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Salivary cortisol and depression in public sector employees: Cross-sectional and short term follow-up findings

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Summary
Introduction: Increased cortisol levels have been suggested to play a role in the development of depression. An association has been shown in some studies but not consistently. The timing of an association is uncertain, and long-term follow-up studies may miss associations in narrower time windows. In the present study, we examined the association of several cortisol measures and depression in a repeated cross-sectional and short-term follow-up design. Depression was assessed by both self-reported symptoms of depression and clinical interviews.

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Method: In 2007, 10,036 public sector employees received a questionnaire along with salivary cortisol test tubes for home administration. Morning (30 min after awakening) and evening (2000 h) salivary samples were collected. Questionnaires and valid saliva samples were returned from 3536 employees. Approximately 3.6 months later a subsample of the participants collected three morning saliva samples (at awakening, 20 min and 40 min after awakening) plus an evening sample (2000 h); participants with high baseline scores of self-reported depressive symptoms, burnout and perceived stress were invited to a standardized interview (SCAN) to detect clinical depression; and the symptom questionnaire was repeated for subsample participants. The study was repeated in 2009 with questionnaires and salivary test tubes ($n = 2408$). In four cross-sectional and two short-term follow-up analyses odds ratios of depressive symptoms and of clinical depression were estimated by logistic regression for morning, evening, mean and the difference between morning and evening cortisol (slope). For the subsample, awakening response (CAR) and area under the curve (AUC) cortisol measures were calculated. We adjusted for sex, age, income, education, family history of depression, physical activity and alcohol consumption.
Results: None except one of the measures of salivary cortisol were associated with self-reported depressive symptoms or clinical depression, neither in the four cross-sectional analyses nor in the two short term follow-up analyses. E.g. in 2007, the adjusted odds ratios (OR) of depressive symptoms by a one unit increase in morning and evening cortisol (ln(nmol/litre saliva)) were 1.01 (95% CI: 0.88—1.17) and 1.05 (0.93—1.18), respectively. The one exception was significant at $p = 0.04$ and was considered as due to chance.
Conclusion: In this large study, salivary cortisol was not associated with self-reported symptoms of depression or with clinical depression.

1. Introduction

Depression is a leading cause of disability and a major contributor to the global burden of disease (Burcusa and Iacono, 2007). Reduced quality of life, increased somatic illness, long-term sick leave and increased mortality are associated with depression (Brown et al., 2004; Hammen, 2005; Sinokki et al., 2009; Chang et al., 2010). Serious life events or other stressors may play an important role in the development of depression (Brugha et al., 1985) and it is discussed, whether a possible mechanism in the development of depression involves changes in hypothalamic-pituitary-adrenal (HPA) activity and cortisol levels (Hellhammer et al., 2009; Kristenson et al., 2012). We know that acute stressors create an immediate strong increase in the cortisol level (van Eck et al., 1996; Kudielka et al., 2004). However, it is still uncertain whether continuous stress leads to persistent changes in cortisol homeostasis and if these changes lead to a higher risk of depression (Kristenson et al., 2012).

Studies of patients with depression have formed the basis for the hypothesis that elevated cortisol levels is associated with an increased incidence of depression (Holsboer et al., 1995; Bhagwagar et al., 2003; Pariante and Lightman, 2008). Patients with Cushings syndrome (hypercortisolaemia) have an elevated prevalence of depression (Brown et al., 2004) supporting the hypothesis. However, evidence of no association or even lower cortisol among depressed patients has also been found (Young et al., 2002; Peeters et al., 2003; Ahrens et al., 2008; Stetler and Miller, 2011).

Studies of the relation between cortisol and depression in population studies or outpatient populations have shown diverging results. Phillips et al. found in a large population of 4256 US army veterans lower levels of serum cortisol among those who were depressed. Pointing in the same direction, a flat diurnal cortisol profile was associated with depression in two studies of randomly selected men and women (Sjogren et al., 2006; Power et al., 2011). This was contrasted by a study of outpatients recruited from general practise with current major depression, a history of depression, and controls. Here, cortisol levels (awakening response and 1000 h) were higher in the depressed groups (Vreeburg et al., 2009). Other studies have suggested a U-shaped curve (Bremmer et al., 2007) as well as no associations (Burke et al., 2005). Thus, these studies show mixed picture of associations in cross-sectional settings.

There have only been published few follow-up studies on adult populations. In one study, high morning cortisol predicted onset of major depression 13 months later (Harris et al., 2000). In another study, a low cortisol awakening response predicted depression after two years (Vreeburg et al., 2013).

We have recently published 2-year follow-up results from a large study of public sector employees showing that a low mean saliva cortisol level and a flat morning-to-evening cortisol slope at baseline predicted clinical depression (Grynderup et al., 2013). Morning and evening cortisol levels did not predict depression. However, considering the course of a depression, two years may be a too long follow-up period as half of those affected with major depressive episodes recover within three months (Spijker et al., 2002).

The aim of the present study was to test if cortisol levels are associated with depression. We had the opportunity to test the associations in the same study of public sector employees using both repeated cross-sectional and short-term follow-up data including a range of cortisol measures as well as depressive symptoms and clinical depression.