

A photograph of a pregnant woman wearing a white, flowing dress. She is holding a large, vibrant yellow flower with orange-tipped petals against her bare pregnant belly. Her hands are gently cradling the flower and her abdomen. The background is a soft, out-of-focus white.

Pearl
Ghaemmaghami

**Investigating
the Psychobiological Stress Response
and
the Conversion of Cortisol to Cortisone
in Human Pregnancy**



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ABSTRACT

Stress during human pregnancy is associated with various adverse consequences for the physiological and psychological wellbeing of mother and child. A main focus for the research field of stress during pregnancy is to identify the underlying biological mechanism by which the maternal psychological stress is transferred to the developing foetus. Glucocorticoids, such as cortisol seem to play a pivotal role, since an overexposure of maternal cortisol, for example due to psychological stress is capable of crossing the placental barrier and thereby reaching the foetus. Heightened cortisol levels in the prenatal period have been associated with preterm birth and low birth weight. In animal studies, the placental enzyme 11β -hydroxysteroid dehydrogenase type 2 (11β -HSD2) which converts active cortisol into its inactive metabolite cortisone, protects the developing foetus against an overexposure to maternal cortisol concentrations. This enzyme is also present in the adult salivary glands, where it exerts the same conversion of cortisol to cortisone.

The aim of the present thesis was to examine the psychological and physiological stress reactivity of pregnant women confronted with a standardized stressor and to concurrently investigate the conversion of cortisol to cortisone in the saliva and amniotic fluid of pregnant women. The empirical study results of the present thesis are divided into two parts.

In part 1 (see chapter 7, page 63), the response of salivary cortisol, cortisone and the ratio between the two compounds, as an indicator of 11β -HSD2 activity in the salivary glands, were compared to the stress elicited by an amniocentesis with cortisol, cortisone and again the ratio between the two compounds in the amniotic fluid which served as an indicator of 11β -HSD2 activity in the foetal system. This ratio was calculated by dividing cortisone (the end product of 11β -HSD2 activity) by the total sum of cortisone plus cortisol and has been adopted in previous studies to investigate the 11β -HSD2 activity.

An aliquot of amniotic fluid and repeated saliva samples were collected from 34 healthy pregnant women undergoing an amniocentesis for karyotyping. Mood alterations due to the intervention were surveyed using questionnaires. Subjects were re-examined in a

control condition 2.7 weeks later after having been informed about the inconspicuous result of the amniocentesis.

The results revealed that subjects with a stronger acute stress response seem to have higher 11 β -HSD2 activity levels in the foetal system as measured by the above mentioned ratio of cortisone to cortisol in the amniotic fluid.

In part 2 (see chapter 8, page 80), we investigated the role of the maternal autonomic nervous system (ANS) in response to the stress of the amniocentesis and compared this stress response with amniotic fluid cortisol, cortisone and the conversion of cortisol to cortisone. Similar to the results in part 1, the amniocentesis revealed significant autonomic alterations compared to the control condition. Links between the ANS stress response and the ratio of cortisone to cortisol in the amniotic fluid were detected as well.

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ABBREVIATIONS

11 β -HSD	11 β -Hydroxysteroid Dehydrogenase
11 β -HSD1	11 β -Hydroxysteroid Dehydrogenase Type 1
11 β -HSD2	11 β -Hydroxysteroid Dehydrogenase Type 2
ACh	Acetylcholine
ACTH	Adrenocorticotrophic hormone
AF	Amniotic fluid
AME	Apparent mineralocorticoid excess
ANOVA	Analysis of variance
ANS	Autonomic nervous system
AUC _i	Area under the curve with respect to increase
AVP	Arginine vasopressin
BNST	Bed nucleus of the stria terminalis
BMI	Body mass index (kg/m ²)
bmp	Beats per minute
CBG	Corticosteroid binding globulin
CG	Control group
CNS	Central nervous system
CRH	Corticotropin-releasing hormone
D	Dopamine
DBP	Diastolic blood pressure
DNA	Deoxyribonucleic acid

E	Cortisone
EG	Experimental group
EPDS	Edinburgh Postnatal Depression Scale
EPI	Epinephrine
IUGR	Intrauterine growth restriction
F	Cortisol
GR	Glucocorticoid receptor
HF	Power in the high frequency range
HPA	Hypothalamic-pituitary-adrenal
HR	Heart rate
HRV	Heart rate variability
HSD	Hydroxysteroid dehydrogenase
LC	Locus coeruleus
LF	Power in the low frequency range
LF/HF ratio	Ratio LF [ms ²] / HF[ms ²]
MAP	Mean arterial pressure
MDBF	Multidimensional Mood Questionnaire (Multidimensionaler Befindlichkeitsfragebogen)
MESA	Measure for Assessment of General Stress Susceptibility (Messinstrument zur Erfassung der Stressanfälligkeit)
MR	Mineralocorticoid receptor
mRNA	Messenger ribonucleic acid
NN	Normal to normal intervals
NE	Norepinephrine

NTS	Nucleus of the solitary tract
PSNS	Parasympathetic nervous system
PVN	Paraventricular nucleus
RSA	Respiratory sinus arrhythmia
SA	Sinoatrial
sAA	Salivary alpha-amylase
SalE	Salivary cortisone
SalF	Salivary cortisol
SAM	Sympatho-adrenomedullary
SBP	Systolic blood pressure
SCN	Suprachiasmatic nucleus
SDNN	Standard deviation between normal consecutive beats
SEM	Standard error of the mean values
SNS	Sympathetic nervous system
STAI	State-trait anxiety inventory
STAI-s	State anxiety
STAI-t	Trait anxiety
T	Time
T3	Triiodothyronine
T4	Thyroxine
TSH	Thyroid-stimulating hormone
TSST	Trier Social Stress Test
VAS	Visual analogue scale