



# Resting cortisol level, self-concept, and putative familial environment in adolescents at ultra high-risk for psychotic disorders



Emily E. Carol<sup>a,\*</sup>, Vijay A. Mittal<sup>b</sup>

<sup>a</sup> University of Colorado Boulder, Department of Psychology and Neuroscience, Boulder, CO 80309, USA

<sup>b</sup> Northwestern University, Department of Psychology, Evanston, IL 60208, USA

Received 11 December 2014; received in revised form 20 March 2015; accepted 21 March 2015

## KEYWORDS

Cortisol;  
HPA axis;  
Prodrome;  
High-risk;  
Schizophrenia;  
Expressed emotion

**Summary** A growing body of evidence suggests that resting cortisol levels are elevated in patients with schizophrenia and closely tied to symptom severity. However, there is limited research on the biological stress system during the ultra high-risk (UHR) period immediately preceding the onset of psychosis, and cortisol has not been examined in relation to individual characteristics such as self-concept or potential stressors such as putative familial environment in this critical population. In the present study, salivary cortisol samples were collected on 37 UHR and 42 matched control adolescents, and these individuals were assessed with clinical interviews as well as a measure of self-concept. For a subsection of the sample (23 UHR and 20 control adolescents), a participating relative/caretaker was also assessed with an expressed emotion interview designed to gauge psychosocial environment. Consistent with previous studies, UHR participants exhibited elevated resting cortisol levels when compared with controls. In addition, UHR adolescents exhibited increased negative self-concept and their relatives/caretakers endorsed significantly fewer initial positive statements about the participant. Interestingly, a strong trend in the UHR group suggests that higher cortisol levels are associated with higher rates of critical statements from relatives/caretakers. Furthermore, elevated cortisol levels in the participants were associated with increased negative self-concept as well as fewer initial positive comments from relatives/caretakers. Results suggest that hypothalamic-pituitary-adrenal axis (HPA) dysfunction is closely associated with both individual and environmental-level characteristics. Taken together, these findings support a neural diathesis-stress model of psychosis and future studies, designed to examine causal relationships, stand to inform both our understanding of pathogenic processes in the high-risk period as well as early intervention efforts.

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\* Corresponding author at: University of Colorado at Boulder, Department of Psychology and Neuroscience, Center for Neuroscience, 345 UCB, Boulder, CO 80309-0345, USA. Tel.: +1 303 492 4616.

E-mail address: [emily.carol@colorado.edu](mailto:emily.carol@colorado.edu) (E.E. Carol).

## 1. Introduction

Accumulating evidence suggests that hypothalamic-pituitary-adrenal (HPA) axis dysfunction can have detrimental effects on mental health (Goodyer et al., 2001) and that adolescence is a period that is characterized by both increased sensitivity as well as significant changes in this integral system (Walker et al., 2008). A neural diathesis-stress model posits that an early biological vulnerability to the HPA system later interacts in the adolescent period with both individual factors and environmental stressors as well as normative and pathological neuroendocrine development, eventually leading to the onset of psychotic disorders such as schizophrenia (Walker et al., 2008). Consistent with this research, elevated stress hormones have been observed in individuals with chronic psychosis (Corcoran et al., 2003). An emerging body of evidence supports this theory and suggests that resting cortisol levels are elevated in the psychosis-risk period as well (Mittal and Walker, 2011; Walker et al., 2013; Karanikas and Garyfallos, 2014). However, while individual characteristics, such as self-concept (Fowler et al., 2006; Smith et al., 2006; Taylor et al., 2013), and psychosocial stressors, such as family environment (Barrowclough and Hooley, 2003), have been reliably linked to psychosis outcome, to the best of our knowledge, there have been no empirical studies examining relationships between these factors and markers of HPA dysfunction. Understanding the association between neuroendocrine dysfunction, self-concept, and environmental stressors in the period immediately prior to the onset of psychotic disorders is integral, as the prodrome is a viable period of intervention in which considerable neuroendocrine development is still underway (Sowell et al., 1999; Dahl, 2004; Spear, 2004).

As noted, studies have observed that cortisol levels are elevated in patients with schizophrenia when compared to healthy controls (Belvederi Murri et al., 2012) and are closely associated with positive symptoms (Franzen, 1971; Walder et al., 2000; Collip et al., 2011). Recent investigations are also now observing similar elevations in psychosis risk (Walker et al., 2010, 2013; Karanikas and Garyfallos, 2014); however, the relationship is nuanced, and group differences are not always observed (Cullen et al., 2014; Day et al., 2014). The root of stress hormone elevations in UHR individuals remains unclear as HPA dysregulation in this population has been linked to anxiety (Corcoran et al., 2012; Karanikas and Garyfallos, 2014), suspiciousness (Corcoran et al., 2012), stressful life events (Labad et al., 2014), and stress intolerance (Pruessner et al., 2013; Karanikas and Garyfallos, 2014). Alternatively, several studies have reported that abnormal stress hormone levels are closely tied to the illness progression in the UHR period and are ultimately predictive of transition to psychosis (Walker et al., 2010, 2013).

Self-concept formation (i.e., the development of beliefs about the self) occurs during childhood and adolescence (Cole et al., 2001), and cognitive theorist have posited that the development of negative beliefs about the self can result in maladaptive responses and mental states (Beck, 1979; Garety et al., 2001). Interestingly, negative beliefs about the self have been linked to cortisol activity in healthy

individuals (Kirschbaum et al., 1995) and have consistently been exhibited by individuals with chronic psychosis (Fowler et al., 2006; Smith et al., 2006; Taylor et al., 2013). Given this finding, researchers have theorized that dysfunctional self-concept, particularly negative self-beliefs, plays a role in the development of psychosis symptoms (Garety et al., 2001; Smith et al., 2006). Although the literature is limited, available studies examining this phenomenon in UHR adolescents have produced inconsistent results leading to a lack of understanding of how poor self-concept relates to illness development. While some investigations observed that UHR individuals endorse more negative self-beliefs than healthy controls (Perivoliotis et al., 2009; Stowkowy and Addington, 2012; Saleem et al., 2014), other studies have not observed a relationship with symptomatology (Saleem et al., 2014).

In normative samples, family environment during adolescence has been tied to endocrine function (Flinn and England, 1995; Luecken et al., 2009) as well as aspects of self-concept, such as self-esteem (Schmidt and Padilla, 2003). Within the context of psychosis, family environment is most commonly assessed through measuring expressed emotion (EE), which is defined as the attitudes and feelings a relative or caretaker expresses about their mentally ill family member (Barrowclough and Hooley, 2003). More specifically, high levels of criticism and hostility in the family environment are linked to increased risk in relapse in schizophrenia (Bachmann et al., 2002). There is a small but accumulating body of literature examining the relationship of EE and symptoms in UHR adolescents, and the findings generally show that greater levels of criticism and emotional over-involvement are associated with higher positive and negative symptoms (O'Brien et al., 2006; McFarlane and Cook, 2007; Schlosser et al., 2010; Dominguez-Martinez et al., 2014). However, to date, there have been no studies comparing EE in a UHR sample to healthy controls and it remains unclear as to how this social risk factor is linked to endocrine activity or self-concept.

In the present study, including a total of 79 adolescents (37 UHR and 42 matched healthy participations), we evaluated resting cortisol levels as well as links with self-concept, family environment, and symptomatology. We made the following predictions based on the available research. First we predicted that the present sample of UHR participants would exhibit elevated cortisol levels when compared to matched healthy controls and that this would be associated with increased symptomatology (i.e., higher positive and negative symptoms). We also predicted that the UHR group would exhibit elevated negative self-concept compared to healthy controls, and that increased negative self-concept would be associated with elevated cortisol levels in turn. Because there is not yet a strong guiding literature to inform predictions, the relationships between cortisol levels and positive self-concept, as well as the relationship between both categories of self-concept and symptoms, were examined in exploratory analyses. In an analysis of family environment, assessed in a subset of 43 participants (23 UHR and 20 control adolescents), we predicted that the family environment of UHR individuals would be characterized by lower levels of positive initial statements and warmth, and elevated criticism and emotional over-involvement compared to the family environment of control participants. Finally,

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