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Physiological reactivity to psychological stress in human pregnancy: Current knowledge and future directions

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ABSTRACT

Cardiovascular and neuroendocrine reactivity to acute stress are important predictors of health outcomes in non-pregnant populations. Greater magnitude and duration of physiological responses have been associated with increased risk of hypertensive disorders and diabetes, greater susceptibility to infectious illnesses, suppression of cell-mediated immunity as well as risk for depression and anxiety disorders. Stress reactivity during pregnancy has unique implications for maternal health, birth outcomes, and fetal development. However, as compared to the larger literature, our understanding of the predictors and consequences of exaggerated stress reactivity in pregnancy is limited. This paper reviews the current state of this literature with an emphasis on gaps in knowledge and future directions.

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Abbreviations: TSST, Trier Social Stress Test; CO, cardiac output; TPR, total peripheral resistance; HRV, heart rate variability; HPA, hypothalamic-pituitary-adrenal; GR, glucocorticoid receptor; CPT, cold pressor test; PTB, preterm birth.

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1. Introduction

Cardiovascular and neuroendocrine reactivity to acute stress are important predictors of health outcomes in non-pregnant populations. Greater magnitude and duration of physiological responses have been associated with increased risk of hypertensive disorders and diabetes, greater susceptibility to infectious illnesses, suppression of cell-mediated immunity as well as risk for depression and anxiety disorders (McEwen, 2004, 2008; Segerstrom and Miller, 2004; Treiber et al., 2003; Linden et al., 1997; Stewart and France, 2001; Cacioppo et al., 1998).

In pregnancy, maternal stress (i.e., perceived stress, depressive symptoms, racial discrimination, stressful life events, and pregnancy-specific anxiety) has been associated with preterm birth, low birth weight, risk of gestational hypertension, and adverse health and behavioral outcomes in offspring (Hetzel et al., 1961; Landbergis, 1996; Kurki et al., 2000; Paarlberg et al., 1995; Grote et al., 2010; Weinstock, 2005; Welberg and Seckl, 2001; Bale et al., 2010; Bilbo and Schwarz, 2009). Thus, differential reactivity to daily life stressors may have unique implications in the context of pregnancy. However, as compared to the larger literature, our understanding of the predictors and consequences of exaggerated stress reactivity in pregnancy is limited. This paper reviews the current state of this literature with an emphasis on gaps in knowledge and future directions.

2. Stressor exposure versus physiological responses: implications for health

The current review focuses on physiological reactivity as an individual difference which has cumulative effects over the course of the life span; that is, the magnitude and duration of physiological activation in the context of psychological challenge. Exposure to stressors is predictive of adverse perinatal outcomes in groups of women. The number and severity of major life events (e.g., divorce, death in the family, illness, loss of a job) during pregnancy has been associated with risk of preterm birth (Nordentoft et al., 1996; Dole et al., 2003; Whitehead et al., 2002). Similarly, exposure to chronic (e.g., homelessness) or catastrophic (e.g., earthquake, terrorist attack) events has been associated with adverse birth outcomes (Stein et al., 2000; Glynn et al., 2001; Lederman et al., 2004). However, clearly, not all women experience adverse outcomes upon stressor exposure. The biological impact of stress is ultimately a function of stressor exposure as well as the magnitude/duration of one's physiological response. Importantly, these factors interact. The experience of chronic or repeated stressors, such as that conferred by racial minority status, may sensitize physiological stress responses. Indeed, as compared to Caucasians, African-Americans exhibit greater cardiovascular reactivity to a variety of acute stressors (Anderson et al., 1988; Lepore et al., 2006; Light and Sherwood, 1989; Hatch et al., 2006; Light et al., 1987). Thus, assessment of individual differences in stress reactivity in addition to assessment of frequency and severity of exposure to stressors is critical for both delineating the impact of stress on prenatal health and predicting which individuals are at greatest risk for adverse outcomes upon stressor exposure.

3. Basal physiological adaptation during pregnancy

Key to stress responding, functioning of the hypothalamic-pituitary-adrenal (HPA) axis is altered dramatically during pregnancy, largely due to the influence of the placenta (Fig. 1). Placental production of corticotropin-releasing hormone (CRH) increases exponentially as pregnancy progresses, with up to 1000-fold increases in plasma CRH by term (Lindsay and Nieman, 2005). There is strong evidence that plasma CRH serves as a marker of the progression of the 'placental clock' which determines the timing of delivery, with differential patterns of plasma CRH levels across pregnancy among women delivering at term, preterm, and post-term (McLean et al., 1995; McLean and Smith, 2001). Notably, placentally-derived CRH is identical to hypothalamic CRH in structure, immunoreactivity, and bioactivity (Lindsay and Nieman, 2005; Magiakou et al., 1997). The bioavailability of CRH is buffered somewhat by CRH-binding-globulin (CBG). CBG drops considerably in the days prior to parturition and is a key factor instigating labor onset.

Increases in placentally-derived CRH across pregnancy stimulate secretion of adrenocorticotropic hormone (ACTH) from the pituitary. This, in turn, stimulates production of cortisol from the adrenal glands, resulting in hypercortisolism. While the diurnal cortisol rhythm is generally maintained across pregnancy, both total and free plasma cortisol concentrations rise in parallel as pregnancy progresses, with plasma cortisol levels 2–3-fold higher than nonpregnancy by term (Mastorakos and Ilias, 2000). These substantial increases in ACTH and cortisol result in gradual hypertrophy of both the pituitary and adrenal glands. Despite these pregnancy-related changes, psychosocial stress is associated with measurable effects on cortisol levels (Obel et al., 2005) and higher cortisol early in gestation has been linked to risk of spontaneous abortion (Nepomnaschy et al., 2006). Moreover, it has been suggested that placental-production of CRH is a stress-sensitive, thus influencing the timing of parturition (Hobel et al., 2008; Lockwood, 1999).

The maternal cardiovascular system also undergoes substantial changes to support fetal development during pregnancy (Fig. 1). Blood volume increases by approximately 45%. Due to increases in stroke volume and heart rate, cardiac output increases by 30–50% while systemic vascular resistance decreases. A decrease in blood pressure is seen, with a nadir at mid-gestation followed by an increase to pre-pregnancy levels by term. Lack of such adaptation has been associated with adverse outcomes. Higher blood pressure during the first trimester of pregnancy is predictive of greater risk of subsequent preeclampsia (Moutquin et al., 1985; Sibai et al., 1995). Moreover, higher blood pressure has been associated with lower birth weight, even among normotensive women (Churchill et al., 1997; Hilmert et al., 2008). Stress may contribute to this association. For example, in a study of 170 African-American and white women assessed longitudinally across pregnancy, stress was associated with higher systolic and diastolic blood pressure among African-Americans only (Hilmert et al., 2008). In addition, an interaction between stress and blood pressure was evidenced whereby the combination of higher stress and high DBP predicted increased likelihood of low birthweight among African-Americans.

There is conflicting evidence regarding pregnancy-related changes in plasma catecholamines (i.e., epinephrine and norepinephrine); there are reports of no changes (Barron et al., 1986; Oshaughnessy et al., 1984; Lederman et al., 1989), and increasing