Psychoneuroendocrinology (2014) 50, 264—273

Available online at www.sciencedirect.com

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24-h urinary free cortisol from mid-pregnancy to 3-months postpartum: Gender and parity differences and effects

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Received 17 January 2014; received in revised form 18 August 2014; accepted 25 August 2014

KEYWORDS
Cortisol;
Pregnancy;
Postpartum;
Women/men;
1st/2nd time parents

Summary
Background: Pregnancy and postpartum have been associated to several physiological changes; however, empirical evidence was almost exclusively obtained in primiparous women and few studies focus on hormonal changes in men and second-time parents. The main aim of this study is to examine 24-h urinary free cortisol from mid-pregnancy to 3-months postpartum, comparing women/men and first/second-time parents.
Methods: Twenty-six women and 22 men ($N = 48$) were recruited from an antenatal obstetric unit in Porto, Portugal. 24-h urinary free cortisol was measured at the 2nd and 3rd trimester and at 3-months postpartum. Repeated measures analyses of variance were conducted, in order to analyze 24-h urinary free cortisol patterns of change over this period. Gender and parity were included in the analyses as potential modifiers, in order to compare women and men, and first- and second-time parents.
Results: An increase from the 2nd to the 3rd trimester ($p = .006$) and a decrease from the 3rd trimester to 3-months postpartum ($p = .005$) were reported in all parents' 24-h urinary free cortisol. The interaction effects for Time * Gender ($p = .03$) and Time * Parity ($p = .02$) were found. Women and first-time parents revealed higher levels, while men and second-time parents showed lower 24-h urinary free cortisol levels at the 2nd trimester than at 3-months postpartum.
Conclusions: Findings appear to clarify the direction, as well as, the timing, gender and parity extension of 24-h urinary free cortisol changes from mid-pregnancy to 3-months postpartum. The same pattern of change in all parents' 24-h urinary free cortisol from mid-pregnancy to 3-months postpartum is consistent with the proposed role of hormones in preparation to parenting.

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http://dx.doi.org/10.1016/j.psyneuen.2014.08.013

Gender and parity differences and effects on 24-h urinary free cortisol are also consistent with cortisol as a stress biomarker for higher challenges associated to pregnancy and childbirth in women and first-time parents *versus* higher demands related to after childbirth parenting in men and second-time parents.

1. Introduction

Pregnancy and postpartum have been associated to several physiological changes, namely the dysregulation of the hypothalamic—pituitary—adrenal axis (HPA) and the autonomic nervous system (ANS) functioning (Brunton et al., 2008; Lazinski et al., 2008; O'Keane et al., 2011; Duthie and Reynolds, 2013). However, empirical evidence was almost exclusively obtained in primiparous women and few studies focus on hormonal changes in men and second-time parents.

Theoretical approaches concerning HPA axis functioning during pregnancy and postpartum have mainly assumed two pathways. The HPA axis was considered an important system involved in the regulation of parental behavior (Carter and Porges, 2012; Gonzalez et al., 2009). The HPA axis was also believed to play a fundamental role in the response to external and internal stimuli and to provide a regulatory network linking the brain with the body's behavioral and physiological responses to stress (Dipietro, 2012; Reynolds et al., 2013). Both paths will subsequently be analyzed in further detail.

Research on human parenting psychobiology is receiving new attention. An association between the HPA axis activity and the subsequent expression of social behaviors and bonds has been proposed. Positive social behaviors, including social bonds, may reduce HPA axis activity, while negative social interactions can have the opposite effect (for a revision see Carter, 1998). Findings revealed a decrease in cortisol with pair-bond formation (Ziegler et al., 1996; Carter, 1998; Reburn and Wynne-Edwards, 1999) and higher cortisol levels are significantly and strongly associated with maternal approach behaviors and positive maternal attitudes (Fleming et al., 1997; Stallings et al., 2001). While some reference was made to relevant research on men, the emphasis on women continues to reflect the state of art on physiological influences in terms of parental behavior. Focus on both women and men's hormonal changes to establish patterns of changes over pregnancy and postpartum is relevant to fully understand the psychobiology of parenthood.

The HPA axis has also been pointed out as the primary biological mechanism underlying stress regulation and adaptation (Dipietro, 2012; Reynolds et al., 2013). Changes in the HPA axis, mainly in the postpartum period, were associated to mood disturbances and several puerperal disorders (Corwin and Pajer, 2008; Meinlschmidt et al., 2010; O'Keane et al., 2011). Considered as the end product of the HPA axis, cortisol has been viewed as a biomarker of psychological stress (Harville et al., 2007). Some studies associate high-cortisol levels to psychological symptoms during pregnancy and the postpartum period (Field et al., 2004; Obel et al., 2005), while others show that stress and anxiety levels assessed by self-report measures do not necessarily correlate with maternal cortisol levels (Harville et al., 2009; Voegtline et al., 2013).

1.1. Changes in cortisol during pregnancy and the postpartum period

Findings from previous research suggest that levels of cortisol generally increase as pregnancy progresses (Obel et al., 2005; Jones et al., 2006; D'Anna-Hernandez et al., 2011), reaching peak levels during the third trimester (Jung et al., 2011). After childbirth, maternal cortisol levels were usually reported to decrease (Field et al., 2004; de Weerth and Buitelaar, 2005; Figueiredo and Costa, 2009; Cheng and Pickler, 2010). Nevertheless, conflicting results depended on the type of cortisol matrices used. Jung et al. (2011), for example, observed that total plasma cortisol and cortisteroid-binding globulin remained high at 2—3 months postpartum, whereas urinary free cortisol and plasma free cortisol returned to baseline level, and mean total cortisol concentrations were lower after childbirth compared with pregnancy.

Cortisol changes during pregnancy and postpartum were analyzed with a variety of matrices and different assessment time points. Little is known about 24-h urinary free cortisol pattern of changes over pregnancy and postpartum, as proposed by the present study.

1.2. Gender differences in cortisol levels

Empirical research on HPA axis sex differences has produce inconsistent or even contradictory findings, especially in humans (for a revision see Kudielka and Kirschbaum, 2005). The sample size, composition in relation to health status, age at testing, the type of stressor/challenge and the duration of stress exposure are some of the proposed factors to explain conflicting results (for a revision see Kudielka and Kirschbaum, 2005). Men and women with similar stage-specific differences in hormone levels, including higher concentrations in cortisol in the period just before birth, were suggested (Storey et al., 2000). In women these changes result, at least, partially from the secretion of corticotropin-releasing hormone (CRH) from the placenta (Magiakow et al., 1996; Mastorakos and Ilias, 2003), stimulated by maternal cortisol and a positive-feed forward mechanism (Mastorakos and Ilias, 2003). Less is known about the basis of such changes in men. Recent studies put forward the hypothesis that the underlying neuroendocrine control of mammalian parental behavior may be homologous in males and females (for a revision see Wynne-Edwards and Reburn, 2000; Nunes-Costa et al., 2015). The study of gender differences and effects in 24-h urinary free cortisol levels and changes from mid-pregnancy to 3-months postpartum can bring further empirical evidence to this hypothesis.