrary, others found higher saliva cortisol levels among subjects reporting low job strain (Steptoe et al., 1998; Fujiwara et al., 2004). Also when considering other theoretical concepts for job stress such as the effort–reward imbalance model, overall results for HPA-axis activity are conflicting (Chandola et al., 2010). The clearest evidence for job characteristics on HPA-axis activity in a recent meta-analysis appeared to exist between high job stressor levels and a high CAR (Chida and Steptoe, 2009).

Studies on *recent life events* and HPA-activity are difficult to compare, since the assessment of life events vary in time. Associations have been found between increased morning cortisol and life events during the last three years (Gerritsen et al., 2010) and between increased evening cortisol and life events within a month but not within six months (Strickland et al., 2002). In contrast, another study found no associations between morning or evening cortisol and life events within one to six months (Harris et al., 2000).

It has also been hypothesized that particularly *childhood trauma* leads to alterations in HPA-axis regulation (Nemeroff, 2004; Carpenter et al., 2007). However, results are conflicting. Some studies have indicated that persons exposed to childhood trauma in the past have indications of higher basal or reactive cortisol levels later in life (Heim et al., 2001, 2000b, 2008; Rinne et al., 2002; Faravelli et al., 2010). On the contrary, others showed negative childhood events to be associated with lower morning or reactive cortisol levels (Elzinga et al., 2008; Gerritsen et al., 2010), which could be explained by the fact that adaptational processes result in hypocortisolism later in life. These inconsistent findings have not been clearly explained yet, but it has been hypothesized that exact timing, severity of trauma, or co-occurring psychopathology such as PTSD or depressive disorder might play a moderating role in the link between trauma and HPA-axis functioning (Heim et al., 2000b, 2008; Elzinga et al., 2008).

Taken together, there is evidence that different types of stressors generally are associated with HPA-axis functioning. Mainly higher HPA-axis activity has been observed for recent stressors such as job stressors and recent life events, but for childhood trauma both higher and lower HPA-axis functioning have been observed. Since results have not always been consistent, there is a need for further research. Studies on the association of stressors and HPA-activity with a large cohort are scarce, especially with a broad set of stressors and cortisol measurements and covariates. Therefore, we examined the relationship between work stressors, important life events and childhood trauma with various salivary cortisol measures (cortisol awakening response, evening level and suppression after dexamethasone), correcting for detailed covariates.

2. Methods

2.1. Study sample

Data are from the Netherlands Study of Depression and Anxiety (NESDA), a large cohort study on the course of depressive and anxiety disorders. In total 2981 respondents participated in the study. Included were 652 subjects with no current or past psychiatric disorders ('healthy controls') obtained through a screening approach conducted among 65 general practitioners, as well as 628 subjects with earlier and 1701 subjects with current episodes of depressive or

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