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Maternal cortisol during pregnancy is related to infant cardiac vagal control

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Summary
Background: Prenatal exposure to maternal psychological distress and glucocorticoids result in neurobiological adaptations within the fetus that increase risk for developing exaggerated emotional, behavioral, and stress responses to novelty and challenges in childhood. The current study investigated the influence of maternal depressed mood and cortisol during pregnancy on infant cardiac vagal control (CVC) to standardized laboratory challenge tasks.
Methods: The sample comprised 194 women and their infants. Maternal reports of depressed mood and salivary cortisol were assessed at 14 and 32 weeks gestational age. Linear regression was used to examine associations between maternal measures during early and late pregnancy, and infant CVC indexed via respiratory sinus arrhythmia (RSA) at rest and in response to laboratory tasks designed to elicit frustration when infants were 6 months of age. It was hypothesized that maternal depressed mood and cortisol would be associated with lower basal RSA and smaller decreases in RSA from baseline to challenge.
Results: A significant decrease in infant RSA from baseline to frustration tasks indicated that laboratory tasks elicited a reliable decrease in RSA from baseline to frustration among infants which is characterized by reduction in vagal efferent activity on the heart in response to challenge. Higher maternal cortisol, but not depressed mood, was associated with lower basal RSA and greater decrease in RSA from baseline to frustration. Associations between maternal cortisol and infant basal RSA were observed for both early and late pregnancy whereas the associations between prenatal cortisol and decrease in RSA from baseline to frustration were observed for early, but not late, pregnancy.

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Conclusions: Maternal cortisol during pregnancy was associated with infant CVC at 6-months of age. Such influences may have enduring impacts on the child and important implications for the development of physical and mental health outcomes.

1. Introduction

There has been increasing awareness that many physical and psychological disorders commonly observed in adulthood such as hypertension, diabetes, and depression have origins in fetal development (Barker, 2002; Calkins and Devaskar, 2011; Glover, 2011). Vulnerability may be conferred through the fine-tuning of stress-regulatory systems that occurs following exposure to insults during a sensitive period in utero or early postnatal life (Van den Bergh, 2011). To date, human and animal evidence has convincingly reported that exposure to excess cortisol and maternal prenatal psychological distress (i.e., an amalgamation of comorbid subjective stress, anxiety, and depressed mood) alters the function of one of the co-acting stress-regulatory systems—-the hypothalamic—adrenal—pituitary (HPA) (Braun et al., 2013; Field, 2011; Kajantie, 2006; Kapoor and Matthews, 2008; Seckl and Holmes, 2007). Relatively less attention has been paid to the influences of prenatal maternal cortisol and psychological distress on the second stress-regulatory system (i.e., the autonomic nervous system; ANS). The current study focuses on the associations between maternal prenatal cortisol and depressed mood on infant autonomic function.

Empirical evidence suggests that exposure to prenatal maternal depressed mood results in neurological adaptations within the fetus that increase risk for low birth weight (Grote et al., 2010) and the development of exaggerated emotional (Davis et al., 2007; Hayes et al., 2013), behavioral (van der Wal et al., 2007), and HPA-axis responses (Fernandes et al., 2014; Oberlander et al., 2008) to stressors. While the mechanisms by which antenatal exposure to depressed mood confers future risk are not well understood, a central claim of the fetal programming hypothesis is that the maternal HPA-axis is a central component in the cascade from maternal depressed mood to fetal and infant development. Nevertheless, it is not clear whether depressed mood and glucocorticoids have combined (joint or interactive effects) or independent effects on infant development. Despite compelling theoretical reasons to believe that the effects of prenatal glucocorticoids may be greatest when they are accompanied by high levels of psychological distress, the evidence to date suggests that they may be independent predictors of child outcomes (e.g., Davis and Sandman, 2010).

Glucocorticoids readily cross biological barriers such as the placenta (Seckl and Holmes, 2007) and exert a direct influence on fetal development. Although the placental enzyme 11β-hydroxysteroid dehydrogenase type 2 (11β-HSD2) regulates fetal exposure by converting cortisol to inactive cortisone, human studies have indicated that increased cortisol consequent to depressed mood (Diego et al., 2009; Field et al., 2004b) and subsequent decreased efficiency of the placenta at converting cortisol to cortisone (Oberlander et al., 2008) may lead to elevated in-utero cortisol exposure. Given that cortisol receptors are highly expressed in the developing brain (Sánchez et al., 2000) and are important for maturation of the developing CNS (Kapoor et al., 2008), prenatal exposure to glucocorticoids can impair feedback mechanisms of the fetal HPA-axis, resulting in altered basal function and responsiveness in the offspring (Kapoor et al., 2008; Maccari and Morley-Fletcher, 2007; Seckl and Holmes, 2007). For example, among premature infants, prenatal maternal treatment with synthetic glucocorticoids is reported to suppress HPA-axis responses to heel lance and physical examination stressors (Davis et al., 2006).

1.1. The autonomic nervous system

Compared to our understanding of the associations between maternal depressed mood and cortisol during pregnancy and fetal/infant HPA-axis development, relatively little is known about the influences of depressed mood and cortisol on the developing ANS (Porges and Furman, 2011). The relative dearth of literature in this area is surprising for several reasons. First, many adult diseases that have origins in fetal development are related to cardiovascular/ANS health (Barker, 2002; Calkins and Devaskar, 2011). Second, catecholamine's (e.g., epinephrine) are synthesized by the adrenal gland when the sympathetic branch of the ANS predominates; these hormones act to down regulate 11β-HSD2 gene expression in human placental cells (Sarkar et al., 2001) and may increase cortisol exposure in-utero. Elevation of catecholamines have been noted among women with antenatal depression compared to non-depressed controls (Field et al., 2004b; Lundy et al., 1999). Finally, cortisol is involved in the maturation of neurobiological areas involved in ANS regulation (Harris and Seckl, 2011).

The ANS comprises sympathetic and parasympathetic branches which innervate most internal body organs and generally act in an opposing fashion—in general, the sympathetic branch acts as an accelerator system and the parasympathetic branch acts as a decelerator system. Considerable interest has been paid to the role of the parasympathetic nervous system in the development of physical and psychological disorders (Rottenberg, 2007; Thayer et al., 2009; Thayer and Lane, 2007). Parasympathetic function can be measured noninvasively using cardiac vagal control (CVC)—the neural regulation of heart rate (HR) by parasympathetic influences emanating from the vagus nerve. The vagus represents an integrated bidirectional neural system between visceral organs and the brain. Vagal stimulation of the heart serves as a ''brake'' to maintain HR below the heart's autonomous rhythm. In this sense, basal CVC can be thought of as a physiological reserve capacity with higher levels reflecting more efficient vagal control and a greater capacity to adjust to environmental demands.