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The association between perceived emotional support, maternal mood, salivary cortisol, salivary cortisone, and the ratio between the two compounds in response to acute stress in second trimester pregnant women

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ABSTRACT

Objective: Little is known about the effect of social support on the reactivity of the hypothalamic–pituitary–adrenal (HPA) axis during pregnancy. Moreover, when investigating the HPA axis most studies do not consider the activity of 11β-hydroxysteroid dehydrogenase type 2 (11β-HSD2), an enzyme within the salivary glands that inactivates cortisol to cortisone. This study explores the association between perceived emotional support and the maternal psychobiological stress response to a standardized naturalistic stressor by assessing maternal mood and the reactivity of salivary cortisol (SalF), salivary cortisone (SalE), and the SalE/(E + F) ratio as a marker of 11β-HSD2 activity.

Methods: Repeated saliva samples and measures of maternal mood were obtained from 34 healthy second trimester pregnant women undergoing amniocentesis which served as a psychological stressor. The pregnant women additionally responded to a questionnaire of perceived emotional support and provided sociodemographic (e.g., maternal educational degree) and pregnancy-specific data (e.g., planned versus unplanned pregnancy).

Results: Perceived emotional support neither showed a significant effect on mood nor on the SalF or SalE response to stress. However, a moderately strong positive association was found between perceived emotional support and SalE/(E + F) ($r = .49$). Additionally, the final regression analysis revealed a significant negative relationship between educational degree, planned/unplanned pregnancy and SalE/(E + F).

Conclusion: Findings suggest a higher metabolization of cortisol to cortisone in pregnant women with higher emotional support. In contrast, higher maternal education and unplanned pregnancy appear to be associated with decreased salivary 11β-HSD2 activity. The current study emphasizes the importance of taking the activity of 11β-HSD2 into account when examining SalF.

Introduction

A growing body of research suggests that maternal prenatal stress can influence the course of human gestation, affect fetal development, impact maternal postpartum well-being, and potentially set the trajectory for subsequent child, adolescent, and adult development [1–4]. Findings also imply that a stress-induced dysregulation of the maternal hypothalamic–pituitary–adrenal (HPA) axis and excessive maternal cortisol concentrations during pregnancy may exert programming effects on the structure and function of the developing fetal tissues and organs [5]. In the pursuit of elucidating the underlying biological mechanisms of prenatal stress, research has begun to examine the acute psychobiological stress response in pregnant women more systematically by using standardized stressors [1,6–12]. Similar to the non-pregnant state, salivary cortisol levels in pregnant women rise significantly in response to laboratory-based psychosocial stress tests [1,6–8] or in response to morning awakening [9,13,14]. But, due to the various endocrine changes the reactivity of the HPA axis seems to diminish with progressing gestation [15]. The stress response nevertheless demonstrates sufficient inter-individual variability in order to research its association with maternal psychological parameters, offspring development, and birth outcome [15]. For example, increased salivary cortisol reactivity during pregnancy has been associated with shorter

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gestational length [16,17], reduced neonatal birth weight [16], and increased maternal postpartum depressive symptoms [1]. Few studies, however, have investigated the extent to which psychosocial resources may be linked with the acute maternal stress response. In a previous study, our workgroup discovered that higher self-efficacy in second and third trimester pregnant women predicted a less extensive salivary cortisol response to a standardized psychosocial stress test [7]. In line with our results, a recent finding showed that pregnant women, who at 10 to 20 weeks of gestation had indicated that they had experienced more positive life events within the past year, exhibited a dampened salivary cortisol awakening response between 35 and 36 gestational weeks [18]. Further studies in this field are needed to identify those psychological and psychosocial resources that exert a protective effect on the maternal stress response in order to better comprehend the underlying biological pathways of prenatal stress and to help develop stress prevention programs for pregnant women at risk of high stress exposure.

A psychosocial factor well-known from epidemiological studies for its beneficial influence on physical and mental health is social support [19]. In the non-pregnant state, the HPA axis response to acute psychosocial stress seems to be attenuated in participants with higher social support [19,20], although not all studies have been able to confirm this [21]. In pregnant women under non-stressed conditions, an inverse association was found between social support and maternal plasma adrenocorticotropin releasing hormone (ACTH) and plasma cortisol concentrations obtained from single plasma measures [22]. No study thus far has examined the relationship between social support and the acute HPA axis stress reactivity during pregnancy. Pregnancy research has mainly focused on the impact of social support on 1) maternal psychological well-being, 2) maternal health behavior and 3) pregnancy complications and birth outcome. Briefly, results indicate that increased support from the pregnant woman's partner, family members, and friends is associated with reduced state anxiety, pregnancy-specific anxiety, depressive symptoms, and better life quality and satisfaction with pregnancy [23–25]. Moreover, higher social support is related to enhanced health behavior in pregnant women, including reduced smoking [24,26], alcohol [27], and drug [28] consumption, a better diet, and an increased likelihood of prenatal vitamin intake [26]. Findings also report associations between social support and increased gestational length [29], a lower incident of preterm birth [30,31], higher birth weight [32,33], and higher APGAR-scores (an indicator of neonatal health status) [32,34]. However, studies have also produced conflicting results with regard to social support and birth outcome possibly due to differing conceptualizations and measurements of social support as well as other methodological issues [3,35]. The additional assessment of stress biomarkers might contribute to elucidate these inconsistencies. Therefore, first basic information on the association between social support and the acute HPA axis reactivity during pregnancy is required.

One method of examining the acute maternal stress response in a standardized but nevertheless more naturalistic setting than provided by laboratory stress tests, is by making use of pregnancy-specific medical examinations as stressors. Undergoing amniocentesis, for example, is known to increase state anxiety and perceived stress in pregnant women [36–38].

Also, researchers have recently recommended exploring the use of new biomarkers in the investigation of stress during pregnancy [4]. With regard to the HPA axis, it is important to note that salivary cortisol (SalF) levels only mirror 50 to 60% of the plasma cortisol levels due to the conversion of biologically active cortisol into inert cortisone by the enzyme 11β-hydroxysteroid dehydrogenase type 2 (11β-HSD2) in the parotid and submandibular glands [39,40]. Consequently, the activity of 11β-HSD2 influences SalF concentrations, and recent findings suggest that SalE may reflect plasma cortisol levels more accurately than SalF [41]. Thus, 11β-HSD2 might explain some of the conflicting findings with regard to SalF in stress literature [42]. Moreover, one of the major limitations of conventionally used immunoassays in determining SalF levels is the cross-reactivity by other steroids such as cortisone [43]. It has accordingly been recommended to measure SalF and SalE utilizing more precise methods such as liquid chromatography–tandem mass spectrometry (LC–MS/MS) [43].

Besides the salivary glands, the 11β-HSD2 enzyme is also expressed in other tissues such as the kidney, colon, and placenta [44]. The ratio between cortisol and cortisone in the different body fluids (e.g., saliva, umbilical cord blood, urine) is frequently used as a non-invasive marker for the enzyme activity in the respective tissues (e.g., salivary glands, placenta, kidney) [43,45]. In a previous study by our workgroup, we were able to show that the SalE/(E + F) ratio in pregnant women decreased in response to the stressful experience of an amniocentesis while SalF and SalE levels increased [46]. Besides, a higher SalE/(E + F) ratio during the second trimester of pregnancy predicted increased neonatal birth weight and size.

The aim of the study at hand was to research the influence of social support on the acute psychobiological stress response induced by having to undergo amniocentesis in healthy second trimester pregnant women. In addition to examining the effect of social support on the SalF response, we intended to explore the effect of social support on SalE and the SalE/(E + F) ratio, which served as an index of salivary 11β-HSD2 activity.

Methods

Overview

The present study is part of a large prospective research project investigating the psychobiology of stress during human pregnancy [46].

Participants

The participants were recruited in Switzerland at the Department of Obstetrics of the University Hospital Zurich and in collaboration with the Cantonal Hospitals of Schaffhausen and Lucerne, the Hospitals of Bülach, Uster, Wetzikon, and two private gynecological practices in Winterthur and Zurich between April 2009 and January 2011. The participants were informed in detail about the ongoing study after they received an appointment for the amniocentesis procedure and were asked whether they would be interested in participating. Exclusion criteria for study participation were multifetal pregnancy, pregnancy via artificial insemination, maternal or fetal complications, current maternal mental disorder, current use of psychotropic substances or medication, protein restricted diet, smoking, alcohol consumption of more than one glass of wine or beer per week, and obesity. A final sample of 34 healthy second trimester pregnant women scheduled to undergo amniocentesis for fetal karyotyping was included into the study. The participants were required to abstain from heavy physical exercise, alcohol, caffeine, and chewing gum for 24 h prior to the appointment and were asked to abstain from eating for 2 h and from tooth brushing 1 h beforehand. Written informed consent was obtained from all participants prior to the study examination. The participants received 200 Swiss Francs for their time and efforts, as well as a gift set containing skincare products for pregnant women, mothers, and babies. The study protocol was approved by the cantonal ethics committees of Zurich, Schaffhausen, and Lucerne and was conducted in accordance with the Declaration of Helsinki.

Study design and procedure

All amniocenteses were scheduled in the morning hours due to hospital procedures and logistics. The pregnant women arrived at the hospital approximately 50 min prior to the amniocentesis appointment, provided written informed consent, and responded to study administrative questionnaires. The stressful nature of the amniocentesis served as a standardized, real-life stress provocation situation. The average duration of this invasive medical procedure is approximately 10 min. Repeated saliva samples and psychological state questionnaires