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Cortisol secretion in depressed, and at-risk adults

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Summary Distinct patterns of cortisol secretion have been associated with depression in past research, but it remains unclear whether individuals at-risk for depression may also have similar patterns of cortisol secretion. This is the first study to date of both naturalistic diurnal cortisol secretion and cortisol reactivity to a psychosocial laboratory stressor in depressed and at-risk adults. Cortisol secretion patterns were compared for 57 currently depressed, at-risk (based on trait-level positive and negative affect), and control participants over 5 days and in response to a laboratory stressor. After controlling for potentially confounding biobehavioral variables, the depressed group had a larger cortisol awakening response (CAR) and higher average diurnal cortisol compared to control participants. Individuals at-risk for depression also had significantly higher waking cortisol levels than control participants. Results for the psychosocial laboratory stressor did not show the predicted elevations in cortisol for depressed and at-risk participants compared to controls. The at-risk group recovered more quickly when compared to the depressed group both in levels of cortisol and concurrent measures of negative affect. The at-risk and depressed participants were similar on the diurnal cortisol measures, but differed on response to the laboratory social stressor, suggesting divergence in cortisol secretion patterns between currently depressed and temperamentally at-risk individuals. Further investigation of HPA functioning of individuals at-risk for depression may clarify the stress processes involved in risk for depression onset.

Stressful life events are risk factors for major depressive disorder (MDD) onset and recurrence (Hammen, 2005; Mazure, 1998). An estimated 20—50% of individuals develop depression after experiencing a recent major life stressor (Brown and Harris, 1989; Monroe and Simons, 1991). Psychosocial and biological factors may exist that create increased sensitivity to the effects of stressors, but the more proximal mechanisms underlying this diathesis—stress relationship have yet to be fully understood. One possible mechanism is dysregulation of the biological stress response system, in the form of altered hypothalamic-pituitary-adrenal (HPA) axis functioning (Gotlib et al., 2008). Alterations in the HPA axis have been linked to depression in past research (Carroll et al., 2007; Knorr et al., 2010; Vreeburg et al., 2009), and may also be related to several factors that could indicate risk for depression, such as the serotonin transporter

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gene (5-HTT) linked polymorphic region (5-HTTLPR) (Alexander et al., 2009; Chen et al., 2009; Goodyer et al., 2009; Gotlib et al., 2008), personality traits such as negative affect and neuroticism (Polk et al., 2005; Portella et al., 2005; Hauner et al., 2008), and family history of depression (Mannie et al., 2007; Vinberg et al., 2008). The current investigation uses a community sample to compare HPA functioning in currently depressed individuals and those believed to be at-risk for depression as a result of one of these factors, trait levels of positive and negative affect.

Cortisol, the hormonal endpoint of the HPA axis, is one of the primary coordinators of the bodily response to a stressor and follows a circadian rhythm in concert with the sleep/wake cycle (Tsigos and Chrousos, 2002). Results of studies examining cortisol levels in depressed individuals appear to vary based on patient characteristics and severity of depression. Currently depressed individuals in inpatient samples typically have diurnal patterns characterized by high morning cortisol and a high, flat pattern of cortisol secretion across the day (Holsboer, 2000; Plotsky et al., 1998). However, there is some indication that this pattern may not hold true for less severely depressed populations outside of the hospital setting, nor for non-melancholic/psychotic depression (Carroll et al., 2007; Maes et al., 1994; Peeters et al., 2004; Strickland et al., 2002). Notably, a recent meta-analysis of 20 studies reported that the small observed difference in morning and evening cortisol did not reliably distinguish depressed and non-depressed persons, except for more severely depressed individuals (Knorr et al., 2010). In contrast, Vreeburg et al. (2009) reported that depressed participants in a large community-based study had higher morning and higher evening cortisol levels when compared to non-depressed participants, similar to the findings for depressed inpatients. Higher morning cortisol (Bhagwagar et al., 2005) and a larger cortisol awakening response (CAR: the peak in cortisol secretion occurring 30—45 min post awakening) (Pruessner et al., 2003) have also been found in some studies involving depressed populations, whereas other studies have reported a blunted CAR (Huber et al., 2006; Stetler and Miller, 2005). Thus, there appears to be support for higher morning cortisol levels in community samples of depressed individuals, but evidence remains inconclusive.

Similarly mixed results have been reported for individuals at-risk for depression. However, certain findings have been consistently replicated over time. A number of prospective longitudinal studies have indicated that elevated waking cortisol (Goodyer et al., 2000, 2009; Harris et al., 2000; Halligan et al., 2007) or a larger CAR (Adam et al., 2010) in at-risk individuals predicts later depression onset. Cross-sectional studies have also reported higher waking cortisol in individuals at-risk for depression based on family history (Mannie et al., 2007), genotype (Chen et al., 2009), and neurotic personality style (Portella et al., 2005). Taken together, the most robust findings suggest greater waking cortisol and a larger CAR in those at-risk for depression.

Patterns of cortisol secretion in response to a psychosocial laboratory stressor or chemical challenge can also reveal HPA axis dysfunction (Adam and Kumari, 2009). Most studies of cortisol reactivity in depressed individuals have assessed cortisol secretion in response to a chemical challenge (i.e., the dexamethasone-/corticotropin-releasing hormone test; Holsboer, 2000) rather than the cortisol response to a laboratory stressor (Heim et al., 2000; Young et al., 2000), and therefore, research investigating the cortisol response to psychosocial laboratory stressors for depressed individuals is needed. Burke et al. (2005) conducted a meta-analysis of seven such studies, and reported that depressed individuals had higher cortisol levels during the recovery period following a stressor, although levels did not differ at baseline or immediately post-stressor. However, their meta-analysis only examined mean levels and not variation of cortisol secretion over time or total cortisol exposure. Moreover, only two of the seven studies involved social evaluative threat which has been shown to contribute to a reliable cortisol response (Dickerson and Kemeny, 2004).

There is also a paucity of research on the cortisol response to psychosocial laboratory stressors in individuals considered at-risk for depression due to behavioral or personality factors. Young and Nolen-Hoeksema (2001) found no difference between high and low ruminators on cortisol response to the Trier Social Stress Test (TSST: Kirschbaum et al., 1993). Schommer et al. (1999) reported no association between cortisol in response to the TSST and neuroticism. Tyrka et al. (2006) did report elevated cortisol response to the TSST based on temperament, specifically novelty seeking, but novelty seeking had no relationship to risk for depression. Kudielka et al. (2007), in a review of research involving the TSST, reported that personality variables were not related to the TSST on first exposure because of the effect of novelty (Brandstadter et al., 1991; Kirschbaum et al., 1992), but that high neuroticism, low self-esteem, and extraversion were associated with lack of habituation to the TSST upon repeated exposure (Kirschbaum et al., 1995; Pruessner et al., 1997a,b).

High negative affect (NA), a personality style defined as temperamental sensitivity to negative stimuli, and low positive affect (low PA; e.g., lack of enjoyment or energy) have been associated with both increased risk for depression and dysregulation of the HPA axis in past research (Clark et al., 1994; Gunderson et al., 2000; Hirschfeld et al., 1989). Additionally, NA and PA are reliably assessed via self-report and, if they are related to dysregulation of the biological stress system, may provide an easy means of identification of stress sensitive individuals. Clark et al. (1994) reported that individuals who later develop depression have NA scores that fall between those of normal controls and those with a current depressive episode. Hirschfeld et al. (1989) reported that individuals who went on to develop depression scored higher than those who did not on a measure of NA. Additionally, Gunderson et al. (2000) reported that neuroticism, which the authors state is essentially identical to NA, was associated with later onset of depression. The evidence for low PA as a risk factor for future depression is less clear, although it has been associated with current depression (Clark et al., 1994). Elevated diurnal cortisol production has been linked to high NA, most clearly for men, with a weaker relationship between elevated diurnal cortisol and low PA (Polk et al., 2005; Smyth et al., 1998; van Eck et al., 1996a,b). There is currently no empirical evidence for greater cortisol response to a laboratory stressor for those high in NA and low in PA — the risk profile for depression according to Clark and Watson's tripartite model (Clark and Watson, 1991) — although high NA appeared to mediate the relationship between naturalistic