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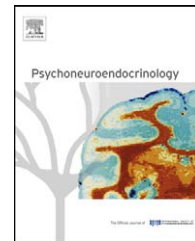**ScienceDirect**

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# Psychological traits and the cortisol awakening response: Results from the Netherlands Study of Depression and Anxiety

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**Summary**
*Background:* Hypothalamus—Pituitary—Adrenal (HPA) axis dysregulation is often seen in major depression, and is thought to represent a trait vulnerability — rather than merely an illness marker — for depressive disorder and possibly anxiety disorder. Vulnerability traits associated with stress-related disorders might reflect increased sensitivity for the development of psychopathology through an association with HPA axis activity. Few studies have examined the association between psychological trait factors and the cortisol awakening response, with inconsistent results. The present study examined the relationship between multiple psychological trait factors and the cortisol awakening curve, including both the dynamic of the CAR and overall cortisol awakening levels, in a sample of persons without psychopathology, hypothesizing that persons scoring high on vulnerability traits demonstrate an elevated cortisol awakening curve.
*Methods:* From 2981 participants of the Netherlands Study of Depression and Anxiety (NESDA), baseline data from 381 controls (aged 18—65) without previous, current and parental depression and anxiety disorders were analyzed. Psychological measures included the Big Five personality traits (neuroticism, extraversion, openness to experience, conscientiousness, and agreeableness) measured using the NEO-FFI, anxiety sensitivity assessed by the Anxiety Sensitivity Index, cognitive reactivity to sadness (hopelessness, acceptance/coping, aggression, control/perfec-

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tionism, risk aversion, and rumination) as measured by the LEIDS-R questionnaire, and mastery, assessed using the Pearlin and Schooler Mastery scale. Salivary cortisol levels were measured at awakening, and 30, 45, and 60 min afterwards.

*Results:* In adjusted analyses, high scores of hopelessness reactivity ($\beta$ = .13, $p$ = .02) were consistently associated with a higher cortisol awakening response. In addition, although inconsistent across analyses, persons scoring higher on extraversion, control/perfectionism reactivity, and mastery tended to show a slightly flatter CAR. No significant associations were found for neuroticism, openness to experience, agreeableness, conscientiousness, anxiety sensitivity, and acceptance/ coping, aggression, or risk aversion reactivity.

*Conclusion:* Of various psychological traits, only hopelessness reactivity, a trait that has been associated with depression and suicidality, is consistently associated with HPA axis dysregulation. Hopelessness reactivity may represent a predisposing vulnerability for the development of a depressive or anxiety disorder, possibly in part mediated by HPA axis activity.

## 1. Introduction

Depressive illness has been associated with a dysregulation of the Hypothalamus—Pituitary—Adrenal (HPA) axis (Pariante and Lightman, 2008). Although not always consistent, the preponderance of evidence indicates that cortisol hypersecretion is associated with major depression (Holsboer, 2001; Pariante and Lightman, 2008), and possibly anxiety disorder (Mantella et al., 2008; Vreeburg et al., 2010a). Of various HPA axis activity indicators, the most consistent association with depressive disorder in depressed outpatients has been observed for the cortisol awakening response (CAR; Bhagwagar et al., 2005; Cowen, 2010). The CAR reflects the natural response of the HPA axis to awakening, and is not strongly associated with cortisol sampled later in the day (Schmit-Reinwald et al., 1999; Edwards et al., 2001), suggesting that it may represent a discrete aspect of HPA axis function.

Our findings of a higher cortisol awakening curve both among current and remitted depressive and anxiety disorder (Vreeburg et al., 2009a, 2010a), and the presence of cortisol hypersecretion in asymptomatic individuals at familial risk of depression (Mannie et al., 2007; Vreeburg et al., 2010b), suggest that HPA axis dysregulation represents a trait vulnerability — rather than merely an illness marker — for mood disorder and possibly anxiety disorder. If this is true, the CAR might also be related to psychological vulnerability markers of depression in never depressed individuals. To exclude effects of current and previous psychopathology, it is essential to examine the link between psychological traits and the cortisol awakening curve in persons who never experienced a depressive or anxiety disorder. The goal of the present study is to examine the association between multiple personality characteristics and the cortisol awakening curve in a sample free of depressive and anxiety disorders.

Several psychological traits are closely linked to depression and anxiety, such as the Big Five personality factors neuroticism and extraversion (Costa Jr. and McCrae, 1995; Furukawa et al., 1998; Bienvenu et al., 2001; Spinhoven et al., 2009). Other psychological traits that are related to depression and anxiety include depression-related cognitions such as hopelessness and rumination, anxiety sensitivity and mastery (Kennedy et al., 1998; Kuehner and Weber, 1999; American Psychiatric Association, 2000; De Graaf et al., 2002).

Few studies examined the association of these psychological traits with HPA axis function in persons free of current psychopathology, of which only a small number focused on the cortisol awakening response, with mixed results. For example, for neuroticism, both positive (Portella et al., 2005), negative (Hauner et al., 2008) and absent (Chan et al., 2007) associations were found. High scores of introversion were associated with lower cortisol awakening responses (Hauner et al., 2008), whereas traits associated with introversion, such as high harm avoidance and low novelty seeking, showed higher cortisol awakening levels (Rademaker et al., 2009). In a study of personality traits and morning cortisol among older persons, no associations were found for neuroticism, mastery and self-esteem (Gerritsen et al., 2009). Other traits, such as conscientiousness, openness, and agreeableness have not been investigated yet.

Taken together, these results are indicative, but far from conclusive, of an association between psychological vulnerability traits and morning cortisol levels. Overall, both the number of studies and the sample sizes are limited (highest $n$ = 230, but the majority is well below this), resulting in low power to detect correlations. Furthermore, most studies focused only on one trait, thereby missing out on the contribution of multiple traits to HPA axis functioning.

In the present study we investigated the association between the cortisol awakening curve, including both the dynamic of the CAR and overall cortisol awakening levels, and multiple psychological trait factors related to depression and anxiety disorders (the Big Five personality traits, cognitive reactivity to sadness, anxiety sensitivity, and mastery) in a large sample of participants free of current and past psychopathology. We hypothesize that persons scoring high on vulnerability traits demonstrate an elevated cortisol awakening curve.

## 2. Methods

### 2.1. Sample

Study participants come from the Netherlands Study of Depression and Anxiety (NESDA), a large cohort study conducted among 2981 adults (18—65 years). The study examines the long-term course and consequences of depressive and anxiety disorders. Respondents were recruited from the community, general practice, and secondary mental health care, and included persons with psychopathology as well as