Psychoneuroendocrinology 92 (2018) 21–28

Contents lists available at ScienceDirect

Psychoneuroendocrinology

journal homepage: www.elsevier.com/locate/psyneuen

Hair cortisol concentration (HCC) as a measure for prenatal psychological distress — A systematic review

Paula Mustonen[a,b,*], Linnea Karlsson[a,b], Noora M. Scheinin[a,c], Susanna Kortesluoma[a], Bárbara Coimbra[d], Ana João Rodrigues[d], Hasse Karlsson[a,c]

[a] FinnBrain Birth Cohort Study, Turku Brain and Mind Center, Institute of Clinical Medicine, University of Turku, Finland
[b] Department of Child Psychiatry, University of Turku and Turku University Hospital, Turku, Finland
[c] Department of Psychiatry, University of Turku and Turku University Hospital, Turku, Finland
[d] Life and Health Sciences Research Institute (ICVS), School of Medicine, University of Minho, Braga, Portugal

ARTICLE INFO

Keywords:
Hair cortisol
Cortisol
Pregnancy
Psychological distress
Prenatal stress
Fetal programming

ABSTRACT

Prenatal environment reportedly affects the programming of developmental trajectories in offspring and the modification of risks for later morbidity. Among the increasingly studied prenatal exposures are maternal psychological distress (PD) and altered maternal hypothalamus-pituitary-adrenal (HPA) axis functioning. Both prenatal PD and maternal short-term cortisol concentrations as markers for HPA axis activity have been linked to adverse child outcomes and it has been assumed that maternal PD affects the offspring partially via altered cortisol secretion patterns. Yet, the existing literature on the interrelations between these two measures is conflicting. The assessment of cortisol levels by using hair cortisol concentration (HCC) has gained interest, as it offers a way to assess long-term cortisol levels with a single non-invasive sampling. According to our review, 6 studies assessing the associations between maternal HCC during pregnancy and various types of maternal PD have been published so far. Measures of prenatal PD range from maternal symptoms of depression or anxiety to stress related to person's life situation or pregnancy. The aim of this systematic review is to critically evaluate the potential of HCC as a biomarker for maternal PD during pregnancy. We conclude that HCC appears to be inconsistently associated with self-reported symptoms of prenatal PD, especially in the range of mild to moderate symptom levels. Self-reports on PD usually cover short time periods and they seem to depict partly different phenomena than HCC. Thus, methodological aspects are in a key role in future studies evaluating the interconnections across different types of prenatal PD and maternal HPA axis functioning. Further, studies including repetitive measurements of both HCC and PD during the prenatal period are needed, as timing of the assessments is one important source of variation among current studies. The significance of prenatal HCC in the context of offspring outcomes needs to be further investigated.

1. Introduction

Starting from the Barker hypothesis (Barker, 1986) on the developmental origins of adult disease, the importance of fetal environment for human development has been increasingly recognized (O'Donnell and Meaney, 2017). The characteristics of prenatal environment prepare the fetus for postnatal circumstances but the impact may also be maladaptive, ultimately leading to negative developmental outcomes in the offspring. One of the environmental factors gaining increasing interest is exposure to maternal prenatal psychological distress (PD), a heterogenic concept that comprises varying types of maternal distress, such as symptoms of depression or anxiety, experiences of stress related to either pregnancy itself or to everyday life situations and major life events (Dunkel Schetter, 2011; Scheinost et al., 2017). The topic is clinically very relevant as it has been estimated that the effects of prenatal PD could explain up to 17% of the variance in childhood cognitive abilities (Bergman et al., 2007) and that exposure to prenatal anxiety may double the prevalence of child psychiatric disorders (O'Donnell et al., 2014). Although PD has sometimes been associated with accelerated development of the offspring (e.g. DiPietro et al., 2006; Li et al., 2013), it has more consistently been linked to impaired neurological and psychosocial development (for a review, see van den Bergh et al., 2017; Capron et al., 2015; Grace et al., 2016; Pearson et al., 2016; Rijlaarsdam et al., 2017). Thus, prenatal PD is an important target for focused prevention and intervention programs (Glover, 2014), and identification of phenotypes with the greatest risk to affect the fetal programming is essential.

* Corresponding author at: FinnBrain Birth Cohort Study, Turku Brain and Mind Center, Institute of Clinical Medicine, University of Turku, Finland.
E-mail address: pmmust@utu.fi (P. Mustonen).

https://doi.org/10.1016/j.psyneuen.2018.03.019
Received 14 March 2017; Received in revised form 26 March 2018; Accepted 26 March 2018

1.1. Maternal prenatal psychological distress (PD) and cortisol concentrations

Cortisol, the hormonal end-point of the main human stress regulation system hypothalamic-pituitary-adrenal (HPA) axis, has been suggested to have a significant role in mediating the effects of maternal stress on the fetus. In general, increased maternal prenatal glucocorticoid levels as measured by maternal salivary, blood or urine cortisol concentrations have been linked with similar child developmental outcomes as prenatal PD (Braun et al., 2013; Moisiadis and Matthews, 2014; Painter et al., 2012). Elevated maternal prenatal cortisol concentrations are reportedly associated with compromised cognitive and motor development, affective problems, blunted cortisol reaction to stress, and alterations in regional brain volumes and connectivity in children (Buss et al., 2012; Davis and Sandman, 2012; Huizink et al., 2003; Kim et al., 2017; O'Connor et al., 2013). However, the data are inconsistent (Zijlmans et al., 2015), and also positive associations between maternal cortisol concentration and child cognitive performance have been reported (Davis et al., 2017).

Associations between maternal cortisol concentrations and prenatal PD are also inconsistent, partially due to the biological heterogeneity of and variety between the phenotypes of PD. Maternal symptoms of pre- and postnatal depression were correlated with maternal salivary, blood or urine cortisol concentrations in only 24 out of 47 studies assessing their associations (Seth et al., 2016). Some studies have reported increased prenatal maternal salivary cortisol concentrations in the context of pregnancy-related anxiety (Kane et al., 2014; Obel et al., 2005). Interestingly, maternal exposure to traumatic events during pregnancy has been associated with lower maternal plasma cortisol concentration (Perroud et al., 2014). However, assessing long-term cortisol levels with momentary measurements is challenging and multiple sampling is varyingly applied (Seth et al., 2016; Short et al., 2016).

One factor potentially producing variance in these findings is that maternal HPA axis functioning alters significantly during the normal course of pregnancy (see Fig. 1; Benediktsson et al., 1997; Challis et al., 2001; Petraglia et al., 1992). It is known that the physiological 2–3-fold increase in maternal cortisol levels towards the end of pregnancy (Jung et al., 2011) is essential to the maturation of several organ systems of the fetus and plays an important role in initiating parturition (Moisiadis and Matthews, 2014). Thus, the timing of assessments is of special importance during pregnancy and findings in a given trimester cannot necessarily be generalized to other trimesters (Kane et al., 2014). On the other hand, HPA axis overall reactivity is attenuated during pregnancy (de Weerth and Buitelaar, 2005; Schulte et al., 1990), further illustrating the complexity of the picture.

Importantly, maternal cortisol is not the only mechanism relating prenatal PD to offspring outcomes. The importance of placental functioning – specifically, the placental enzyme 11β-hydroxysteroid dehydrogenase type 2 (11β-HSD2) in converting cortisol into inactive metabolites – is gaining support from recent evidence (Janssen et al., 2016). Other mechanisms that could mediate the fetal programming effects of PD include direct effects of placental CRH (pCRH), changes in maternal immune system functioning, gut microbiota composition, serotonin levels and epigenetic changes as well as maternal lifestyle during pregnancy (Abbott et al., 2018; Beijers et al., 2014; Elwenspoek et al., 2017; Glover, 2015; Howland et al., 2016; Karlén et al., 2015; Zijlmans et al., 2015).

1.2. Rationale of using hair cortisol concentration (HCC) as a measure of prenatal PD

During the past few years, hair cortisol concentration (HCC) has been presented as a method to assess *long*-term levels of cortisol (Stalder and Kirschbaum, 2012). Cortisol is accumulated into hair as it grows and thus, with the generally accepted average hair growth rate of one centimeter per month (Wennig, 2000), one or several segments of selected length can be analyzed for the mean levels of cortisol during the corresponding months. Instead of the more traditional short-term measurements of cortisol assessing either the reactivity or diurnal profile of cortisol by repetitive samples of saliva or blood (Adam and Kumari, 2009; Vining et al., 1983), HCC provides a possibility to measure retrospectively cumulative cortisol levels of previous months to gain a more complete picture of the mean cortisol levels during the chosen period, via a single sample (Davenport et al., 2006; Kirschbaum

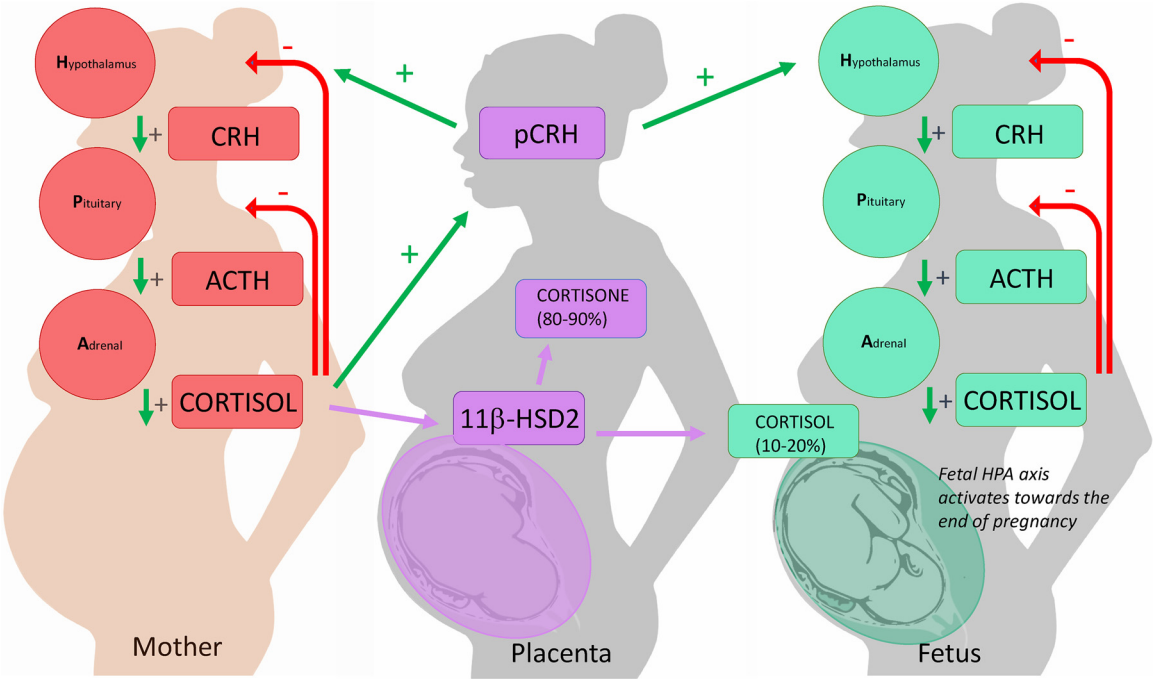

Fig. 1. Functioning of the HPA-axis during pregnancy. Maternal HPA-axis (in left) continues to funtion similarly as in non-pregnant states, but with the effects of placental pCRH (in the middle) and its positive feedback, the amounts of circulating CRH and cortisol increase. In left is pictured how the fetus is affected both by maternal pCRH (activating the fetal HPA-axis towards the end of pregnancy) and the inconverted proportion of maternal cortisol passing through the placenta.