Assessment of psychobiological stress reactivity and its relation to postpartum mood states

Bratsikas, Aliki

Abstract: Eine Schwangerschaft stellt für die meisten Frauen ein einschneidendes Ereignis dar und bedarf diverser physiologischer und psychologischer Anpassungsprozesse. Psychosoziale Belastungen in der Schwangerschaft scheinen diese Anpassungsprozesse, u.a. auf der hormonellen Ebene, in ungünstiger Weise zu beeinflussen und das Risiko für Komplikationen in der Schwangerschaft und bei der Geburt zu erhöhen. Im ersten Teil der vorliegenden Arbeit bestand das Ziel darin, psychosoziale relevante Faktoren, die einen ungünstigen Einfluss auf den Schwanger- und Geburtsverlauf haben können, in einem neuen Messverfahren zu integrieren. Der Fragebogen soll als mögliches Screeninginstrument zur Früherkennung von Frauen mit einem erhöhten psychosozialen Risiko für die Entwicklung von Schwangerschafts- oder Geburtskomplikationen eingesetzt werden können. Anhand von Interviews mit Schwangeren und unter Einbeziehung bestehender Messinstrumente zur Erfassung von Belastungen in der Schwangerschaft, wurden fünf Skalen mit je zehn Items konstruiert: Das Zürcher Inventar zur psychosozialen Befindlichkeit in der Schwangerschaft (ZIPS). In zwei aufeinander folgenden Substudien (N = 154 bzw. N = 60) wurde die interne faktorielle Struktur des ZIPS überprüft und die Reliabilität und Validität untersucht. Insgesamt liefern die vorliegenden Befunde dieser Fragebogenanalyse erste Hinweise auf eine plausible Faktorenstruktur, gute psychometrische Kennwerte und interessante erste Validitätsbefunde. Beim ZIPS handelt es sich um ein psychometrisch solides Verfahren, das die psychosoziale Befindlichkeit von Schwangeren umfassend zu erheben vermag. Dementsprechend könnten anhand eines Screenings Frauen mit einem erhöhten psychosozialen Risiko von einer frühen Intervention präventiver Art profitieren. Im zweiten Teil der Doktorarbeit wurde der Zusammenhang zwischen der psyochobiologischen Stressreaktivität während der gesunden Schwangerschaft und der psychischen Befindlichkeit postpartum untersucht. Hierzu nahmen 57 gesunde Schwangere an einem standardisierten psychosozialen Stresstest (Trier Social Stress Test, TSST) teil. Die biologische Stressreaktivität wurde im Speichel anhand des endokrinen Parameters Cortisol gemessen, während psychologische Faktoren mittels Fragebogen erhoben wurden. Es konnte gezeigt werden, dass Frauen, die nach der Geburt eine depressive Symptomatik (Postpartum Blues) entwickelten, bereits während der Schwangerschaft eine auffällige psychobiologische Stressreaktivität aufwiesen. Frauen mit einer depressiven Gestimmtheit postpartum zeigten im Stresstest höhere Cortisolanstiege, eine höhere Ängstlichkeit und eine schlechtere Befindlichkeit nach der Stresskonfrontation. Zudem wurde bei den Frauen dieser Gruppe generell eine erhöhte Ängstlichkeit und Stressanfälligkeit sowie vermehrt Appetit- und Schlafstörungen festgestellt als bei den Frauen, die nach der Entbindung keine depressive Verstimmung berichteten. Die Ergebnisse weisen darauf hin, dass gesunde Schwangere mit einem erhöhten Risiko für postpartale depressive Verstimmung bereits während der Schwangerschaft anhand einer höheren Cortisolreaktivität und einer höheren psychologischen Reaktivität auf einen psychosozialen Stressor frühzeitig identifiziert werden können. For most women pregnancy represents an incising event and requires various physiological and psychological adaptive processes. Psychosocial stress seems to have adverse impact on these adaptive processes and is known to increase the risk for pregnancy and birth complications. The purpose of the first part within this research project was the development and validation of a new inventory assessing important aspects of the psychosocial well- being during pregnancy. The development of the questionnaire based on interviews with pregnant women as well as on the comprehension of existing instruments measuring pregnancy related psychosocial strain. The development resulted in an inventory consisting of five scales, with ten items each: The Zurich Inventory of

Psychosocial Well-being in Pregnancy (ZIPP). In order to investigate its factorial structure the inventory was applied to a sample of 154 pregnant women. The reliability and validity was examined by means of the data of 60 pregnant women. The results show a consistent factorial structure and strongly support good psychometric properties of the scales and validity. Taken together, the findings indicate that the ZIPP is a short psychometric instrument which validly and reliably assesses psychosocial well-being in pregnancy. In regard to the results concerning the predictive validity the questionnaire is applicable as a screening tool helping to identify women at risk for an adverse birth outcome. Thus, the possibility for early preventive intervention is given. The purpose of the second part of this work was to examine the association between psychobiological stress reactivity during healthy pregnancy and depressive symptoms in the early puerperium. A sample of healthy nulliparous pregnant women (N = 57) between the ages of 21 and 35 years underwent a standardized psychosocial stress test (TSST) during pregnancy. Women with depressive symptoms postpartum showed significantly higher cortisol responses to the stress test compared to women without depressive symptoms in the puerperium, whereas baseline levels did not differ. Additionally, women in the depressive group showed significantly higher state anxiety and lower mood state throughout the experiment. Furthermore, women in this group showed higher stress susceptibility, higher trait anxiety and higher levels in the Symptom Checklist. No differences were found for prior episodes of psychiatric disorders, obstetrical complications, birth weight or mode of delivery. Our data provide evidence that healthy pregnant women developing postpartum depressive symptoms might be identified already during pregnancy by means of their higher cortisol reactivity and their higher psychological reactivity in response to psychosocial stress. The higher cortisol stress response might be interpreted as a biological prodromal symptom, preceding postpartum depressive mood changes.

ASSESSMENT OF PSYCHOBIOLOGICAL STRESS REACTIVITY AND ITS RELATION TO POSTPARTUM MOOD STATES

Abhandlung zur Erlangung der Doktorwürde
der Philosophischen Fakultät der Universität Zürich

vorgelegt von
Aliki Bratsikas

von Winterthur / Zürich

Angenommen auf Antrag von Frau Prof. Dr. Ulrike Ehlert
und Herrn Prof. Dr. med. Roland Zimmermann

Zürich, 2006

Acknowledgements

First I would like to thank Professor Ulrike Ehlert, for giving me the opportunity to do scientific research in one of the most interesting interdisciplinary fields of psychology and obstetric research.

I also wish to express my thanks to all cooperating obstetricians, midwives and health care staff, and particularly to my Co-Supervisor Professor Roland Zimmermann, MD, and Urs Lauper, MD, from the Department of Obstetrics, University Hospital of Zurich, for their valuable advice and support in regard to the recruitment of the pregnant women. I also thank Kurt Bischofberger, MD, from the Department of Obstetrics, St. Elisabethen Hospital, Lörrach, Germany, for his support in data collection.

I would like to thank all the women for participating in the studies.

I also like to thank my students, Daniela Klaus, Gabriela Schöbi, Christine Wehrli, Nicole Fluri, Christine Wolfinger, Lea Hauri, Karin Meier, Sandra Voser, Selina Fischer, Somea Gisler and Barbara Schmid for their help in conducting the experiments. Special thanks also to Changiz Mohiyeddini for his valuable statistical support.

I thank the two further members of our “Triple A-Team”, Ada and Ariadne, for carrying out this project.

I thank my colleagues at the Department of Clinical Psychology and Psychotherapy and especially my friends Tanja Schad, Ulrike Rimmele and Petra Wirtz for having a great time besides the heavy work.

A special thanks goes to Tania Kongstad. She read and corrected parts of the manuscript.

I express my sincere thanks to my parents, my sister Christina and brother George and my best friend Nina for the support, understanding and encouragement throughout the years.

My most deep thanks go to Leo, who supported me in every single way and is a never-ending source of strength, happiness and joy, thank you!

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1 Introduction

The present research project sought to investigate psychosocial well-being and physiological parameters during pregnancy and to examine its association to postpartum mood states. This project consisted of two empirical parts. The objectives of the first part were the development of a new questionnaire for the assessment of psychosocial well-being during pregnancy and its validation, whereas the second empirical part incorporated the examination of the association between psychobiological stress reactivity to psychosocial stress during pregnancy and the potential development of depressive symptoms in the puerperium.

Etiological factors of complications such as preterm labor or gestational hypertension remain unclear in up to 50%. However, there is growing evidence that psychosocial factors contribute to adverse pregnancy and birth outcomes (Ehlert, Sieber, & Hebisch, 2003). Thus it is not surprising that in the recent years, applied researchers have become increasingly interested in the relation between psychosocial stress and its negative effects on the course of pregnancy, birth outcomes and the postpartum (Sandman, Wadhwa, Chicz-DeMet, Dunkel-Schetter, & Porto, 1997). The majority of studies though focus predominantly either on the stimulus based or the reaction centered aspect of stress during pregnancy.

In order to avert the limitations of the present conceptualisations of stress in prenatal research it seems to be inalienable to combine both stimulus and response properties, as well as transactional aspects, in the sense of Lazarus' transactional stress-theory, into one single measure.

Hence, the purpose of the first part within this research project was to create a questionnaire comprising the most important factors known to affect gestational complications, grouped into reaction, stimulus and transactional based aspects. This aim was achieved by means of the three following steps:

(a) The item generation, which has been conducted in an explorative way, by interviewing a sample of 14 women with idiopathic premature labour, about their psychosocial well-being. Additionally, the item generation was based on the consideration of existing questionnaires concerning the measurement of stress and well-being in pregnancy.

(b) The exploratively developed questionnaire was then applied to a sample of 154 pregnant women, in order to explore its internal factorial structure and to evaluate its psychometric values, and to shorten the item pool on the basis of these factorial and psychometric parameters.

(c) The third step included the study of the factorial structure in the sense of a cross-validation on the basis of a sample of 60 healthy pregnant women. The analyses were extended in examining the convergent and discriminant validity, in relating the new developed questionnaire with other measures assessing similar constructs. In addition, construct validity (predictive validity) was calculated in correlating the scales of the new inventory with birth outcomes (length of gestation and birth weight), as well as birth complications (secondary caesarean section, loss of blood > 500 ml, initiation of delivery and perineal rupture of second and third grade).

The second empirical part of this research project was devoted to the investigation of the psychophysiological stress reactivity during pregnancy in relation to the potential development of postpartum depressive symptomatology. Postpartum depressive symptoms occur in about 50% of women who have recently given birth, while postpartum major depression occurs in approximately 10% to 20% of women within 6 months postpartum (Ehlert, Patalla, Kirschbaum, Piedmont, & Hellhammer, 1990). Postpartum disorders can

have long-term effects for both mother and child if remain untreated. Therefore it is important to discover potential etiological factors to identify pregnant women at risk for postpartum depressive mood changes to initiate prevention as early as possible. While different psychosocial factors such as marital discord, number of critical life events or a previous history of depression may be associated with postpartum depression, a number of hypotheses have been stated to account for postpartum depressive symptoms in terms of neuroendocrinological dysfunction.

Up to now, investigations have been confined to the research of the hormones estradiol and progesterone and little attention has been paid to the role of cortisol regarding mood changes in the puerperium. However, all studies regarding cortisol are based on the research of unprovoked basal cortisol levels measured either during pregnancy or postpartum, with controversial findings.

So far, none of these studies has looked at HPA *reactivity* during pregnancy and the occurrence of depressive symptoms in the postpartum period. We therefore investigated a sample of 57 healthy primiparous pregnant women, who underwent a standardized psychosocial stress situation (Trier Social Stress Test, TSST, Kirschbaum, Pirke, & Hellhammer, 1993) and sought to find out whether the stress reactivity to psychosocial stress during pregnancy played a predictive role in terms of depressive symptoms postpartum. The pregnant women participated in the TSST, which consists of an unprepared speech and a mental arithmetic task performed in front of an audience. The TSST (Kirschbaum et al., 1993) has repeatedly induced profound endocrine and cardiovascular responses in 70-80% of the subjects tested (Dickerson & Kemeny, 2004). Besides the assignment of various psychological measures, physiological reactivity was measured via salivary cortisol samples throughout the whole experiment. On the average of 13 days after delivery, depressive symptoms were assessed using the German version of

the Edinburgh postnatal depression scale (EPDS, Cox, Holden, & Sagovsky, 1987). According to a cut-off score of 9/10 the sample was divided into two groups with an EPDS score ≤ 9 (N = 41) and an EPDS score ≥ 10 (N = 16).

The results indicate a distinct pattern of physiological as well as psychological stress reactivity during pregnancy for women developing postpartum depressive symptoms. This is the first study to show that postpartum depressive symptoms are significantly associated with higher cortisol reactivity as a response to psychosocial stress. Further, women with an EPDS score higher than nine showed increased state anxiety and showed lower mood state throughout the experimental procedure. Additionally, the same group showed higher levels of depressive symptoms, trait anxiety and higher stress susceptibility during the time of pregnancy, compared to women whose postpartum mood stayed unobtrusive. Thus, women at high risk for depression after delivery might already be identified during pregnancy by means of their distinct pattern of psychobiological stress reactivity. These results might help provide a better understanding in the etiology of postpartum mood disorders and their prevention, respectively.

2 Theoretical Background

The theoretical background describes the constitutional constructs in this work. These constructs are arranged in terms of psychological concepts specific to stress in pregnancy, its diverse definitions, the adverse impact of stress on the ongoing of pregnancy, birth outcomes and the postpartum period. Furthermore, the psychological well-being after delivery will be discussed, confined to postpartum depressive symptoms and its psychological and endocrinological agents.

2.1 Assessing psychosocial well-being in pregnancy

There is great evidence that stress is thought to be one of the psychophysiological factors that may contribute to adverse pregnancy and birth outcomes, for instance preterm labor, gestational length, preeclampsia, birth weight or complications during delivery. But how is stress defined? A body of studies have been conducted regarding the concept of stress itself, and additionally, there is strong effort to adapt stress concepts for use among pregnant populations. First, a selection of some of the most important theories of the stress-concept will be presented. Subsequent, the comprehension of the association of various stress concepts in obstetric research will follow.

2.1.1 Definitions of stress in general

The expression of the term “stress” has lately become a buzzword and is often used without being precisely defined. Thus, its broad construct should be accurately described. However, since the first reports of the stress concept in the 1920’s, extensive research has been conducted in the field of stress conceptualization.

Some of the early investigation on stress has been conducted by Walter Cannon (1929) in establishing the well-known fight-or-flight response to a stressor. When potentially threatening cues are present, neuroendocrine responses are initialized to optimize the survival of the individual, e.g. in releasing hormones, which increase heart rate and blood pressure, delivering more oxygen and blood sugar to power important muscles (Cannon, 1929).

Hans Selye (1950) took a different approach from Walter Cannon. While the fight-or-flight response applies to the very short term, Cannon focussed on the longer-term response to stress. According to Selye (1950), organisms facing a stressor will immediately enter into alarm state where different physiological changes take place, followed by the second stage, the resistance. This phase is characterised by trying to remain aroused while the organism works to defend against and adapt to the threatening stimuli. If the stressor persists for a certain period of time, the object will step in to a third stage of this 3-phasic model, called exhaustion, where the organism suffers seriously and looses balance (Selye, 1950).

Lazarus (1984b) implemented a cognitive theory of stress appraisal and coping. According to this theory, what matters is not the event itself, but *how* somebody perceives and interprets that event. The first stage consists of the so-called primary appraisal, where a stimulus is appraised as positive, negative or neutral. If the potential stressor is being appraised as negative the next question to be posed is if the stimulus is interpreted as harmful, threatening or challenging. The secondary appraisal involves evaluating the resources, whether a person has the capability to cope with a particular stressor at the moment. Thus, the definition of stress includes consideration of the interaction between environmental demands and the power of the organism to deal with these demands trying not to exceed resources.

2.1.2 Stress in pregnancy-research

There are only few studies which consequently applied the stress-concept of Lazarus to the bio-psychological obstetric research. Lobel (1994) summed up the adaptation of Lazarus framework in pregnancy research as follows: *According to Lazarus' conceptual approach to stress, robust stress measurement calls for the identification of stressful stimuli, subjects' appraisals of these stimuli, and their responses, particularly emotional responses. No single measure exists which assesses each of these dimensions. [..]. The ideal in prenatal stress research would be to examine effects of a single underlying latent construct from a variety of [..] indicators, casting the "wide net" that is advised by methodologists to establish the construct validity of an abstract concept such as stress* (Lobel 1994; p. 231). As reported above, a broad body of research exists regarding the concept of stress itself. However, the interpretation of the applicability of general stress research in the context of pregnancy is difficult and definitions are often inconsistent (Istvan, 1986). To summarize, stress in prenatal research has been defined predominantly focusing either on stimulus-based *or* response-based stress definitions. To avert the limitations of the present conceptualisations of stress in prenatal research it seems to be inalienable to combine both the stimulus and response properties of stress (Lazarus, 1984a; Lobel, Dunkel-Schetter, & Scrimshaw, 1992).

In the following sections, different psychological concepts of stress used among pregnant populations will be presented by discussing the most important psychosocial factors related to adverse pregnancy and birth outcomes. The factors will be grouped according to their operational definition of stress, i.e. *stressors* will be distinguished from *stress responses*.

2.1.3 Reaction centered aspects of stress in pregnancy and their influence on adverse birth outcome

2.1.3.1 Prenatal maternal anxiety

Initially, the measurement of prenatal anxiety was narrowed to the application of questionnaires originally made for the assessment of general anxiety (Allen, Lewinsohn, & Seeley, 1998; Barnett & Parker, 1986; Bhagwanani, Seagraves, Dierker, & Lax, 1997) such as the use of the State-Trait Anxiety Inventory (STAI, Laux, Glanzmann, Schaffner, & Spielberger, 1981). Surprisingly, even recent studies (e.g. Leithner et al., 2004) still abstain from using pregnancy and birth specific questionnaires regarding the measurement of prenatal anxiety in obstetric research. Even though women with high pregnancy and birth related anxiety tend to be anxious in general (Areskog, Uddenberg, & Kjessler, 1983), it is necessary to extend the application of general inventories by the use of specified tools in order to assess prenatal anxiety, which has been implemented by some researchers (Dunkel-Schetter, 1998; Sjogren, 1997).

Now, what exactly is prenatal maternal anxiety? In literature, a variety of definitions can be found. For instance, Standley and colleagues (1979) identified three dimensions or prenatal maternal anxiety: pregnancy and childbirth, parenting the child, and general psychiatric symptomatology. Later, in the early 1990's Levin (1991) presents the following three aspects of prenatal anxiety in his model: being pregnant, childbirth and hospitalization. The two approaches have one feature in common: both of them distinguish between pregnancy related anxiety and birth related anxiety.

According to Huizink, Mulder, Robles de Medina, Visser and Buitelaar (2004) *pregnancy* related anxiety is described as being a result of having fear of the oncoming birth, concerns about one's appearance and fear of bearing a physically or mentally handicapped. As apparent, Huizink et al. (2004) do not separate pregnancy specific and birth specific anxiety, but denote "fear of giving birth" as a part of pregnancy related anxiety. In

contrast, Lukesch (1983) separates pregnancy related fears from birth related anxiety. According to his definition, birth anxiety comprises solely of fear associated with the childbirth itself: fear of pain, and therefore fear of pain itself, fear of losing control, fear of complications during birth. In a similar way, Melender (2002) specifies childbirth related anxiety in her definition of *birth related anxiety* as fear of pain, obstetric injury, emergency caesarean obstetric injury or fear of dying during childbirth. She also includes lack of trust in the health care staff assisting in childbirth, fear of not being allowed to participate in making important decisions or worries about an unfriendly staff or of being alone (Melender, 2002), whereas *pregnancy related anxiety* can be characterized as fears concerning the course of pregnancy: fears about the health of the unborn child, fears of complications during pregnancy and worries about one's own health and appearance. In line with the reported comments of Lukesch (1983) and Melender (2002), prenatal maternal anxiety is divided into two categories in the present research: pregnancy and birth related anxiety.

Pregnancy and birth related anxiety does not remain stable throughout pregnancy, but proceeds in a u-shaped course. While higher anxiety levels were observed during the first and the third trimester, prenatal maternal anxiety was lower during the second trimester (Da Costa, Larouche, Dritsa, & Brender, 1999; Huizink et al., 2004; Rofe, Blittner, & Lewin, 1993). According to the summary of Melender (2002) women are predisposed to prenatal anxiety when the following factors apply: young maternal age, low education level, psychological problems before and/or during pregnancy, sexual abuse or problems concerning sexuality, low self-esteem, lack of social support as well as high exposure to daily hassles. She also mentions previous adverse experiences in pregnancy or delivery, lack of knowledge and not attending the childbirth preparation classes.

There is evidence that prenatal anxiety might be related to an adverse birth outcome. One investigation conducted by Wadhwa et al. (Wadhwa, Sandman, Porto, Dunkel-Schetter, & Garite, 1993) revealed that prenatal maternal anxiety was negatively associated with

gestational age at birth and positively associated with the clinical incidence of preterm birth, replicating previous findings (Lobel et al., 1992). Wadhwa et al. (1993) measured prenatal anxiety by means of five items concerning fears related to the health of the unborn, towards the labor and delivery process, and fears of not having confidence in the obstetrician and other health care providers. This finding was replicated in a subsequent study conducted by Rini et al. (1999), where pregnancy anxiety was found to be an important component of stress in predicting the length of gestation in a sample of 230 women (half Hispanic and half non-Hispanic white), even after controlling for obstetric and socio-demographic risk.

To sum up, prenatal maternal anxiety seems to be a fundamental factor in the assessment of stress during pregnancy.

2.1.3.2 Attitude towards pregnancy

A considerable number of studies investigating women's psychosocial state during pregnancy have been published nearly thirty years ago and represent an improper view of the pregnant woman of today (Dunkel-Schetter, Gurung, Lobel, & Wadhwa, 2000). The image of pregnant women has changed over the years. For instance, the majority of women today are engaged in a work process, in comparison to the situation twenty or thirty years ago. Women today have to face up to their multiple roles as housewifes, mothers and business women. The way pregnant women view themselves has changed completely and should be taken into account in modern research regarding the attitude of pregnant woman towards pregnancy.

Pregnancy represents a period of significant change for women. The way how women adapt to this new state influences women's psychological well-being and their attitude towards pregnancy. The manner of coping with the conflicts of physical change, alterations in roles, additions of responsibilities and concerns about a woman's own mothering

capabilities influences her ability to enjoy pregnancy and to feel good during the gestational period.

The concept of the attitude towards pregnancy has been extensively investigated by Lukesch and Lukesch (1976). In their view, attitude towards pregnancy is defined by three factors, which are also the basis of their German inventory "Attitude towards pregnancy, birth and sexuality" (SSG, Lukesch & Lukesch, 1976). Firstly, attitude towards pregnancy is characterized by the degree of the unfavourability of pregnancy (e.g. for items of the SSG: "Pregnancy is a frustration for the majority of pregnant women", "The movements of the unborn child are annoying"). The second factor is the attitude towards breast feeding which is described by the degree of the desirability of the opportunity to slake the child. Thirdly, the SSG includes aspects of inadequate over-solicitude towards children, fear of childbirth and attitude towards sexuality.

De Muylder et al. (1992) investigated the attitude towards pregnancy and its relation to preterm labor in a prospective study among 434 pregnant women at 24-28 weeks of pregnancy. In their study, attitude towards pregnancy was defined as the degree to which pregnancy was planned/wished and to what degree activities and attitudes had been modified due to pregnancy. They found out that preterm labor was better predicted by the attitude towards pregnancy and the antepartum fetomaternal relationship than by the sociomedical risc score (De Muylder, Wesel, Dramaix, & Candeur, 1992).

The degree of an adverse attitude towards pregnancy might depend on the successful (or unsuccessful) maternal adaptation during pregnancy. Kiehl and White (2003) use Roy's adaptation model as the conceptual framework in their study. According to this model individuals are considered to be in constant interaction with an ever changing environment. Individuals have to adapt in order to be able to respond positively to these changes (Kiehl & White, 2003). This model works well in explaining the general adaptation throughout life and is also well transferable to issues of childbearing. Accordingly,

pregnant woman need to adapt to react to changes of maternity in a positive way and – finally - to have a favourable attitude towards pregnancy.

Maternal adaptation during childbearing has been conceptualized by Lederman (1979). In her view, maternal adaptation consists of the following seven factors: well-being of self and the baby, acceptance of pregnancy, identification of a motherhood role, preparation for labor, help/control, relationship with mother, relationship with husband/partner. Maternal adaptation is influenced by various factors such as marital support, age, parity, (un-) planned pregnancy, financial issues and working situation .

2.1.3.3 Locus of control

Rotter (1996) introduced the concept of locus of control, defined as a generalized expectancy that affects the extent to which behaviour are under internal or external control. People showing an internal locus of control put more emphasis on personal initiative, capability and effort, whereas people with an external locus of control believe that enhancements are particularly determined by other people, fate and luck (Rotter, 1996).

In the field of research regarding risk factors for adverse course of pregnancy and birth outcome, locus of control can have different impacts. For one, locus of control might have an influence on the occurrence of pregnancy complications, as for instance preterm delivery, in the following way: Women with a high locus of control feel more powerful to influence their own pregnancy outcomes and are less likely to engage in unhealthy behaviour such as smoking and drug use. Furthermore, locus of control might also affect the way pregnant women cope with stressors. This in turn may affect her adoption of unhealthy behaviours (McCormick et al., 1990). Additionally, a primipara with a high internal locus of control might feel more competent to handle the pregnancy and birth as

ambiguous and totally new situations, than a woman with an external locus of control. However, locus of control has been rarely examined in pregnancy research. One of the few research groups examining this factor was the one of Shiono, Rauh, Park, Lederman and Zuskar (1997). They found that the belief, chance plays a major role in determining one's health status, was negatively associated with birth weight (Shiono et al., 1997). Another study revealed that low mastery (i.e. external locus of control) predicted a higher probability of giving birth to a child who was small for gestational age (Cliver et al., 1992), whereas known risk factors such as smoking, maternal education, height, weight and age have been controlled. Rini et al. (1999) showed significant associations between mastery and birth weight, too. Contrastingly, Copper, Goldenberg, Das, Elder, Swain, Norman, Ramsey, Cotroneo, Collins, Johnson, Jones and Meier (1996) failed in replicating the relation between locus of control and fetal growth restriction, examining a sample of 2593 pregnant women. The authors assumed that differences in measuring locus of control might account for the contradicting findings (Copper et al., 1996).

2.1.4 Stimulus centered aspects of stress and their influence on adverse birth outcome

2.1.4.1 Major life events

Life events are the most intensive investigated stimulus-based definitions of stress used in pregnancy research. Life events can be characterized as negative (e.g. the death of a loved one), as well as positive (e.g. marriage), whereas most of the life event measures focus on events with negative connotation. If such a critical event happens, adjustment and adaptation is needed, often accompanied by major changes and consequences, respectively. However, life events are typically measured by using a self-reported total number of live events that happened during a specific duration, usually during pregnancy or the time prior conception. The findings of studies investigating the relation between stressful life events during pregnancy and adverse birth outcomes are very inconsistent (Istvan, 1986). Berkowitz and Kasl (1983) assessed exposure to life events during pregnancy in a sample of 166 mothers delivering preterm and 299 mothers who delivered at term. The two groups differed significantly in their number of experienced life events. Similar results were found by several other research groups (Georgas, Giakoumaki, Georgoulias, Koumandakis, & Kaskarelis, 1984; Newton, Webster, Binu, Maskrey, & Phillips, 1979). However, all these studies have a retrospective design. Studies with such a construction usually focus on life-event questionnaires which are answered by mothers who have experienced preterm delivery. The problem of such a design is the fact that women, who deliver preterm, are trying to explain their preterm delivery and hence, the probability to overreport the past events is highly elevated (Omer, Palti, & Friedlander, 1986).

A better way to investigate the role of life events in adverse birth outcome is obviously a prospective design. Interestingly, the majority of studies with such a design show rarely results with significant effects. Honnor and his colleagues (Honnor, Zubrick, & Stanley, 1994) measured life events prospectively, but failed to show any predictive value of life

events in relation to preterm birth. The same applies for several other studies with respect to a variety of adverse birth outcomes (Dudenhausen & Kirschner, 2003; Lu & Chen, 2004; Pagel, Smilkstein, Regen, & Montano, 1990).

A further important aspect is the rating of life events. There are a few studies in which life events have not only been counted, but also rated according the subjects' own assessment of the extent of stress they experienced from reported live events. Norbeck and Anderson (1989), for example did not find an effect of life events related to gestational age, but found an interaction between high support and life stress, associated with longer labours. Another study conducted by Hedegaard and colleagues (Hedegaard, Henriksen, Secher, Hatch, & Sabroe, 1996) showed interesting results. In their study design they applied a prospective design and rating of occurring life events. The authors revealed no association between occurrence of life events and the duration of gestation or risk of preterm delivery. By taking into account women's appraisals of the reported life events, Heedegard et al. (1996) found that women with one or more highly stressful life events had a higher risk of preterm delivery than those reporting no stressful events.

As major events are unlikely to appear with sufficient frequency during the narrowed time period of gestation, several authors suggested, to focus on the minor event approach (e.g. Levin et al., 1988).

2.1.4.2 Minor daily events (Daily hassles and uplifts)

There is evidence, that the so-called "daily hassles and uplift approach" may provide a more direct and broader estimate of the stimulus based component of stress in comparison to major life events (Da Costa et al., 1999; Kramer et al., 2001). This concept was introduced to the stress literature by Kanner and his colleagues in 1981 (Kanner, Coyne, Schaefer, & Lazarus, 1981). In addition to major life events, the authors also investigated on minor daily events called hassles and uplifts. Daily hassles, which are also described as microstressors, are defined as "*the irritating, frustrating, distressing demands that to*

some degree characterize the everyday transactions with the environment" (Kanner et al., 1981, p. 3), whereas Lazarus defined daily uplifts as "*experiences and conditions of daily living that have been appraised as salient and positive or favourable to the endorser's well-being*" (Lazarus, 1984, p. 376).

One reason why the focus changed from major to minor events was that major life events were only weakly related to the outcomes of interest (see chapter 2.1.4.1) and theory could not explain the process how major events might have influence on psychological or physiological functioning. Since then, many studies have shown that the sum of a variety of recent daily hassles is a stronger predictor of psychological distress and health outcomes than major life events (Chamberlain & Zika, 1990; Kanner et al., 1981). Additionally, it has been suggested that major life events may affect the pattern of a person's daily hassles (Ruiz & Fullerton, 1999), which means that minor stressors could represent a kind of mediators on the impact of life events. Another point in favour of applying the minor approach is that minor event measure may be more easily adaptable to prospective studies of the impact of stress on the course of pregnancy and birth outcomes (Da Costa et al., 1999).

As for the major life event approach, a prospective study design is recommended, because studies measuring minor life events with a retrospective design, might be biased if a gestational, intrapartal or neonatal complication occurred. One prospective study has been derived from Da Costa, Brender and Larouche (1998) with a sample of 102 pregnant women. The authors measured daily stress events on a monthly basis and examined their influence on complications during gestation and delivery. In a postpartum follow-up measurement the authors built three groups consisting of women who experienced gestational complications, intrapartum complications and women with no complications at all. Da Costa et al. (1998) found out that the two groups, with complications during pregnancy or delivery, both reported higher levels of daily hassles over the course of their

pregnancy, compared to the group without any complications. However, in another study also conducted by Da Costa et al. (1999), this finding could not be replicated. No significant relation to pregnancy complications was found, but the authors showed that the level of daily hassles, measured monthly with beginning in the third month, stayed stable throughout the course of pregnancy. This finding is in contrast to the result of Thompson, Murphy, O'Hara and Wallymahmed (1997) who found that the severity on the hassles-score was highest in the first trimester. Another result revealed by Da Costa et al. (1999) was that daily hassles were significantly more frequent (during the first trimester of pregnancy) for women, who thought that the pregnancy would have a negative impact on their career. This finding may highlight one of the negative stereotypes women are encountering when they face themselves to reconcile pregnancy, motherhood and work.

2.1.4.3 Job strain

Job strain has gained increasing importance as a psychosocial risk factor for complications during pregnancy and birth in the last past decades, as the number of working women has increased. Despite this increasing number of employed women and women continuing to work until just a few days before giving birth, the incidence of complications such as preterm birth stayed equal, indicating that women who are not employed may still have high rates of stressful and fatiguing work in the home setting (Creasy, 1991).

Job strain can be divided into two characteristic aspects: physically strenuous work and psychosocial strain at work. Characteristic physical workload are prolonged standing, prolonged working hours, shiftwork, sleep deprivation, toxic exposures, strenuous postures (e.g. kneeling, bending, squatting or holding the arms at shoulder level or above), heavy lifting and work on vibrating machines (Papiernik, 1984).

As far as the psychosocial aspect of job strain is concerned there are several attempts of definitions. Ruiz et al. (1999) defined psychosocial demand as follows: work at high speed, work to tight deadlines, too simple work and repetitive or monotonous work. Another

definition was used in the study of Henriksen, Hedegaard and Secher (1994) classifying jobs into four dimensions: relaxed jobs (low demands and high control), active jobs (high demands and high control), passive jobs (low demands and low control), and high-strain jobs (high demands and low control).

Another dimension of job strain which must not be underestimated is the aspect of social stress at work, which consists of arguments with the superior, collaborator or subordinate (Weiss, 1999). Zapf and Friese (1991) found that social stressors are just as important as other aspects of job strain (e.g. physical job strain). Despite this fact the aspect of social stress at work has not been considered in pregnancy research. Most studies have focused on the physical aspect of job strain, with contradicting findings. Some research groups suggested that physical workload has as harmful effect on the course of pregnancy (e.g. Launer, Villar, Kestler, & de Onis, 1990), whereas other groups could not replicate these findings (Fortier, Marcoux, & Brisson, 1995; Savitz, Olshan, & Gallagher, 1996). As mentioned, work does not have to be physically strenuous, to be stressful. There are only few studies which examined the effect of mother's psychosocial working environment on preterm birth. In the aforementioned study of Henriksen et al. (1994), investigations revealed that the group with the so-called relaxed job had the lowest risk for small-for-gestational age (SGA), whereas the high job strain group showed the highest risk for SGA and preterm delivery. Both risks, SGA and preterm delivery were higher for the groups with low control. These reports are limited because the results represent only risk scores while all group differences remained unsignificant (Henriksen et al., 1995). Another study conducted by Oths and colleagues (Oths, Dunn, & Palmer, 2001) revealed that women with psychosocial high strain jobs (high in demands, low in control) had significantly lower birth weights in offspring than mothers with low strain jobs or unemployed women. A more recent study found that pelvic pain during pregnancy was influenced by both physical and psychosocial working conditions (Juhl, Andersen, Olsen, & Andersen, 2005).

However, results concerning the relation between working conditions and pregnancy outcome remain controversial. Regarding the above mentioned literature it can be argued that the two different parts of job strain might have detrimental effects on pregnancy outcome as proposed of Creasy (1991). He suggested that physical strenuous work may increase the incidence of low birth weight and/or preterm delivery, while non strenuous but psychologically stressful work might increase only preterm delivery. However, further research is needed, above all regarding the social stress component at work.

2.1.4.4 Marital discord

One can imagine that emotional support from the marital partner is of great benefit for the general coping with stress. Research shows that persons, who experience their partner as empathetic and supportive, e.g. to commit oneself to the concerns of the other and to propose solutions for problems, appraise their general coping with stress as highly efficient (Weiss, 1999). Partnership quality seems to have an important influence over health and Weiss (1999) describes marital support as the major source of social support at all. Men as well as women seem foremost to turn to their partner in case of problems or anxiety. As proposed by Burke and Weir (1982), effects of partnership quality can be considered as preventive, therapeutic as well as stress-buffering. The authors investigated a sample of 189 married couples and found that marital support affected psychological as well as physiological well-being. Interestingly, a positive effect on job satisfaction was also observed.

From a system-theoretical perspective, partner-specific interaction and communication have been stated as relevant factors for partnership satisfaction. If partners do not feel emotionally supported and understood, not appreciated by the other, or if communication is confused and characterized by negative escalations, this might have disadvantageous effects on both physical health and psychological well-being.

Against the background of these considerations it is conceivable that marital relationship has been investigated in terms of possible effects on the course of pregnancy and birth outcomes. The quality of marital relationship is known to play a role in maternal adjustment during pregnancy.

Westbrook (1978) showed that women in good relationships had the least pregnancy-specific worries and concerns. Also, impaired marital relationship has been associated with higher stress levels during pregnancy, as well as with postpartum mood disorders (see chapter 2.4.2.2).

Da Costa and colleagues (1999) also investigated the relation between marital discord and pregnancy. The authors revealed that marital adjustment, which has been measured in the first trimester, was significantly related to pregnancy-specific stress, higher state-anxiety during the last trimester and to higher daily hassles during the time of pregnancy. Da Costa et al. (1999) suggested that women who are more adjusted in their partnership might get more support from their partner, resulting in a reduction of experienced stress. Furthermore, the absence of a partner also seems to have a negative impact on pregnancy-related anxiety, circumstantiated by Pagel et al. (1990). Additional studies seem to support the association between marital discord and pregnancy related anxiety (Bernazzani, Saucier, David, & Borgeat, 1997; Saisto, Salmela-Aro, Nurmi, & Halmesmaki, 2001a). Saisto et al. (2001a) endorsed that the lack of marital support and dissatisfaction with the partner have been strongest predictors for birth anxiety. Furthermore, partner-specific support was significantly related with low stress, less substance abuse and more positive attitudes towards pregnancy (Zambrana, Scrimshaw, Collins, & Dunkel-Schetter, 1997).

Support of the baby's father seems to have an indirect effect on pregnancy and birth outcome via the pathway of occupying prenatal health care. Sable et al. (1990) showed in a sample of 1464 participants that pregnant women who were at greater risk for receiving inadequate prenatal care, have been less-educated, had unwanted pregnancies, higher

parity and were single. Thus, there is evidence that marital relationship or marital discord seems to be associated with a variety of factors influencing the course of pregnancy and birth outcomes. Hence, it is important to assess quality of marital relationship, as this is the most important source of social support.

In order to assess psychosocial well-being during pregnancy including the factors described in this chapter, several separate scales or inventories would be required. To our knowledge, there is no questionnaire which measures stimulus as well as reaction centered aspects of stress in one single measure.

2.2 Physiology of the HPA axis in pregnancy

2.2.1 HPA axis in non pregnant healthy humans

Cortical areas involved in the detection of a stressor send signals down pathways which activate certain areas of the hypothalamus in the limbic system. The challenge to homeostasis or even its anticipation, results in an increased activity of the hormones of the hypothalamic-pituitary-adrenocortical (HPA) axis to improve the ability for the organism to align its homeostatis and increase its opportunities for survival. The endocrine response to stress consists of a chain reaction of hormonal responses from the hypothalamus, the pituitary gland and the adrenal cortex (the outside of the adrenal glands) (Tsigos & Chrousos, 2002). First, the release of corticotropin-releasing hormone (CRH), a 41 amino acid long peptide, from the hypothalamus is initiated, which in turn results in the release of adrenocorticotropin hormone (ACTH) into general circulation. ACTH then has an impact on the adrenal cortex resulting in the secretion of a species-specific glucocorticoid (in humans: cortisol) into blood (D. B. Miller & O'Callaghan, 2002).

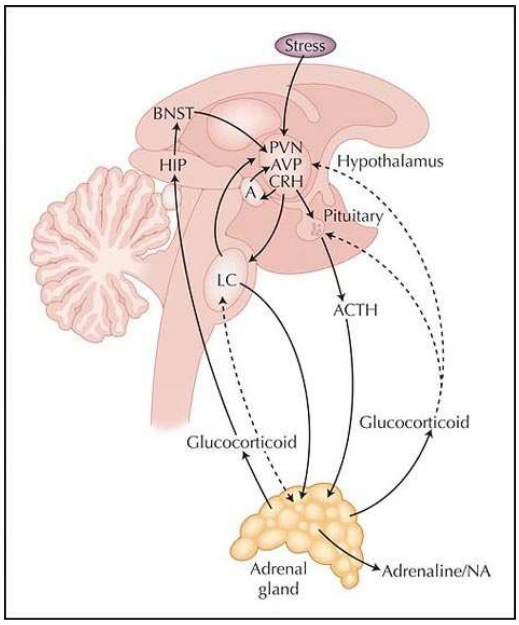

Figure 2.1 HPA axis modulation in response to stress (www.images.md)

After the stressor subsides, the homeostasis is regained by a negative feedback loop: glucocorticoids, for instance cortisol, act debilitating in order to terminate the release of CRH in the hypothalamus. Cortisol also controls its own secretion by a fast negative-feedback, inhibiting ACTH release. Cortisol production follows the ACTH circadian rhythm, which is overlaid on the episodic release of ACTH (Mastorakos, Weber, Magiakou, Gunn, & Chrousos, 1994).

The psychophysiologic stress reaction of the HPA axis described above can also be seen as an adaptation to challenge that maintains stability, also called "allostasis". This expression was introduced by Sterling and Eyer (1988) and reflects the active process of handling with stress on a physiologic and behavioural level. Systems such as the HPA axis or the autonomic nervous system are also called "allostatic systems" (McEwen, 1998). In case of chronic or very intense stress experiences these allostatic systems can cause problems and the repeated effort to adapt to challenges has a price which is called "allostatic load". Allostatic load is caused by either an overactive or an underactive allostatic system. In other words: High allostatic load occurs when an allostatic system is overworked or fails to shut off after stress exposure and hence fails to respond adequately. Thus, it has been suggested that HPA axis functioning might represent some kind of indicator for allostatic load. There is vast evidence that a high level of allostatic load in terms of a dysfunctional HPA axis is associated with a variety of psychiatric disorders, such as posttraumatic stress disorder, cognitive impairment or depression (McEwen, 1998).

2.2.2 Maternal pituitary-adrenal function in human pregnancy

Pregnancy implicates a large body of neuroendocrine and psychological changes. During pregnancy the plasma level of circulating immunoreactive CRH is characterised by an exponential increase up to a thousand times compared to its non-pregnant values, whereas the increase begins from 8^{th} to 10^{th} week of gestation (Goland, Wardlaw, Blum, Tropper, &

Stark, 1988; Riley, Walton, Herlick, & Challis, 1991), while free cortisol starts its increase much later, about 25th week of gestation (Allolio et al., 1990). Analyses of purified extracts of term human placenta revealed that the tissue contained CRH, which has been identical to neuronal CRH in immunoreactivity and bioactivity and was stimulating ACTH secretion from cultured pituitary cells (Shibasaki, Odagiri, Shizume, & Ling, 1982). Studies showed that the human placenta both synthesizes and releases increasing amounts of CRH from the second trimester to term (Frim et al., 1988). Thus, the aforementioned increase of CRH is not of hypothalamic source, but the result of CRH-specific production by the placenta, amniotic fluid, deciduas, membranes and local tissues (Petraglia et al., 1992).
The fact, that maternal CRH levels decline precipitously after parturition support the theory of placental CRH production (Riley et al., 1991).

The well-known negative feedback effect of glucocorticoids on CRH and ACTH secretion in the HPA axis is not appropriate for placental cells (Fadalti et al., 2000). Cortisol stimulates CRH gene-expression in the placenta, which in turn leads to an increased synthesis and secretion of placental CRH and pro-opiomelanocortin (POMC) products such as ACTH and β-endorphin, but the secretion of placental ACTH consists in a moderate extent and remains unpersuaded by the impact of glucocorticoids (Rinne, 1994). Then, placental CRH stimulates the maternal HPA axis and leads to a secretion of cortisol from the adrenal cortex (Magiakou et al., 1996). Thus, in contrast to the negative feedback loops known from the HPA axis, there is a *positive* placental-adrenal feedback mechanism which makes the simultaneous rise of CRH, ACTH and cortisol levels possible (Goland, Conwell, Warren, & Wardlaw, 1992).

Placental CRH affects not only maternal, but also fetal and placental divisions. As the concentration of CRH is significantly higher in the umbilical veins than in the arteries of

the umbilical cord, it was presumed that there is a placental secretion in fetal tissues (Egarter & Husslein, 1998). It was showed that placental CRH has a positive effect on the fetal HPA axis in releasing cortisol from the adrenal cortex of the fetus (Challis & Hooper, 1989), which leads to a positive CRH release in the placental region (see figure 2.2).

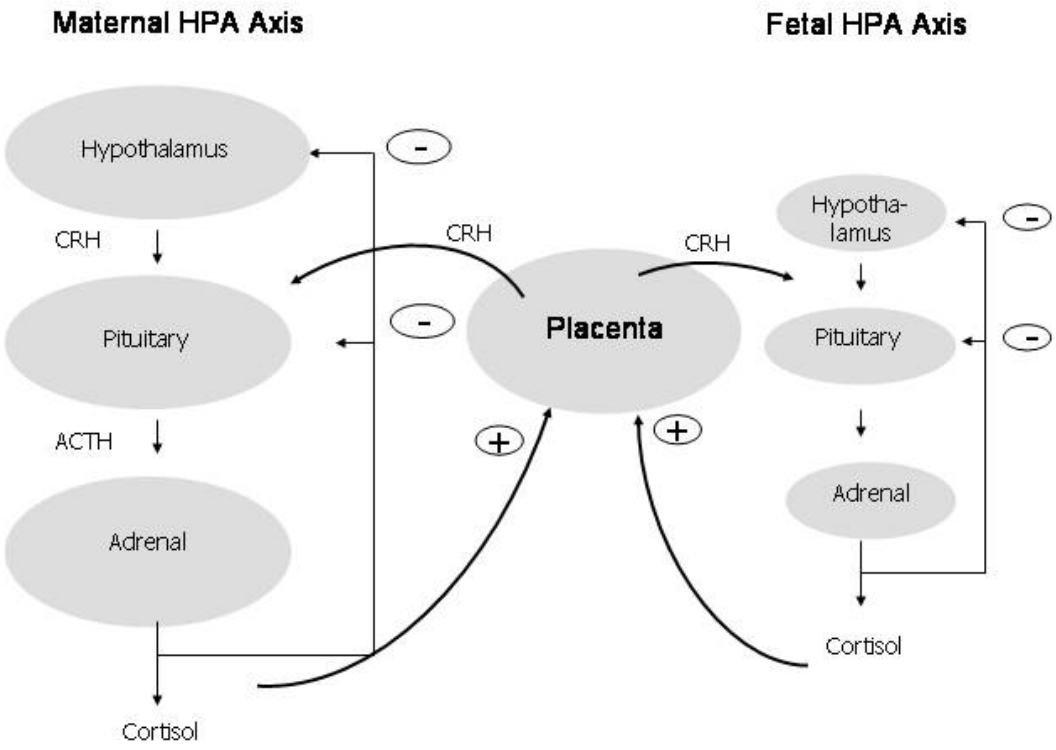

Figure 2.2 Positive placental-adrenal feedback mechanism during human pregnancy (Bratsikas, 2003)

Furthermore, placental CRH implicates various other endocrine and paracrine effects. Placental CRH is also a effectful local regulator of myometrial contractility and of prostaglandin release (Fadalti et al., 2000).

While prostaglandins have a direct positive effect on myometrial contractility itself, placental CRH acts in a synergistic way with oxytocin or prostaglandin (Quartero, Noort, Fry, & Keirse, 1991). In addition CRH is a potent vasodilator and may therefore play a role in the onset of parturition. Circadian rhythm during pregnancy is maintained (Magiakou et al., 1996), although placental CRH release does not underlie circadian pulse.

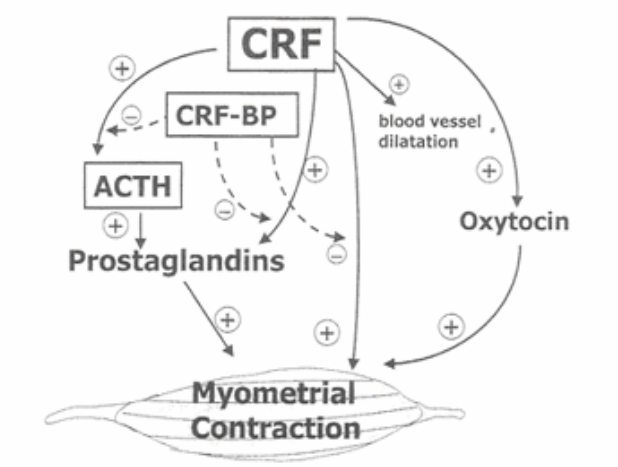

Figure 2.3 Effects of placental CRH (Fadalti et al., 2000)

As the placental CRH is the main source of maternal CRH and as there exists a normal functioning circadian rhythm it is hypothesized that arginine-vasopressin may be responsible for the circadian rhythmicity (Mastorakos & Ilias, 2000).

Furthermore it was revealed that cortisol and plasma ACTH do not respond sufficiently to exogenous human CRH during pregnancy. It was suggested that the prolonged high CRH and cortisol levels may desensitize the maternal pituitary corticotroph to further elevations of CRH (Schulte, Weisner, & Allolio, 1990). Thus the desensitization exerts inhibitory influences on hypothalamus and pituitary.

Despite the described immense increase of maternal CRH due to the placental CRH, hypercortisolism appears only mildly in the second half of pregnancy, whereas the increase of cortisol and ACTH levels stay comparatively low (Carr, Parker, Madden, MacDonald, & Porter, 1981). The presence of a CRH-binding protein (CRHbp) in plasma and amniotic fluid, which is unique to humans, makes this phenomenon possible in considering to reduce

the bioactivity of circulating CRH (Sehringer et al., 2004). Main source of the CRHbp is the liver, whereas it is also produced by placental tissues as well (Egarter & Husslein, 1998). Notably, CRHbp plasma levels in pregnant women remain similar to concentrations of non-pregnant women until the third trimester of gestation (Hobel, Dunkel-Schetter, Roesch, Castro, & Arora, 1999), but fall then precipitously to one-third of prior levels or even to those of the non-pregnant state (Linton et al., 1993). Contemporaneously, plasma levels of unbound CRH rise in a reciprocal way. Keelan, Coleman and Mitchell (1997) suggested that this mechanism may have relevance for the onset of parturition. After delivery, CRHbp levels decrease within 48 hours to those of non-pregnant state (McLean & Smith, 2001).

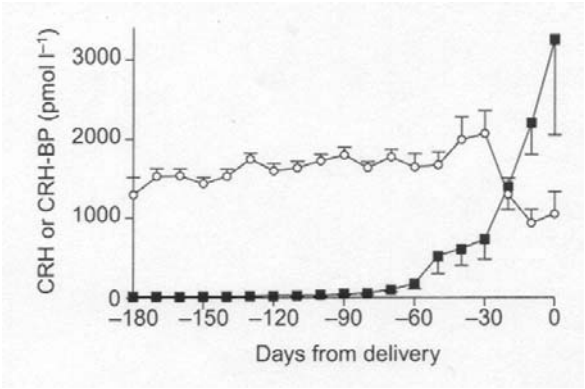

Figure 2.4 Maternal Plasma levels of CRH (▫) and CRH-BP (o) (McLean & Smith, 2001, p. 497)

2.2.3 General pathophysiologic adrenal aspects in pregnancy

The described regular neuroendocrinological changes during pregnancy (see prior chapter) may deviate in case of illness. The placenta is described as a stress-susceptible organ (Sandman et al., 1997). Symptoms of a threatening preterm delivery indicated in preterm labour or a premature cervix are the expression of disturbances of a complex and susceptible balance of diverse biological cycles (Schneider, 2000). Pregnant women with premature labour show significantly higher plasma CRH concentrations than healthy women (Egarter & Husslein, 1998). Hobel et al. (1999) explored in a prospective study CRH concentrations of women developing premature labour, hypertension and healthy pregnant women by measuring three times in the course of pregnancy. The authors found a specific

biochemical profile in women who developed premature labour in the course of pregnancy: Compared to the control group those women showed significantly higher CRH concentrations while the CRHbp levels were lower (Hobel et al., 1999). McLean and Smith (1999) replicated these findings in showing that women with premature labour showed increased CRH levels from the very beginning of pregnancy, suggesting that the activation of the HPA axis may represent a "placental clock", which controls the length of pregnancy. Thus, placental CRH is the "timing starter", determining the course of gestation (McLean et al., 1995).

2.3 Psychobiological model of stress in pregnancy

There are many diseases in the array of gynaecology whose etiology is thought to be associated with psychological factors as for instance premature labour. The incidence of preterm labour continues unabated and there has been no decrease in the rate of preterm labour since the implementation of tocolytic drugs (Leveno, Little, & Cunningham, 1990). Prematurity is commonly caused by ascending urogenital tract infections of the mother or uterine overdistention (Challis, 2000). In half of all cases of premature labour the so called idiopathic premature labour is diagnosed which means that no agent could be found. At this point it is to state that psychosocial factors might play a putative role. This idea is not a new one. Ancient physicians already knew about the adverse effect of stress on the reproductive system (Chrousos, Torpy, & Gold, 1998) and as aforementioned, Sandman et al. (1997) described the placenta as a stress-sensitive organ. As a mechanism of the activation of the HPA axis under stress (see chapter 2.2.1) and a positive interaction between the HPA axis and placental tissues exists, it might be hypothesized that this could be a possible pathway regarding the association between maternal stress and its adverse impact on human pregnancy. Chrousos et al. (1998) demonstrated in the following model the different pathways from stress to premature labor, mediated by placental CRH. Increased levels of cytokines, caused by infection or inflammation, anoxia as a result of

preeclampsia and increased levels of corticosteroids, incidental after physical or emotional stress, can provoke CRH secretion which culminates in premature labour. As the placenta is responding with a positive placental CRH secretion to glucocorticoids Sandman and authors (1997) postulated that the placental organ might even intensify the stress signal.

Based on these considerations, further studies have been conducted. Several authors investigated the association between psychological and endocrine factors. One of the first studies was the one of Wadhwa et al. (1996). Among the assessment of psychosocial factors by means of prenatal stress, social support and personality traits there were also measured endocrine parameters as the two POMC derivates ACTH and b-endorphin and cortisol.

2.4 Postpartum depressive mood disorders

> "… within two weeks of the birth, the wife finds herself feeling overwhelmed and exhausted. She has trouble sleeping even when the baby is asleep, cannot concentrate well, and is forgetful and distracted. The baby is fussy and difficult to soothe, leading the woman to worry about her adequacy as a mother. She also worries that her poor appetite and significant weight loss are causing her breast milk to be less nutritious for the baby. Her guilt and worry are greatly heightened by hostile feelings she develops towards the infant. Her relationship with her husband becomes increasingly strained by her belief that he does not understand or support her. She does not return phone calls and begins feeling lonely and isolated."
>
> (Hendrick & Altshuler, 1999, p. 65).

Reports of mood disturbances related to childbearing date back to antiquity (Hamilton & Harberger, 1992). Regardless of the broad body of research which has been conducted since then, the nature of the association between childbirth and mental disturbance is still not clarified (M. D. Miller, 1999).

Today, postpartum symptoms occur in approximately 50% of women who have recently given birth (Ehlert et al., 1990). In case of postpartum symptomatology the mother's ability to respond sensitively and competently to her new born is compromised (Beardslee & MacMillan, 1993). A large body of research indorsed that postpartum depressive mood disorders have an adverse impact on the course of the early postpartum period, where the foundation of the mother-child dyad is constituted (Murray & Cooper, 1997). Considering its high prevalence and devastating consequences prevention, identification and treatment should be a high priority.

Postpartum mood disorders are typically divided into three broad categories: postpartum blues, postpartum depression and puerperal psychosis. There is a growing body of research suggesting that these three may be qualitatively diverse states, with differing etiologies, predictive factors and treatments (Miller, 1999). Postpartum blues could be described as being more like a reactive state and may be a concomitant phenomenon of regular neuroendocrine changes during the puerperium. In contrast, postpartum depression,

analogue to depressive illness at other times, may be determined by numerous factors like genetic predisposition, situational, personal and physiological factors (Miller, 1999). In the following both the postpartum blues and depression will be shortly dwelled on. Postpartum psychosis will not be discussed, as it has no relevance for this paper (for further informations see Pfuhlmann, Stober, Franzek, & Beckmann, 2000).

As aforementioned there is evidence that postpartum blues und postpartum depression may have qualitatively diverse etiologies, predictive factors and treatments. Firstly, data about the phenomenology and etiological factors of postpartum blues will be summarized, and then the focus will lie on the aspects valid for puerperal depression.

2.4.1 Postpartum blues

2.4.1.1 Phenomenology of postpartum blues

Postpartum or "baby blues" is the most commonly observed puerperal mood disturbance (Robertson, Grace, Wallington, & Stewart, 2004). The blues is characterized by mild symptoms such as depressed mood, tearfulness, irritability, generalized anxiety, confusion, emotional lability and sleep and appetite disturbance (Hamilton & Harberger, 1992; Kennerley & Gath, 1989; Pitt, 1973). Typical symptoms begin within a few days of childbirth with a peak 3 to 5 days after delivery (Kendell, McGuire, Connor, & Cox, 1981). Symptoms may last from a few hours to several days and remit without being treated (Pitt, 1973). Seyfried and Marcus (2003) note that the blues resolves by day ten after delivery. Maternity blues is clinically significant because women suffering from postpartum blues sometimes show continuous episodes of postpartum depression or do have higher vulnerability to postpartum depression in subsequent pregnancies than women without a history of maternity blues (Okano & Nomura, 1992).

Reports of the prevalence of maternity blues in western cultures range from 27 to 76% (Murata, Nadaoka, Morioka, Oiji, & Saito, 1998). These differences in prevalence of

postpartum blues are mainly due to methodolocigal problems in defining and classifying the blues.

2.4.1.2 Etiological factors of postpartum blues

The etiology of the maternity blues is unknown. This phenomenon is present in a range of cultures, albeit in a different prevalence (Okano & Nomura, 1992) and there has been a wide number of studies researching psychosocial variables which could be related to the maternity blues, without consistent findings. The prevalence of maternity blues is unrelated to psychiatric history, cultural context, breastfeeding, parity, or – as aforementioned – cultural context (Hapgood, Elkind, & Wright, 1988). Furthermore, the blues is not related to demographic variables (O'Hara, Zekoski, Philipps, & Wright, 1990), current stressors (B. Harris, 1980) or obstetric complications (Best, Wiley, Stump, Elliott, & Cowen, 1988), either. A number of studies revealed that primiparous have a higher risk for the blues (Yalom, Lunde, Moos, & Hamburg, 1968). Murata et al. (1998) investigated a sample of 111 women and found out, that 15.3% of women developing postpartum blues appeared to have been cared for less in their own childhood and had significantly less social support than women without postpartum blues, while the authors failed to show any association to obstetric factors.

However, as the blues is cross-culturally present, psychosocial factors are widely unrelated and as the maternity blues occurs with a distinct pattern of timing of delivery, many researchers have suggested physiological causes for postpartum blues (Miller, 2002), although results have been inconclusive (Seyfried & Marcus, 2003).

One of the leading hypotheses for the explanation of postpartum blues is the hormone withdrawal hypothesis. A variety of hormones such as cortisol, estrogens, progesterone and allopregnanolone, a progesterone metabolite, slowly rise to levels several hundred times higher compared to their non-pregnant state. When delivery occurs they fall rapidly and

reach their primordial levels within at least two weeks. At the same time other important physiological changes, such as the onset of breast feeding occur.

These hormonal hypotheses comprise that women with postpartum depressive blues have an abnormal precipitous drop from pregnant to postpartum levels. For example Nott, Franklin, Armitage and Gelder (1976) surveyed pregnant women and found that women, who rated themselves as depressed within 10 days after birth, showed a greater progesterone drop during the time of late pregnancy to the early puerperium. Interestingly, these women rated themselves happier during the time of pregnancy compared to women with a normal progesterone drop, which presumes a characteristic mood lability in these women. Harris, Lovett, Newcombe, Walker and Riad-Fahmy (1994) also examined progesterone in terms of postpartum blues and found that women with a depressive symptomatology showed higher prenatal salivary progesterone levels, lower progesterone levels after birth and greater decrease in concentrations following delivery, while O'Hara, Schlechte, Lewis and Varner (1991) were not able to replicate an association between progesterone and depressive mood changes postpartum. Another study has been conducted by Nappi et al. (2001) who found that serum allopregnanolone was significantly decreased in women with postpartum depressive symptoms after delivery.

While numerous studies focusing on estradiol, progesterone, allopregnanolone, thryptophan and prolactin in terms of postpartum depressive symptoms were conducted, only few studies examined the role of cortisol.

All studies focusing on cortisol in relation to postpartum depressive mood changes are based on the research of unprovoked cortisol baseline levels, with contradiciting findings. As patients with non-pregnant and non-puerperal major depression show a hypercortisolism (Rubin, Poland, Lesser, Winston, & Blodgett, 1987), researchers expected higher cortisol baseline levels in women with postpartum depressive symptoms, too.

Handley, Dunn, Waldron and Baker (1980) determined in addition to free and total tryptophan also plasma cortisol of 71 women on eight occasions between 36 weeks of

gestation and six weeks postpartum. After controlling for seasonal variation, the authors found significantly higher cortisol baseline levels during the 38th gestational week in those women, who developed “blues” in the first five days postpartum (see figure 2.5).

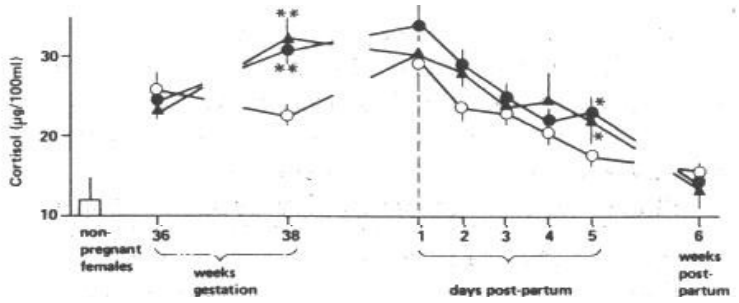

Figure 2.5 Changes in plasma cortisol and tryptophan at parturition and postpartum blues. (o) Subjects not experiencing postpartum blues, (●) Subjects reaching the 80th percentile on at least 1 blues scale, (Δ) Subjects reaching the 80th percentile on at least 3 blues scales

Ehlert et al. (1990) measured cortisol levels too, focusing on the first five days after delivery, measuring three times a day. The authors investigated 70 young mothers and found higher morning cortisol levels on those days when the postpartum blues were experienced by the young mothers. The group of depressed and non-depressed mothers with varying morning cortisol levels did not differ in their afternoon or evening cortisol levels.

Contrastingly, another study (Feksi, Harris, Walker, Riad-Fahmy, & Newcombe, 1984) failed to show any significant associations between cortisol secretion and blues symptoms during the first five days after delivery. It must be noted, that the authors compared only five women with postpartum blues with symptom-free pregnant women. Another study investigating cortisol in terms of postpartum blues was conducted by Pedersen, Stern, Pate, Senger, Bowes and Mason (1993). They found significantly higher levels of plasma cortisol after delivery in women with a previous history of major depression. However, results of relations between unprovoked basal cortisol levels measured either during pregnancy or in the puerperium, and postpartum depressive symptoms remain controversial.

2.4.2 Postpartum non-psychotic depression

2.4.2.1 Phenomenology of postpartum non-psychotic depression

In 1968, the American Psychiatric Association first included the diagnostic classification of "psychosis associated with childbirth" in the second edited Diagnostic and Statistical Manual of Mental Disorders (DSM), DSM II, while the revised fourth edition of the DSM defines "with postpartum onset", utilized as a modifier for brief reactive psychosis and mood disorders, as an episode of depression, mania, or psychosis with an onset within four weeks (Seyfried & Marcus, 2003).

Postpartum depression usually begins within the first 6 weeks of delivery. Sometimes baby blues simply continues and becomes more severe or a period of well-being after delivery is succeeded by a gradual onset of depression (Robertson et al., 2004). This severe mood disorder is usually characterized by discouraged mood, feelings of inadequacy and inability as a parent, suicidal ideation, impaired concentration and memory, fatigue, appetite and sleep disturbances, even when the infant is asleep or others have offered to care for the baby. Furthermore, a lot of women with postpartum depression have thoughts of harming their infants (Jennings, Ross, Popper, & Elmore, 1999).

A meta-analysis conducted by Moses-Kolko and Roth (2004) found that 10 to 15% of new mothers experience various degrees of postpartum non-psychotic depression, while other authors report prevalence with a range from about 10 to 22% (Josefsson et al., 2002). Again, differences in diagnostic criteria are the reason for these divergences. It remains unclear, if the puerperium represents a specific period of vulnerability of developing depressive mood disorders. Besides the fact that the prevalence of depression in a woman's life is about 10 to 15% in any event, Evans and his colleagues (Evans, Heron, Francomb, Oke, & Golding, 2001) found, that symptoms of depression are not more common or severe after childbirth than during pregnancy, but the onset rate for depression appears to be raised in the first three months postpartum compared with the following nine months (Cox, Murray, & Chapman, 1993). However, for many new mothers

delivery represents the trigger of recurrent or chronic episodes of depression (Robertson, 2004) and a mother's ongoing depression can provoke emotional, behavioural, cognitive and interpersonal problems for a child's life (Murray et al., 1997).

There have been some considerations on the phenomenology of postpartum depression compared to non-puerperal depression. Postpartum depression erstwhile has been conceptualized as a separate entity (Pitt, 1973), whereas recent literature suggests that the symptomatology is nearly indistinguishable from depressive episodes occurring at other times (Wisner, Peindl, & Hanusa, 1994). However, there is evidence for subtle differences in the phenomenology of non-puerperal depression and postpartum depression in terms of lower age of onset, lower incidence of suicidality, worse social adjustment following delivery, aggressive obsessional thoughts and higher anxiety in the latter (Seyfried & Marcus, 2003). The diagnosis of postpartum depression is complicated by the fact that many of the symptoms of major depression overlap with usual experiences a new mother undergoes in the period of the puerperium as for instance weight change, fatigue and sleep disturbance. Using common screening measures such as the Beck Depression Inventory, which is not related to pregnancy and the puerperium, lead to a high rate of false positives (Hopkins, Campbell, & Marcus, 1989), suggesting to use pregnancy specific measures such as the Edinburgh Postnatal Depression Scale (see chapter 4.2.4).

2.4.2.2 Etiological factors of non-psychotic postpartum depression

There is no clear etiology posited for postpartum depression, as in the case of postpartum blues (Seyfried & Marcus, 2003). Broad research has been conducted in the field of biological as well as psychosocial factors affecting postpartum depression. Similar as for the postpartum blues significant attention has been paid to the changes in reproductive hormones occurring in the puerperium. In terms of psychosocial etiological factors related to postpartum depression there have been numerous investigations. Consistent results are only shown for some few factors while for the most other factors there seems to be a lack of consistency.

One of the most consistent psychosocial factors is *marital discord*. Women who experience marital problems during or after pregnancy seem to be at higher risk for postpartum depression. Robertson et al. (2004) note that the effects of parenthood on diverse aspects of the new mother's psychosocial functioning should not be underestimated. Robertson et al. (2004) describe the importance of a good functioning relationship as follows: *The mother usually tends to do the greater share of parenting tasks, and the parents must decide how their new roles will affect their previous work patterns and implement the necessary changes. With the added burden of childcare, the relationship between the partners often suffers, [..]. A supportive relationship with the father can help mitigate the stresses of being a new mother. These stresses should be borne in mind when evaluating the role of factors in the development of postpartum depression.*

Gotlib, Whiffen, Wallace and Mount (1991) recruited 730 pregnant women and revealed by a one month follow-up postpartum that marital satisfaction during pregnancy was one of the important predicting factors for the onset of depression in the puerperium. Similar results were found by O'Hara (1986). In a prospective design she studied a sample of 99 women from the middle of pregnancy until nine weeks after delivery. The women who experienced postpartum depression (12% of the total women) reported less support from

their husbands after delivery than women in the non-depressed group. In addition several review-studies have reported an increased risk of postpartum depression in women with marital discord during the course of gestation (e.g. Beck, 2001).

Another well investigated risk factor for the development of postpartum depression is the presence of *depressive symptoms during pregnancy* or shortly after delivery. In a study conducted by Righetti-Veltema, Conne-Perreard, Bousquet and Manzano (1998), depressive state at the end of pregnancy was found to predict the occurrence of postpartum depression in a 3-month follow-up. Chaudron, Klein, Remington, Palta, Allen and Essex (2001) found similar results. The authors examined 465 women in their prospective study and found out that maternal age, depressive symptoms during pregnancy, thoughts of death and dying and difficulties falling asleep (both measured at first month postpartum), were the four strong predictive factors for depression at time of four months postpartum. Accordingly, Gotlib et al. (1991) found depressive symptoms during gestation being a strong predictor for postpartum depression, too. More recent investigations conducted by Verkerk, Pop, Van son and Van Heck (2003) were able to predict postpartum depression in high risk women, which was conceptualized by high depressive symptomatology during pregnancy. Interestingly, the differentiation between the high and low risk group, based on depressive symptoms during pregnancy, was limited to depression in the early 3-month postpartum period, while differentiation was not possible for the later 6- and 12-month period. This led the authors to the conclusion that the etiology of depression might differ between high- and low risk women. Pregnancy and birth associated stress might enhance the development of depression, but only for women with a higher vulnerability for depression (Verkerk et al., 2003). Another prominent explanation for the phenomenon of depressive symptomatology during pregnancy as a predictor for postpartum depression is the occurrence of subsyndromal depression during gestation which may represent a sort of prodromal phase and suggests a predisposition for the development of depression in the

puerperium (Chaudron et al., 2001). Besides depressive symptoms during gestation as a risk factor for postpartum depression, there is little question that a previous history of depression at any time leads to an increased risk of postpartum depression (Johnstone, Boyce, Hickey, Morris-Yatees, & Harris, 2001; Josefsson et al., 2002; O'Hara, Schlechte, Lewis, & Varner, 1991).

In addition to investigations of depressive symptoms during pregnancy as a predictor for postpartum depression, *anxiety* as a personal trait was explored as another psychological predictor. Research indicates that higher levels of anxiety during gestation predicted not only the occurrence but also the intensity of postpartum depressive symptomatology (Robertson et al., 2004). Thus, it can be interpreted that anxiety, operationalized as state or trait, might function as a moderator variable for depression in the puerperium. Neter, Collin, Lobel and Dunkel-Schetter (1995) found that women who reported higher levels of prenatal anxiety were also more likely to feel depressed at two months postpartum. Consistent with these findings, in a study conducted by Saisto and colleagues (2001), puerperal depression was also predicted by general anxiety during early as well as late pregnancy. In their view, pregnancy and delivery-related fears seem to be influenced by personality characteristics as for instance general anxiety. Anxiety in relation to postpartum depression was also explored by Johnstone et al. (2001), but they used anxiety only as a psychiatric history variable, not as a trait or even state variable during gestation. The authors found that women with a past history of anxiety had an increased risk of developing postnatal depression at eight weeks postpartum.

It has to be noted that the role of general anxiety as a predictor or – as previously proposed – as a moderator variable is less frequently examined than depressive symptoms during pregnancy.

More extensively investigated fields are *life events* and their possible relationships with the onset of puerperal depression. According to the importance of life events in the etiology of non-puerperal depression, in this study it is assumed that experiences such as the death of a loved one, losing a job or a divorce are known to be possible triggers for depressive episodes, some researchers have investigated the effects of stressful life events during pregnancy and the puerperium (Robertson et al., 2004). Studies concerning the association of life-events and depressive mood changes show an inconsistent pattern. Several groups of researchers have been able to show a relation between postpartum depression (e.g. Areias et al., 1996) while other could not (Faisal-Cury, Tedesco, Kahhale, Menezes, & Zugaib, 2004; Kumar & Robson, 1984; O'Hara, Schlechte, Lewis, & Wright, 1991).

However, one general inconvenience which attracts attention in life event research is the retrospective study design. Retrospective data collection represents a source of bias because subjects try to associate life events with the actual illness, which leads to an overreporting.

Literature concerning obstetric and *perinatal risk factors* is heterogenic and shows little consistency (Josefsson et al., 2002). Studies examining obstetric factors in relation to postpartum depression can be divided into two broad categories: On the one hand there are pregnancy-related complications including premature labor, hyperemesis gravidarum or preeclampsia, while on the other hand birth-related complications are of particular interest, such as excessive bleeding, caesarean section or premature delivery. Moreover, obstetrical risk factors have also been defined by the factors breast feeding and wanted or unwanted pregnancy.

There are some methodological issues, which have to be considered. Firstly, birth-related factors might be dependent on physicians, hospitals, region and nation, whereas breast feeding depends strongly on cultural factors (Robertson et al., 2004). Furthermore, an

unwanted pregnancy does not mean a disadvantageous aggravation per se. However, results concerning these factors should be interpreted with caution.

Josefsson et al. (2002) found no association between delivery complications and postpartum depression, which is in line with other findings (Nielsen Forman, Videbech, Hedegaard, Dalby Salvig, & Secher, 2000; Patel, Murphy, & Peters, 2005; Saisto, Salmela-Aro, Nurmi, & Halmesmaki, 2001b; Warner, Appleby, Whitton, & Faragher, 1996), whereas pregnancy-related complications such as hyperemesis and premature contractions were more common in the postpartum depressed group (Josefsson et al., 2002).

None of the demographic variables such as education, age and marital status have been identified as increasing a new mother's risk of developing postpartum depression (Beck, 2001; Chaudron et al., 2001; Horowitz, Damato, Duffy, & Solon, 2005; Josefsson et al., 2002).

Similar to the research of etiological factors of biological origin in postpartum blues, investigations in the field of postpartum depression are focused on the dramatic changes in reproductive hormones occurring in the puerperal period. Again, research is basically concentrated on estrogen and progesterone, with conflicting results. Only few studies investigated cortisol in relation to postpartum depression, measured and diagnosed several weeks after delivery.

O'Hara et al. (1991) examined 182 subjects and revealed that women with postpartum depression, diagnosed at nine weeks postpartum, had lower estradiol levels at week 36 of gestation and at the second day postpartum, whereas there were neither differences noted for progesterone and prolactin, nor for cortisol. Harris (1994) investigated a sample of 120 women measuring progesterone levels from 2 weeks before birth to 35 days postpartum. Similar to the findings of O'Hara et al. (1991) Harris failed to show an association between salivary progesterone and depression, measured at day 35 postpartum. Contrastingly,

Abou-Saleh, Ghubash, Karim, Krymski and Bhai (1998) revealed higher progesterone, but not estradiol at day 7 postpartum in women who developed postpartum depression, diagnosed at 6 to 10 weeks postpartum, in comparison to the control group without having developed postpartum depression.

The small number of studies which examined cortisol, related particularly with the development of postpartum depression, and not only with blues, show contradicting results. Pedersen et al. (1993) is to date the only research group who found a significant relation of elevated salivary morning cortisol levels and postpartum depression at six weeks postpartum. In contrast, several groups did not find an association (Gard, Handley, Parsons, & Waldron, 1986; B. Harris, 1994; O'Hara, Schlechte, Lewis, & Wright, 1991).

To sum up, findings of associations between unprovoked baseline cortisol levels measured during pregnancy and/or after delivery and postpartum symptoms are few and remain unclear. Unfortunately, there are no studies investigating the *reactivity* of the HPA axis in women developing postpartum depressive symptoms, by means of applying a stress paradigm.

2.4.3 HPA axis dysfunction in non-puerperal major depression and mood changes in the postpartum period: a comparison

The idea, to compare the HPA axis functioning between non-pregnant and non-puerperal samples with pregnant and postpartum samples, is not a new one. One such a comparison is given by Magiakou et al. (1996). Interestingly, the HPA axis disturbances observed in major depression are similar to those in the condition of a physiologically normal proceeding pregnancy. First reports of a dysfunctional HPA axis in non-puerperal depressed patients have been provided by Carroll and Curtis (1976). Since then, HPA axis disturbances have been approved as one of the most reproducible findings in non-puerperal major depression. Baseline hypercortisolism in non-pregnant individuals with major

depression are a common finding and have been demonstrated in several studies (Carroll & Curtis, 1976; Halbreich, Asnis, Shindledecker, Zumoff, & Nathan, 1985; Rubin et al., 1987). Similarly, the last trimester of healthy human pregnancy is characterized by mild hyperactivity, with increased plasma cortisol levels, mainly due to the additional secretion of CRH by the placenta (Magiakou et al., 1996) (see chapter 2.2.2).

Additionally for a subset of patients with non-pregnant and non-puerperal major depression, blunted ACTH responses and cortisol increases in response to dexamethasone administration are shown to be characteristic (H. M. Burke, Davis, Otte, & Mohr, 2005; Checkley, 1996; Rubin et al., 1987; Young et al., 1993). Likewise, administration of dexamethasone during healthy pregnancy results in a non-suppression of cortisol, too, as well as it is typically shown in patients with non-puerperal and non-pregnant major depression, respectively (Bloch, Daly, & Rubinow, 2003).

Focusing on the *pathological* state of the pregnant and postpartum period, findings about HPA *activity* (unprovoked baseline cortisol) are contradictory (see chapters 2.4.1 and 2.4.2). As far as HPA *reactivity* is concerned, no study has investigated the association of biological reactivity during pregnancy and the occurrence of postpartum depressive symptoms. This is in contrast to the research of non-pregnant and non-puerperal major depression, albeit there are only few findings. H. M. Burke, Davis et al. (2005) summarize in their meta-analysis, that there is evidence for a blunted cortisol reactivity in depressive samples, as response to psychosocial stress. They included studies using different stress paradigms as for instance cognitive stressors, social stressors as well as naturalistic stressors. According to H. M. Burke, Davis et al. (2005) depressed patients show a relatively flat and unresponsive pattern of cortisol secretion compared to their non-depressed counterparts, whereas blunted stress reactivity was most pronounced in older and more severely depressed patients. In contrast, the non-depressed samples showed a

more dynamic pattern of cortisol reactivity, and more rapid recovery following stress exposure.

Up to now, there are no studies, which have investigated the relation of psychobiological response to psychosocial stress during pregnancy and postpartum depressive symptoms in clinical and subclinical populations, respectively.

3 The Zurich Inventory of Psychosocial Well-being in Pregnancy (ZIPP): Development and empirical findings

3.1 Introduction

Pregnancy represents for the majority of women an incising event and requires several physiological and psychological adjustment processes (Ehlert, 2004). A woman's ability to adapt to challenges of pregnancy determines both her physical as well as her psychological health. There is great evidence that psychosocial strain has an unfavourable influence on these adaptational processes and, therefore, increases the risk of complications during gestation and birth (Rini et al., 1999). Premature labour exemplifies a common complication during pregnancy. Considering the serious social and medical consequences of such an adverse birth outcome, as for instance preterm labour, it is not surprising that etiological factors of complications such as preterm labour have been extensively studied in recent years of health research. Infective processes such as ascending urogenital tract infections account for approximately 30-40% of all cases of preterm labour, whereas 40-50% of the cases remain unclear and are therefore called "idiopathic" preterm labour (Challis, 2000). For these idiopathic cases psychosocial factors might play a putative role. Regarding the interaction between psychosocial stress and adverse birth outcomes the HPA axis does have a decisive role (see chapter 2.3). This idea is not a new one. Ancient physicians already knew about the adverse effect of stress on the reproductive system (Chrousos et al., 1998) and as reported in chapter 2.3, Sandman and his colleagues described the placenta as a stress-sensitive organ (Sandman et al., 1997). As a mechanism of the activation of the HPA axis under stress exists and therefore a positive interaction between the HPA axis and placental tissues can result, it might be hypothesized that there is a possible pathway regarding the association between maternal stress and its adverse impact on human pregnancy. As the placenta is responding with a positive placental CRH

secretion to glucocorticoids Sandman and authors (1997) have postulated that the placental organ might even intensify the stress signal.

Up to now, the concept of stress in prenatal research has been defined focusing predominantly either on stimulus based *or* response based stress aspects. Stimulus based measures generally assess subjectively highly relevant events or situations, called stressors (e.g. daily hassles, daily uplifts, perceived stress, chronic strain, major life events). In the response centered approach it is assumed that subjectively stressful situations lead to a number of emotional as well as physical stress reactions. Examples for the assessment of the response based approach in pregnancy research is the assignment of questionnaires measuring e.g. pregnancy and birth related anxiety, state and trait anxiety or adaptation towards pregnancy.

According to the transactional stress-concept of Lazarus and its application to psychobiological obstetric research, stimulus and response based stress measurement should be extended, considering moderator variables such as general or specific locus of control (or mastery). To avert the limitations of the present conceptualisations of stress in prenatal research it is inalienable to join both the stimulus and response properties of stress, as well as mediating factors (Lazarus, 1984; Lobel et al., 1992).

At present, in order to assess the mentioned constructs of stress (response, stimulus and mediator variables), the use of multiple separate scales or inventories is required. Considering the very time-consuming management of these combined instruments, the call for shorter questionnaires including the three above mentioned aspects of stress is justified. Thus, the study at hand was conducted in order to create a questionnaire comprising the most important factors known to affect gestational complications, grouped into reaction, stimulus and transactional based aspects. This aim was achieved by means of several steps: First, the item generation was conducted in an explorative way by interviewing a sample of 14 women having idiopathic premature labour, about their psychosocial well-being. Additionally, the item generation based on the consideration of

several questionnaires concerning the measurement of stress and well-being in pregnancy. In a next step, the explorative developed questionnaire was then applied to a sample of 154 pregnant women, in order to explore its internal factorial structure, to evaluate its psychometric values, and to shorten the item pool on the basis of these factorial and psychometric parameters. Then a restudy of the factorial structure was conducted, in the sense of a cross-validation. This restudy was based on a sample of 60 healthy pregnant women. The analyses were extended in examining the convergent and discriminant validity, by relating the new developed questionnaire with other measures assessing similar constructs. Finally, to investigate predictive validity of the questionnaire, correlations between the subscales and different outcome variables such as birth weight, gestational length and birth complications were calculated.

3.2 Pilotstudy: Development of the Zurich Inventory of Psychosocial Well-being in Pregnancy (ZIPP)

3.2.1 Introduction

The goal of this sub-study was the development and validation of a questionnaire assessing psychosocial well-being in pregnancy. Starting point of the development of the new inventory was the explorative compilation of an item pool. This explorative work was based upon interviews with pregnant women with idiopathic premature labour. In addition, a comprehensive literature research about possible risk factors related to adverse pregnancy and birth outcomes was also taken into account in adapting items of existing questionnaires measuring psychosocial risk factors for adverse birth outcomes.

3.2.2 Methods

3.2.2.1 Subjects

The sample consisted of 14 adult pregnant women with diagnosed idiopathic premature labour. Women whose premature contractions could be explained by the presence of any infections, multiple pregnancy, premature rupture of the membranes, fetal abnormalities, uterine abnormalities or the foregoing of physical stress such as an accident, were therefore excluded (Steer & Flint, 1999). As young or old age and cigarette smoking are known to be risk factors for preterm labour, cigarette smoking women and women younger than 19 or older than 35 years were excluded, too. All patients were hospitalized at the University Hospital of Zurich and underwent a tocolytic treatment (sympathomimetics).

3.2.2.2 Procedure

As reported above the development of a first version of the new inventory was conducted in an explorative way. The preliminary instrument was based on the findings from existing

literature and the interviews with a sample of fourteen pregnant women, whose experience was regarded as expert opinion about experiencing and coping with stress in pregnancy. It was of great interest whether the women with idiopathic premature labour experienced exceedingly foregoing stress prior to the occurrence of their premature labour and if so, what kind of stress this was. According to these informations new items were created and currently modified.

In addition, the following inventories were taken into account: the German questionnaire about health and stress (Fragebogen zu Gesundheit und Stress, GUS; Weiss & Schneewind, 1996), the German version of the attitude towards pregnancy, birth and sexuality (SSG; Lukesch & Lukesch, 1976) and the daily hassles and uplifts subscales (Thompson et al., 1996).

3.2.3 Results

3.2.3.1 Sample characteristics

The mean age of the pregnant participants (N = 14) was 27.4 (SD = 4.0, range 19 – 32 years) and their gestational age averaged out at 28.9 (SD = 4.0). 71% were primiparous whereas the other 29% of the women were multiparas. 29% were unmarried, whereof one woman of the total sample was single. In five (36%) of 14 cases the pregnancy was unplanned. 57% of the pregnant women were employed (part-time or full-time, respectively). All women had the diagnosis of idiopathic preterm labour and were therefore hospitalized and engaged in medical treatment.

3.2.3.2 Preliminary questionnaire

The explorative creation and collection of items resulted in an item pool of 127 items, which can be assigned to the following arrays: major and minor events, leisure time, social support, partnership quality, pregnancy and birth related anxiety, general and

pregnancy/birth locus of control (mastery), personality traits (flexibility, self-esteem), job strain, generally perceived stress and well-being.

The general pattern that emerged from the sample of women with idiopathic premature labour was that all patients reported having experienced high stress prior and during their labour. Interestingly, the majority of the women were aware of a psychosomatic model, which they often adapted to their own situation. To sum up, six women reported problems in their relationship, three women attracted attention with their exceptional high levels of pregnancy and/or birth anxiety, five women reported high job strain, whereof only one was of psychosocial nature, whereas the remaining four cases were physical job strain. Regarding negative major life events, there were three women affected in the past two years. The following case history illustrates one of the fourteen cases, where partnership strain and attitude towards pregnancy were the two balance points:

> Ms. M. was a 29-year old woman, being at 33rd week of gestation, unmarried but in a partnership since 15 months. She was a handycraft teacher and had a part-time job. The pregnancy, her first, was not planned and at the beginning of her pregnancy she and her partner had great difficulties adapting to their new situation. Both of them never planned having children. The insecurity of Ms. M. was heightened by the negative attitude of her partner towards the unborn child and both of them felt stressed by the situation. In addition, it was difficult for her to adapt to changes of pregnancy, i.e. to accept her reduced physical capacity and hence, she felt very constricted and hemmed in due to her pregnancy. Before she got pregnant she was used to be energetic and independent. Now, she felt henpecked by her body and it felt hard for her to accept her new limits. She said that this might have been the cause why she had ignored premature contractions as signals of her body.

3.3 Study 1: Internal factorial structure

3.3.1 Introduction

In order to explore the internal factorial structure and evaluate the psychometric values of the preliminary inventory developed in the foregoing pilot-study, a further study ("study 1") was conducted. With respect to economical considerations regarding the number of items it was intended to diminish the account of items by means of psychometric and factorial criteria. The questionnaire was therefore applied to a sample of 154 pregnant women in order to conduct factorial ananylses.

3.3.2 Methods

3.3.2.1 Subjects

The sample consisted of 154 adult pregnant women receiving prenatal care in the public clinic of a teaching hospital affiliated with the University of Zurich and in obstetricians' offices in the surrounding area of Zurich and Lörrach (Germany). The participants were requested to complete the questionnaire if possible at the time of administration at the physician or to post it in stamped self-addressed envelopes that had been provided.

3.3.2.2 Statistical analyses

In order to test the internal factorial structure of the preliminary questionnaire a principal component factor analysis with varimax rotation was conducted. Each item load should show at least $a_{ij} < 0.40$. To assess the components the following criteria were applied (see Rost & Schermer, 1989): Eigenvalue > 1, one component should have at least 4 marking variables und should explain a total variance of three percent at least. As an indicator for reliability of the ZIPP, Cronbach's alpha and corrected item-total Correlation r_{it} was calculated. Data were tested for normal distribution using a Kolmogorov-Smirnov before

statistical procedures were applied. For all analyses, the significance level was α = 5% and unless indicated, all results represented are means ± standard error of means (SEM).

3.3.3 Results

3.3.3.1 Sample Characteristics

The mean age of the pregnant participants was 30.4 (SD = 5.0, range 19 – 42 years) and their gestational age ranged from 20.2 to 40 weeks. The mean gestational age was 30.1 (SD = 4.2). For further demographic information see table 3.1.

Table 3.1 Sample characteristics of study 1 (N = 154)

SAMPLE CHARACTERISTICS		%
Marital status	Married/partnered	94.1
	Single/divorced	5.2
	Widowed	0.6
Highest (completed) educational level	University	33.8
	College preparatory high school	4.5
	Apprenticeship	53.9
	Secondary school	3.9
	Elementary school	2.6
	Missing data	1.3
Employed	Yes	83.7
	No	16.2
Parity	Primipara	66.9
	Secundipara	24
	Multipara	9
Obstetrical problems	Yes	31
	No	69

3.3.3.2 Internal factorial structure

The principal component factor analysis revealed 53 Eigenvalue greater than one (the first ten values were 27.36; 10.20; 9.34; 7.22; 7.11; 5.36; 4.93; 4.84; 4.33; 3.95; 3.72; 3.52). The progression of the Eigenvalue in the Scree-Test (Cattell, 1966) shows five-, eight- and twelve-factor solutions. Based on this Scree curve, the five-factor solution was considered optimal for the data set. The five-factor solution explained a total variance of 30.1% (explained variance before and after rotation, respectively: component 1 = 13.55% / 7.40%; component 2 = 5.05% / 6.31%; component 3 = 4.62% / 6.22%; component 4 = 3.58% / 5.23%, component 5 = 3.52% / 5.15). The first component comprised 29 marking items, the second 31, the third 23, the fourth 18 and the fifth 20 marking items. All items loading less than 0.4 were therefore excluded from further calculations. After the exclusion of items, whose content did not fit into the factorial structure, corrected item-total Correlation r_{it} of each item was calculated. All items less than $r_{it} < 0.30$ were therefore excluded from further analyses. To test internal consistency, Cronbach's alpha was calculated. Cronbach's alpha should be greater than $\alpha = 0.75$.

After the mentioned exclusion of these items, a second principal component factor analysis with varimax rotation was conducted on the remaining items. Based on economic and textual considerations each subscale was shortened to 10 items. High Correlations (r = 0.8 - 0.9) between the long and the short versions of the subscales indicated no loss of content. The total number of items was therefore 50. Table 3.2 shows the final version of the 50-item instrument, displaying the main factors and the respective question areas.

Table 3.2 The ZIPP

Main Sections	Question Areas
Job strain (JS; Factor one)	5 questions about interpersonal problems 3 questions about hassles with the superior 1 question about difficulties in communication 1 question about feeling non-appreciated at work
General strain (GS; Factor two)	3 questions about manifestations of stress 1 question about a daily hassle 2 questions about feeling under pressure 1 question about a general personal trait 3 questions about the degree of lack of recreation
Partnership strain (PS; Factor three)	3 questions about feeling content with the one's partnership 2 questions about coping with problems 2 questions about lack of marital support 3 questions about lack of marital communication 1 question about the feeling of togetherness
Lack of resources (LR; Factor four)	8 questions about daily uplifts 2 questions about feeling able to recreate in leisure time
Pregnancy and birth related strain (PBS; Factor five)	3 questions about birth anxiety 3 questions about attitude towards pregnancy 3 questions about the belief of control during parturition 1 question about general sense of mastery

Again a third principal component factor analysis with varimax rotation on the new 50-item-version was conducted. The analysis revealed fourteen Eigenvalues (progression of the Eigenvalues: 10.34; 5.32; 4.00; 3.14; 2.48; 1.98; 1.70; 1.49; 1.48; 1.30; 1.19; 1.11; 1.07). Based on the Scree Test again, a five-factor solution was considered optimal for the data set. The resulting five factors explain a total variance of 51.0% (see table 3.3).

The first component includes items concerning "*job strain*" (JS) (e.g. "There often is a tense atmosphere at my workplace."; "I don't get along with some of my colleagues."). This component explains– unrotated 20.7 % - a total variance of 20.7% after rotation. The

second component explains a total variance of 10.77% after rotation and 10.64% unrotated, respectively. In consideration of the marking items the component was labelled "*general strain*" (GS) (e.g. "I have problems with relaxing.", "I still have a lot of things to do before I give birth.").

The third component explained a total variance of 10.46% after rotation and 8.01% before, respectively. The component comprises items concerning relationship problems and is therefore labelled *"partnership strain"* (PS).

The fourth component explains a total variance of 9.32% after and 6.27% before rotation. As the component comprises resource oriented items it is therefore labelled "resources". Due to the polarity of the items the factor was labelled *"lack of resources"* (LR), respectively (e.g. "To do something good for myself.", "I enjoy my leisure time to the full.").

The fifth and last component measures prenatal anxiety, attitude towards pregnancy, as well as the attitude towards birth and breastfeeding, and the pregnancy-specific control expectancy (e.g. "I feel as I am at doctor's and midwife's mercy.", "Every mother is afraid of delivery."). The fifth scale explained a total variance of 4.96% after rotation (unrotated explained variance: 6.98%) and was labelled *"pregnancy and birth related strain"* (PBS).

The shortened questionnaire has been labelled 'Zurich Inventory of psychosocial well-being in Pregnancy', ZIPP.

Table 3.3 Factor loadings (principal component factor analysis) and psychometric evaluation of the ZIPP in study 1 (N=154)

Item	Nr.	F1	F2	F3	F4	F5	M	SD	r_{it}
JS	6	**0.86**					2.22	1.45	0.81
JS	8	**0.83**					2.06	1.37	0.79
JS	1	**0.83**					2.66	1.58	0.79
JS	2	**0.80**				0.25	2.39	1.50	0.83
JS	3	**0.80**					1.82	1.31	0.76
JS	7	**0.79**			0.21		2.02	1.39	0.75
JS	5	**0.78**			0.26		1.63	1.17	0.71
JS	10	**0.73**					1.43	0.90	0.65
JS	9	**0.70**					1.46	0.86	0.64
JS	4	**0.53**				0.25	2.67	1.68	0.47
GS	5		**0.76**				2.54	1.44	0.74
GS	4		**0.75**				2.35	1.35	0.79
GS	2		**0.74**				3.10	1.45	0.69
GS	3		**0.67**				3.01	1.54	0.65
GS	8		**0.66**		0.28		2.93	1.61	0.54
GS	6		**0.65**				3.67	1.48	0.52
GS	7		**0.59**			0.26	3.19	1.58	0.49
GS	10		**0.59**		0.29		3.10	1.30	0.48
GS	9		**0.56**		0.38		2.64	1.20	0.55
GS	1		0.038				2.56	1.45	0.42
PS	2			**0.82**			1.34	0.77	0.79
PS	6			**0.78**			1.43	0.88	0.69
PS	9			**0.76**			1.83	0.90	0.75
PS	3			**0.76**			1.43	0.95	0.75
PS	7			**0.73**			1.41	0.93	0.67
PS	10			**0.71**			1.34	0.64	0.66
PS	5			**0.67**	0.20		1.72	1.03	0.52
PS	4	0.21		**0.60**			1.96	1.01	0.59
PS	8		0.27	**0.54**			1.85	1.1	0.60
PS	1			**0.46**			2.19	1.37	0.50
LR	3				**0.78**		2.31	1.08	0.67
LR	7				**0.71**		2.16	0.98	0.66
LR	4		0.27		**0.70**		2.08	0.98	0.69
LR	5				**0.69**		1.9	0.92	0.66
LR	6				**0.68**		2.49	1.17	0.61
LR	2			0.22	**0.61**		1.52	0.73	0.58
LR	10		0.41		**0.58**		2.60	0.98	0.60
LR	1			0.24	**0.57**		1.92	0.80	0.46
LR	8		0.35		0.50		2.52	1.27	0.53
LR	9				0.31		2.58	1.13	0.45
PBS	6					**0.77**	3.09	1.34	0.49
PBS	9					**0.62**	2.18	1.28	0.44
PBS	3	0.21	0.21			**0.61**	2.16	1.41	0.60
PBS	5					**0.60**	3.57	1.42	0.42
PBS	8					**0.56**	1.58	1.01	0.41
PBS	2		0.23			**0.54**	2.65	1.45	0.47
PBS	7		0.22			**0.43**	2.72	1.07	0.36
PBS	4					**0.42**	2.14	1.27	0.48
PBS	1					0.34	1.99	1.23	0.36
PBS	10					0.24	1.23	0.72	0.30
Cronbach's alpha		0.92	0.87	0.89	0.87	0.77			
Total of variance (in %):					Total = 50.59				

3.3.3.3 Psychometric evaluation of the ZIPP

To test internal consistency, Cronbach's alpha was assessed. As it is shown in table 3.3, the ZIPP scales show reasonable (>0.60) to very good (>0.90) internal consistency ("Job strain": α = 0.92; "General strain": α = 0.87; "Partnership strain": α = 0.89; "Lack of resources": α = 0.87; "Pregnancy-specific strain": α = 0.77). Kolmogorov-Smirnov showed significant deviation from normal distribution concerning the scales "Job strain" and "Partnership strain" (Z_s > 2.01, P_s < 0.01). Both scales show positive skewness and kurtosis and therefore are left skewed. The positive and low intercorrelations between the scales of the ZIPP (divergent validity) conformed to the expectations (range r = 0.09 - 0.39) in indicating independency for the subscales of the ZIPP, and demonstrated logical relationships (see table 3.4)

Table 3.4 Intercorrelations between the subscales of the ZIPP in study 1 (N=154)

	JS	GS	PS	LR	PBS
JS	-				
GS	0.28**	-			
PS	0.14	0.24**	-		
LR	0.19*	0.36**	0.23**	-	
PBS	0.39**	0.28**	0.25**	0.15	-

Note : * p < 0.05; ** p < 0.01

3.4 Study 2: Construct validity

3.4.1 Introduction

The second study addressed first of all the internal factorial validity of the ZIPP once again (cross-validation). In addition, convergent and discriminant validity of the ZIPP were to be tested. Therefore we conducted correlations between the subscales of the ZIPP and measures from different and similar constructs. It was hypothesized that measures from similar constructs would correlate high with the subscales of the ZIPP, while the correlations to different constructs should have much lower correlations, respectively. For instance, instruments measuring negative attitude towards pregnancy should have low positive correlations to the fifth scale of the ZIPP "pregnancy-specific strain". In addition, instruments measuring perceived stress should be highly positive correlated with the second subscale of the ZIPP "general strain". Similar relations are expected for the correlations between instruments measuring stress at the workplace and the first scale of the ZIPP "job strain".

Furthermore, predictive validity was to be tested in a long term study design. The construct validation was conducted by analysing the relationship between the subscales of the ZIPP and objective criteria (birth outcome variables), as for instance gestational age, birth weight, diverse pregnancy complications and birth complications, which were assessed immediately after delivery.

It was hypothesized that each scale represented by the ZIPP should correlate negatively with all birth outcome variables. More precisely, it was suggested that subjects perceiving more stress and having higher values in the subscales of the ZIPP, would have shorter gestational ages, lower birth weights of their children and would experience more pregnancy and birth complications. Based on contradictory results regarding the effect of birth anxiety on birth weight and gestational age (Rini, Dunkel-Schetter, Wadhwa, & Sandman, 1999; Wadhwa et al., 1993) and mode of delivery, for instance secondary

cesaerean section (Ryding, Wijma, Wijma, & Rydhstrom, 1998), it was assumed, that women who experience high birth anxiety would have adverse birth outcomes. In addition, we assumed that the same correlations would also apply for the other aspects, as for instance, pregnancy-specific control expectancy and adverse attitude towards pregnancy, birth and breast feeding.

3.4.2 Methods

3.4.2.1 Subjects

The sample consisted of 60 healthy primiparous women with a singleton intrauterine pregnancy. Subjects were recruited through posted announcements, signs at the University of Zurich, the University Hospital of Zurich, and in obstetricians' offices in Zurich and the surrounding area. The pregnants' physical health was approved by their obstetricians while psychiatric disorders were screened using a structured clinical interview according to DSM-IV (WHO, 1990; Wittchen & Pfister, 1997) and SKID-II (Wittchen, Gruschwitz, & Zaudig, 1996). Exclusion criteria for participation were present psychiatric disorders such as depression, anxiety disorders, substance abuse or dependency, eating disorders or psychotic symptoms; alcohol consumption of more than 1 glass of wine or beer per week, insufficient knowledge of the German language, low school education and any medication. Pregnancy-specific exclusion criteria were artificial insemination, known medical maternal or fetal complications, including hypertension, diabetes mellitus, hyperememesis gravidarum, suspected fetal growth restriction and fetal structural anomaly on ultrasound.

3.4.2.2 Experimental Protocol

Sixty healthy pregnant women at time 1, were given the ZIPP and a battery of questionnaires about similar constructs (see below). The predictive power of the ZIPP (and the other measures) was tested by a postpartum follow-up assessment of the birth outcomes (see below). At time 1, all women who had completed the questionnaires, were

given a leaflet with contact informations. They were requested to make a telephone call or to write an e-mail as soon as they would have given birth. All pregnant women were informed about the course and aim of the study and provided written, informed consent prior to participation. At time 2, on average 13 days after the women had given birth, they were visited at the hospital and at home, respectively. The visit included a half-structured interview and the assessment of psychological and objective variables (see below). The objective variables were taken from medical protocols, given by the obstetricians. Finally, after the postpartum interview, they were given a body lotion as a present.

3.4.2.3 Psychological Assessment

The validated German versions of the following questionnaires were included: the Perceived Stress Scale (PSS, Cohen, Kamarck, & Mermelstein, 1983), the Lederman Prenatal Self-Evaluation Questionnaire (PSEQ, Lederman, 1979) and the Birth Anxiety Scale (GAS, Lukesch, 1983).

The PSS (Cohen et al., 1983) is a widely used self-report measurement to assess general or non-specific stress via 14 items, answered on an five-point scale from 0 (never) to 4 (almost always). The questions in the PSS ask for the perceived stress during the last month. PSS scores were averaged across all items to create a single prenatal perceived stress index for each subject. High scores represent high perceived stress.

The PSEQ (Lederman, 1979), comprising a total of 79 items, asks for psychosocial adaptation to pregnancy on the following seven dimensions: well-being of self and baby (10 items), acceptance of pregnancy (14 items), identification of a motherhood role (15 items), preparation for labor (10 items), help/control (10 items), relationship with mother (15 items), relationship with husband (10 items). The items were answered on a four-point scale from 1 (very much so) to 4 (not at all), which means that high values represent low adaptation to pregnancy. Internal consistencies (Cronbach's alpha) shown are reasonable (0.75) to very good (0.92) (Lederman, 1996, pp. 284). The intercorrelations (divergent validity) indicate independency for the subscales of the ZIPP (range r = 0.06 – 0.54).

The GAS (Lukesch, 1983) examines birth anxiety only on one dimension with a total of 25 items, answered on a four-point scale from 0 (no fear) to 3 (strong fear). Birth anxiety scores were averaged across items, as with the PSS, to create a single prenatal birth anxiety score for each subject.

3.4.2.4 Birth outcomes

The gestational age at the time of delivery was obtained from the medical protocol, received by the physicians. Newborns were weighed in the delivery room immediately after the birth. Birth weight was used as a continuous variable. Furthermore we assessed possible pregnancy complications occurring after time 1 until the time of delivery. We also assessed birth complications as secondary caesarean section, loss of blood > 500 ml, initiation of delivery, perineal rupture of second and third grade, and preterm delivery (delivery > 37 + 0 weeks).

3.4.3 Results

Again, the Scree Test in the principal component analysis with varimax rotation indicates a five-factor solution (course of Eigenvalues: 10.72; 6.94; 4.01; 3.22; 2.93; 2.57; 2.39; 2.34; 2.20; 1.89; 1.75; 1.68; 1.65; 1.39.; 1.36; 1.23; 1.20; 1.02). These five factors collectively account for a total variance of 49.96%. The first component comprises nine marking items and explains – unrotated – a total of variance of 19.18% and after rotation 13.32%, respectively. The second factor is marked with six items and explains a total variance of 6.12% (unrotated) and 9.55% (rotated), while the third factor (or component) accounts for a total of 7.00% before and 9.78% after rotation. This third factor is defined by seven marking items, whereas the fourth component is marked by six items and explains – unrotated –6.12% and after rotation 9.55% total variance. The last and fifth component, marked by seven marking items, explains unrotated 5.11% and after rotation 7.38% of total variance, respectively.

The intercorrelations between the subscales performed in the expected directions and are shown in table 3.5. Merely the comparatively high correlations between the scales “pregnancy and birth related strain” / “general strain” and “marital strain” / “pregnancy and birth related strain” are in contrast compared to the first study.

Table 3.5 Intercorrelations between the subscales of the ZIPP in study 2 (N=60)

	JS	GS	PS	LR	PBS
JS	-				
GS	0.35*	-			
PS	-0.07	0.54**	-		
LR	0.09	0.45**	0.30*	-	
PBS	0.35*	0.61**	0.59**	0.26	-

Note : * p < 0.05; ** p < 0.01

The ZIPP scales showed good internal consistencies, as reflected by the high standardised Cronbach’s Alpha, ranging from acceptable (> 0.76) to good (> 0.90) magnitude. The

lowest alpha coefficient was shown for the scale “lack of resources”, whereas the highest one was revealed for the scale “job strain”.

The tests regarding construct validation were conducted using the following questionnaires: GAS, PSS and PSEQ. Correlations were shown in the expected directions (see table 3.6). As for instance, sum score of the GAS was highly correlated with the ZIPP subscale pregnancy and birth related strain. Similarly, scores of the PSS have been positively correlated with both, the subscales “general strain” and “lack of resources”, respectively. In other words, the higher the birth anxiety of the women was, diagnosed using the GAS, the higher was their pregnancy specific strain, measured by the ZIPP, and, the higher their perceived stress was, the higher was their lack of resources and their general strain.

Table 3.6 Convergent validity of the ZIPP in study 2 (N=60)

Instrument/Subskala	GS	PS	LR	JS	PBS
GAS	0.51**	0.31*	0.32*	0.14	0.**48****
PSS	**0.53****	0.32*	0.49**	0.33*	0.45**
PSEQ – Well-being of self and baby	**0.60****	0.25	0.20	0.25	**0.68****
PSEQ – Acceptance of pregnancy	0.22	0.38**	0.30*	0.05	0.36**
PSEQ – Identification with motherhood role	0.32*	0.31*	**0.58****	0.18	0.36**
PSEQ – Preparation for labor	0.42**	0.36**	0.34*	0.21	**0.45****
PSEQ – Help / control	**0.55****	0.41**	0.07	0.18	**0.68****
PSEQ – Relationship with mother	0.22	0.06	0.12	0.14	0.23
PSEQ – Relationship with husband	0.13	**0.67****	0.21	0.00	0.35**

Note : * $p < 0.05$; ** $p < 0.01$

Correlations to the PSEQ also seem to be consistent with our expectations. The partnership specific subscale of the PSEQ shows significant positive correlations to the partnership subscale of the ZIPP. Also high correlations are shown between the subscales "concern for self" (PSEQ) and "general strain" (ZIPP). Furthermore, *all* subscales of the PSEQ, comprising a total of 59 items concerning pregnancy and birth, were highly positive correlated with the ZIPP scale "pregnancy and birth related strain". This scale includes 10 items, thereof the two strongest correlations were found for the two PSEQ scales "fear of pain/loss of control" and "concern for self" with $r = 0.68$ ($p \leq 0.001$), respectively.

To investigate the predictive validity of the ZIPP, correlations between the ZIPP subscales and different outcome variables were calculated. Gestational length was negatively correlated with the scale "lack of resources" ($r = -0.31$, $P = 0.04$). As expected, significant negative associations are shown between the ZIPP scale "pregnancy and birth related strain" and pregnancy complications, which were inversely coded ($r = -0.32$, $p = 0.03$). In other words: the higher the women were negatively affected by pregnancy related concerns, the higher was the probability to develop complications during the course of pregnancy. Furthermore, negative associations between the birth outcome variable "secondary cesaerean sectio" and the two ZIPP scales "general strain" and "partnership strain" were found, respectively (see table 3.7). Birth complications, such as the need to initiate delivery and perineal rupture of second and third grade, have been significantly correlated with "job strain" and "partnership strain" ($r = -0.41$, $p = 0.01$; $p = -0.35$, $p = 0.01$), approving our expectations (birth complications were also inversely coded). No significant correlations were found between birth weight and the ZIPP scales, nor for the scales of the questionnaires PSEQ, GAS or PSS.

Table 3.7 Criterion validity in study two (N=60)

Variables	Gestational length	Pregnancy complications	Secondary ces. section	Birth initiation	Perineal rupture
ZIPP - General strain	0.04	0.04	**-0.35***	-0.04	-0.08
ZIPP - Partnership strain	-0.06	-0.07	**-0.31***	**-0.35***	0.13
ZIPP - Lack of resources	**-0.31***	0.05	0.01	0.02	-0.20
ZIPP - Job strain	0.23	-0.20	-0.08	-0.09	**-0.41****
ZIPP - Pregnancy and birth related strain	0.04	**-0.32***	-0.25	-0.20	-0.08
PSEQ - Well-being of self and baby	0.04	0.10	-0.09	0.08	-0.13
PSEQ – Acceptance of pregnancy	0.16	-0.26	-0.09	-0.16	-0.02
PSEQ – Identification with motherhood role	0.07	**-0.31****	-0.04	-0.17	-0.08
PSEQ – Preparation for labor	-0.24	-0.08	-0.05	-0.13	-0.07
PSEQ – Help / control	0.10	0.13	-0.22	0.01	-0.10
PSEQ - Relationship with mother	**0.31***	-0.10	-0.01	0.02	-0.11
PSEQ – Relationship with husband	0.11	-0.14	-0.09	-0.25	0.01
GAS	0.08	0.14	-0.11	0.10	-0.03
PSS	0.04	-0.10	-0.13	0.01	-0.13

Note : * $p < 0.05$; ** $p < 0.01$

Regarding the questionnaires used for testing the validity of the ZIPP, there were only few associations with outcome variables found. “Identification of motherhood” (PSEQ) was negatively correlated with the variable “pregnancy complications”, which means that pregnancy complications were less probable, the more a woman had identified herself with becoming a mother. Surprisingly, the PSEQ subscale “relationship with mother” (PSEQ) has been positively correlated with gestational length. In other words: the worse the relationship to the own mother, the longer the gestational length.

3.4.4 Discussion

The aim of this study was the development of a questionnaire to assess psychosocial well-being in pregnancy. In order to achieve this goal, a three-sectional study was conducted. In the initial part of the study (pilotstudy) a first version of the questionnaire was designed, particularly based on interviews with pregnant women and on the consideration of existing questionnaires concerning the measurement of stress and well-being in pregnancy.
In the second part (study one) of this three-sectional study, the exploratively developed questionnaire was then applied to a sample of 154 pregnant women, in order to explore its internal factorial structure and to evaluate its psychometric values.

Further, the third and last part of this study (study two) was addressed to the factorial validity once again, in terms of a cross validation, based on another sample of 60 healthy pregnant women. In line with this purpose, we also investigated convergent and discriminant validity.

However, the development and statistical evaluation led to the ZIPP, a short psychometric instrument comprising five subscales, consisting of ten items each, which validly and reliably assesses psychosocial well-being in pregnancy according to stimulus, response and transactional stress theory.
The ZIPP is characterised by the following three advantages:

- First, the ZIPP comprises not only stress specific aspects of partnership, job and perceived strain, but also resource orientated aspects such as daily uplifts.
- Second, stimulus and reaction centered aspects of stress are considered, at the same time. This is in contrast with the majority of questionnaires used for obstetric research, which are narrowed to single stress aspects, as for instance birth anxiety, life events or even non-pregnancy-specific topics like the state-trait anxiety inventory.

- Third, the ZIPP represents a questionnaire assessing pregnancy related stress in a multi-dimensional but economic way.

The five-factor solution found in the first study by means of a principal component analysis with varimax rotation, could be replicated in the second study. We interpret this as an indicator for the stability of these five factors, although a final verification can only be approved on the basis of a confirmatory factor analysis (Bollen & Long, 1993).

Further, the five factors showed in both studies reasonable up to good internal consistencies. In the first study lowest values were revealed for the scale “pregnancy and birth related strain”. This phenomenon might be due to the relatively high heterogeneity of the items within this scale, compared to the other ZIPP scales. The “pregnancy and birth related strain” scale comprises items of the concepts such as birth anxiety, attitude towards pregnancy and breast feeding, general and pregnancy/birth specific locus of control.

Significant and positive, but low correlations between the factors among each other are evidence of divergent validity. Hence, the factors testify to be independent. The highest intercorrelations were found between the scales “lack of resources” and “general strain”. This goes in line with several findings showing that our psychosocial well-being is not only strain-dependent but also strongly related to our available resources (e.g. Cohen, 1988). Strong correlations were also found for “general strain” and “pregnancy and birth related strain” (see table 3.4). As expected, correlations of “pregnancy and birth related strain” were also highly significant together with “partnership strain”, “jobstrain” and “lack of resources”, which means that the higher a woman scores in pregnancy and birth specific strain, the more probable concerns in her partnership and job are. In addition the result is her having less resources to cope with difficulties.

Compared to the first study, the intercorrelations all turned out to be merely higher in the second study. This effect might be based on the different formation of the samples. In the first study healthy, as well as pregnant women with different pregnancy complications

were included, whereas in the second sample there were only healthy women regarded. Additionally, the second sample comprised only women who were primiparous, while the first study also included mothers.

Convergent validity regarding the pregnancy specific scale was supported by positively strong correlations with other indices assessing pregnancy and birth related strain, as for instance the GAS and the scales of the PSEQ. In particular, the strongest correlation was found for the scales “pregnancy and birth related strain” (ZIPP) and scale “fear of pain/loss of control” (PSEQ). This is not very surprising, as the pregnancy specific ZIPP scale comprises four of ten items regarding either specific or general aspect of locus of control and mastery, respectively. Likewise, a similarly strong correlation was found for the two accordant scales “general strain” and the PSS. Thus, we can conclude, that all scales of the ZIPP are valid and reliable. Nonetheless, considerable differences regarding their predictive validity seem to exist, indicating the ZIPP to be a more valid instrument in comparison to the PSS, GAS and PSEQ.

4 Are stress-induced cortisol changes during pregnancy associated with postpartum depressive symptoms?

4.1 Introduction

Postpartum depressive symptoms occur in approximately 50% of women who have recently given birth, whereas nonpsychotic postpartum major depression occurs in about 10 to 20% of women within 6 months postpartum (Ehlert et al., 1990). In the case of postpartum depressive symptoms, the mothers' ability to respond sensitively and competently to their newborn is compromised (Beardslee & MacMillan, 1993). Postpartum disorders can have long-term adverse effects for both mother and child if it remains untreated (Jacobsen, 1999), and even the presence of mild depressive symptoms has been found to be associated with impaired maternal functioning, comparable to that of women with postpartum depression (Weinberg et al., 2001). A broad range of research into the etiology of postpartum mood disorders has already been conducted. While psychosocial factors such as marital disharmony, number of life events in the previous year, and poor social support may be associated with postpartum depression, a number of hypotheses have been formulated to account for postpartum depressive symptoms in terms of neuroendocrine dysfunction. Research in the field of endocrine factors associated with postpartum mood disorders has mainly focused on estradiol and progesterone, and has produced conflicting findings (B. Harris, 1993; O'Hara, 1997).

As yet, only a small number of studies have examined the role of cortisol. Notably, all studies regarding the role of cortisol in depressive mood changes in the puerperium were based on the examination of unprovoked cortisol baseline levels. One such study, conducted by Handley et al. (1980) (Handley et al., 1980), examined a sample of 71 women and measured cortisol at 36 and 38 weeks gestation, on days 1 to 5 postpartum during hospital admission, and at 6 weeks postpartum. Results revealed significantly elevated cortisol levels during the end of pregnancy (38 weeks) associated with more

severe blues after delivery (Handley et al., 1980). Ehlert et al. (1990) measured cortisol levels after delivery and found that women showed significantly higher elevated morning cortisol levels on those days after delivery when the postpartum blues occurred, compared to days with balanced mood and the non-depressed group (Ehlert et al., 1990). However, other research groups did not find significant associations between elevated postpartum basal cortisol levels and blues symptoms during the first five days after delivery (Feksi et al., 1984; Kuevi et al., 1983). Pedersen et al. (1993) found significantly higher levels of plasma cortisol after delivery in women with a previous history of major depression than those with no such history (Pedersen et al., 1993).

In sum, the sparse findings of associations between unprovoked basal cortisol levels, measured either during pregnancy or after delivery, and postpartum depressive symptoms, are controversial. Notably, no study has investigated the relation between HPA *reactivity* of women during the time of their pregnancy and the occurrence of postpartum depressive symptoms.

In contrast, a broad body of research has clearly demonstrated the dysfunction of the unprovoked hypothalamic-pituitary-adrenal (HPA) axis in non-pregnant and non-puerperal individuals with major depression. Alterations of HPA axis in terms of baseline hypercortisolism in non-pregnant adults with melancholic depression are a common finding and have been demonstrated in several studies (Carroll & Curtis, 1976; Halbreich et al., 1985; Rubin et al., 1987). Besides the findings of elevated baseline cortisol levels and CRH levels at rest, numerous investigations have consistently reported abnormal glucocorticoid feedback in terms of blunted feedback sensitivity of the HPA axis (Checkley, 1996; Nemeroff et al., 1984; Young, Haskett, Murphy-Weinberg, Watson, & Akil, 1991; Young et al., 1993).

Extending the knowledge regarding HPA functioning in depressed individuals demonstrated by studies of basal HPA activity and pharmacological challenge studies, several studies

investigated cortisol in response to psychological stress in depressed individuals. There is evidence that depressed patients show blunted salivary cortisol reactivity compared to non-depressed individuals (H. M. Burke, Davis et al., 2005), with one study, for example, showing blunted cortisol responses after naturally occurring events in the daily lives of depressed outpatients measured by event assessment (Peeters, Nicholson, & Berkhof, 2003). A further study using a naturalistic stressor consisting of an unexpected visit by health professionals at the home of very low-income Mexican women following an in-depth interview and physical assessment showed that women with more severe depressive symptoms exhibited more blunted cortisol responses to stress than those with less severe symptoms (H. M. Burke, Fernald, Gertler, & Adler, 2005). Authors using a mental arithmetic task revealed that clinically depressed individuals also showed blunted cortisol responses (Trestman et al., 1991). Burke et al. (2005) summarize the literature on HPA reactivity following psychological stressors in depressed patients and outline that depressed individuals exhibit a relatively flat and unresponsive pattern of cortisol release compared to their non-depressed counterparts (H. M. Burke, Davis et al., 2005). The authors also showed that blunted stress reactivity in depressed patients was most pronounced in older and more severely depressed patients. In contrast, cortisol activity in the non-depressed samples was characterized by a more dynamic pattern, including greater stress reactivity and more rapid recovery following stress.

Based on these findings, it can be summed up that there is great evidence for elevated basal cortisol levels, a strong suppression of cortisol following pharmacological challenge, and blunted cortisol reactivity in response to psychological stressors in non-pregnant and non-puerperal depressed patients.

However, as reported above, only a small number of studies have actually found evidence for elevated basal cortisol levels during pregnancy and in the puerperium in terms of postpartum depressive symptoms. To our knowledge, there have been no investigations into the association of the psychobiological response to psychosocial stress during

pregnancy and postpartum depressive symptoms in clinical and subclinical populations, respectively.

The aim of this study was therefore to examine the predictive value of psychobiological stress reactivity during pregnancy for the development of depressive symptoms in the puerperium. To date, we are the first to investigate the relation between stress reactivity during pregnancy and depressive mood changes in the postpartum. In this context, we decided to assess the HPA axis reactivity of healthy pregnant women in response to a psychosocial stressor (mock job interview and mental arithmetic task performed in front of an audience) and then relate cortisol reactivity during pregnancy to postpartum depressive symptoms, assessed after delivery. Moreover, we investigated the psychological stress response to this standardized stressor.

4.2 Methods

4.2.1 Subjects

The sample consisted of 57 healthy nulliparous women with a singleton intrauterine pregnancy. Subjects were recruited through postal announcements, flyers at the University of Zurich, the University Hospital of Zurich, and in obstetricians' offices in Zurich and the surrounding area. Pregnant women's physical health was approved by their obstetricians, and psychiatric disorders were screened two weeks prior to the experiment using a structured clinical interview according to DSM-IV and SKID-II (Wittchen, Gruschwitz, & Zaudig, 1996.). Exclusion criteria for participation were presence of psychiatric disorders such as depression, anxiety disorders, substance abuse or dependency, eating disorders or psychotic symptoms, alcohol consumption of more than one glass of wine or beer per week, smoking, insufficient knowledge of the German language, low school education, and any medication. Pregnancy-specific exclusion criteria were artificial insemination, and known medical maternal or fetal complications, including hypertension, diabetes mellitus, hyperemesis gravidarum, suspected fetal growth restriction and fetal structural anomaly

on ultrasound. The study protocol was approved by the ethics committee of the University of Zurich and the ethics committee of the Canton of Zurich. All pregnant women were informed about the course and aim of the study and gave written informed consent before taking part in the experiment.

4.2.2 Procedures

Psychosocial stress test (time 1): All pregnant women participated in the Trier Social Stress Test (TSST) (Kirschbaum et al., 1993), which has been repeatedly found to induce profound endocrine and cardiovascular responses in 70-80% of the subjects tested (Dickerson & Kemeny, 2004). The TSST basically consists of an unprepared speech (five minutes) and mental arithmetic task (five minutes) performed in front of an audience. After a basal salivary-free cortisol sample was taken, women were introduced to the TSST (simulated job interview). After a 10-min preparation phase in a separate room, the women were then taken into the TSST room, which contained a panel of two observers and an ostentatious video camera. Saliva samples were taken ten minutes and immediately before and after the TSST, with additional samples taken at 10, 20, 30, 45 and 60 minutes after stress exposure. The TSST took place between 14.00 and 18.00. Subjects were reimbursed for participation in the study with 150 Swiss francs.

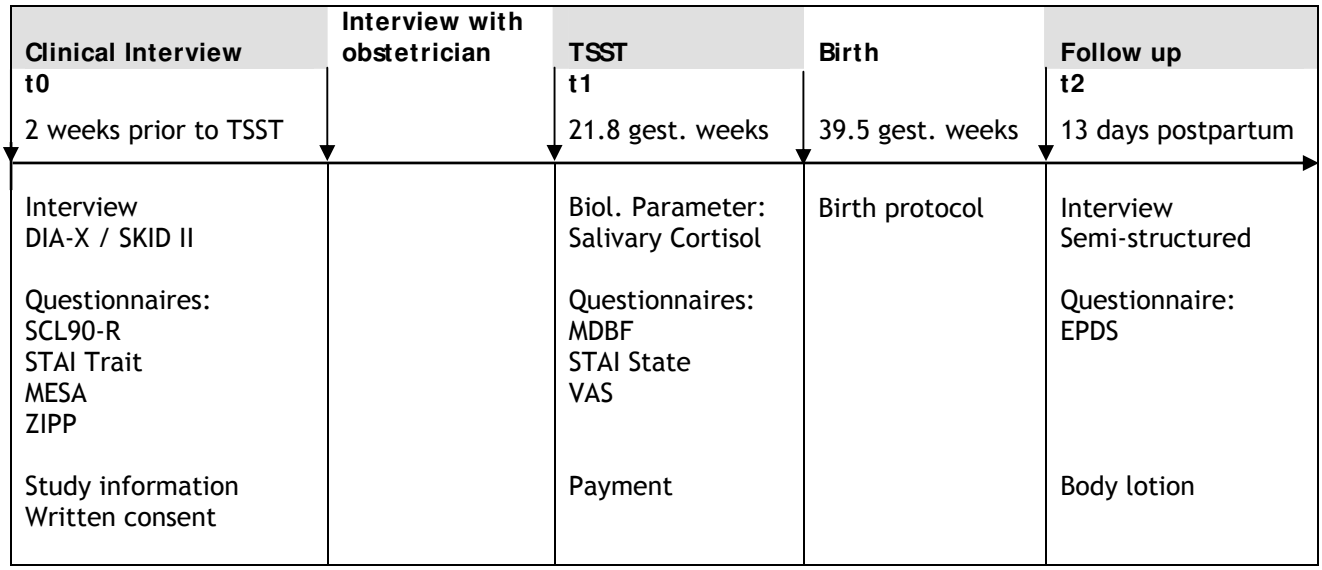

Figure 4.1 Study design

Follow-up assessment (time 2): At the end of the experiment, the pregnant women were given a flyer including contact information with a request to give a notice of birth by telephoning or mailing. At time 2, when the women gave birth, they were then visited within 13 days postpartum, at the hospital or by home visit. The visit included a semi-structured interview and the assessment of the psychological and objective variables (see below). The objective variables were taken from medical protocols given by the obstetricians. Finally, after the interview, the new mothers were given a body lotion as a present.

4.2.3 Sampling methods and biochemical analyses

Salivary cortisol was collected using Salivette collection devices (Sarstedt, Sevelen/Switzerland). After chewing on cotton rolls for approx. 60 seconds, collection devices were kept at room temperature until the end of the session. Saliva samples were then stored at -20°C until biochemical analyses took place. After thawing, saliva samples were centrifuged and spun at 3000rpm for 5 min, resulting in 1.0 ml clear supernatant of low viscosity. To reduce error variance caused by inaccuracy of the intraassay, all samples

of one subject were analyzed in the same run of each assay. Salivary-free cortisol concentrations were measured using a commercially obtainable chemiluminescence immunoassay (LIA) with high sensitivity (IBL, Hamburg, Germany).

4.2.4 Psychometric measures

To assess postpartum depression symptoms, a German validated version of the Edinburgh Postnatal Depression Scale (EPDS) was applied (Bergant, Nguyen, Heim, Ulmer, & Dapunt, 1998). This internationally used and well validated 10-item self-report instrument does not diagnose depression, but is used as a screening tool (Beck, 2001). Using a cut-off point of 9/10, the EPDS has a sensitivity of 84-100% and a specificity of 82-88% when compared to a diagnosis of major postpartum depression assessed through a psychiatric interview (Murray & Carothers, 1990). This cut-off point has been recommended to have sufficient sensitivity for community screening purposes (Zelkowitz & Milet, 1995). In addition, the following German language questionnaires were used to investigate psychological stress factors: The Multidimensional Mood Questionnaire (MDBF) was used to assess current mood on three dimensions (Steyer, Schwenkmezger, Notz, & Eid, 1997). State and trait anxiety was assessed using the State-Trait Anxiety Inventory (STAI) (Laux et al., 1981). A 36-item questionnaire was applied to measure stress susceptibility (MESA). The MESA comprises six subscales: sensitivity to failure, tolerance to work overload, tolerance to social conflict, sensitivity to criticism, tolerance to uncertainty and ability to relax (Schulz, Jansen, & Schlotz, in press). Psychopathological symptoms were assessed using the Symptom-Checklist-90-Revised (SCL90-R) comprising the following ten subscales: somatization, obsessive-compulsive symptoms, interpersonal sensitivity, depression, anxiety, anger-hostility, phobic anxiety, paranoid ideation, psychoticism, and “additional items”, referring to sleep behaviour, appetite and thoughts about dying and death (Franke, 1995). The stressfulness of the TSST was measured by a visual analogue scale (VAS).

4.2.5 Birth outcome measures

For the assessment of objective data postpartum, medical data were obtained from birth protocol. Three birth outcomes were measured: Gestational age at time of delivery, birth weight (as a continuous variable in g) and mode of delivery. Newborns were weighed in the delivery room immediately after the birth. Furthermore, pregnancy complications occurring after the stress exposure and during pregnancy until giving birth were assessed. We also measured the following birth complications: secondary caesarean section, loss of blood > 500 ml, second- and third-degree perineal rupture, and preterm delivery (delivery < 37 + 0 weeks).

4.2.6 Statistical analyses

To assess possible time and group effects, analyses of variance (ANOVAs) for repeated measures were computed. Possible effects of gestational age on cortisol stress reactivity were controlled by conducting analyses of covariance (ANCOVA). All reported ANOVA and ANCOVA results were corrected by the Greenhouse-Geisser procedure where indicated (violation of sphericity assumption). Cortisol areas under the curve were calculated with respect to increase (AUCi) and to ground (AUCg) using the trapezoid formula (Pruessner, Kirschbaum, Meinlschmid, & Hellhammer, 2003). All data were tested for homogeneity of variance and for normal distribution using a Kolmogorov-Smirnov and Levene's test before statistical procedures were applied. For all analyses, the level of significance was □ = 5%. Unless otherwise indicated, all results shown are means ± standard error of means (SEM).

4.3 Results

4.3.1 Sample characteristics

57 healthy nulliparous women with a singleton intrauterine pregnancy participated in the TSST during pregnancy. Allocation based on the EPDS score postpartum resulted in two groups, with 16 (28.07%) participants showing a score of ten or more (probable cases) and 41 (71.93%) participants having a score less than or equal to nine (probable non-cases). The EPDS was applied within an average of 13.4 (SD = 5.17) days postpartum.

Table 4.1 Sample characteristics (N = 57)

SAMPLE CHARACTERISTICS		EDPS ≥ 10 N = 16	EPDS ≤ 9 N = 41
Marital status (N, %)	Married/partnered	16 (100%)	41 (100%)
	Single/divorced	0	0
	Widowed	0	0
Highest (completed) educational level (N, %)	University	6 (37.5%)	11 (26.8%)
	College preparatory high school	6 (37.5%)	9 (22.0%)
	Apprenticeship	3 (18.8%)	14 (34.2%)
	Secondary school	1 (6.2%)	6 (14.6%)
	Missing data	0	1 (2.4%)
Employed (N, %)	Yes	14 (87.5%)	40 (97.6%)
	No	2 (12.5%)	1 (2.4%)
Obstetrical data (Mean, SD)	Week of gestation during TSST	21.1 (6.8)	22.5 (6.5)
	Gestational length	39.5 (1.5)	39.5 (1.6)
	Birth weight	3385.6 (543.2)	3310.1 (399.2)
Preterm delivery	Yes	1 (6.2%)	3 (7.3%)
	No	15 (93.8%)	37 (90.3%)
	Missing data	0	1 (2.4%)
Mode of delivery (N, %)	Vaginal	11 (68.8%)	34 (82.9%)
	Regular section	4 (25%)	4 (9.8%)
	Emergency section	1 (6.2%)	2 (4.9%)
	Missing data	0	1 (2.4%)
Gestational (N, %) complications	Yes	4 (25%)	10 (24.2%)
	No	12 (75%)	30 (73,2%)
	Missing data	0	1 (2.4%)
Complications during Delivery (N,%)	Yes	8 (50%)	25 (61%)
	No	8 (50%)	15 (36.6%)
	Missing data	0	1 (2.4%)

The two groups did not differ with respect to mean age (probable cases: 30.50, SD = 3.18 vs. probable non-cases: 29.20, SD = 3.56) or week of gestation at the time of the experiment (probable cases: 21.06, SD = 6.84 vs. probable non-cases: 22.45, SD = 6.53), complications during pregnancy (probable cases: 1.75, SD = 0.45 vs. probable non-cases: 1.75, SD = 0.44) and complications during birth (probable cases: 1.50, SD = 0.52 vs. probable non-cases: 1.38, SD = 0.49). Furthermore, one-way ANOVAs revealed no group differences in terms of gestational length (probable cases: 39.49, SD = 1.52 vs. probable non-cases: 39.52, SD = 1.62), birth weight (probable cases: 3385.63, SD = 543.23 vs. probable non-cases: 3310.13, SD = 399.16) and mode of delivery (four women in the group of probable non-cases and five women in the group of probable cases delivered by caesarean section). With regard to previous depressive history, no differences were found: In the group of probable cases with postpartum depressive symptoms, there were three women who had experienced depressive episodes in the past, while in the group of probable non-cases, five women were found to have a history of depressive symptoms.

4.3.2 Physiological stress response

4.3.2.1 Salivary cortisol stress response

The TSST resulted in a significant increase in salivary cortisol (in nmol/l) (main effect of time: $F (2.41, 48.09) = 5.58$; $P < 0.00$) from repeated measures ANOVAs.

There was no significant time x group interaction found over all of the nine cortisol measures ($F (1.51, 88.36) = 1.73$; $P = 0.19$), whereas ANOVAs with repeated measures did reveal a significant time x group interaction over the seven cortisol measures that included one measure immediately before, and the remaining six after the stressor (time x group effect: ($F (2.41, 25.74) = 2.99$; $P = 0.04$) (figure 4.2).

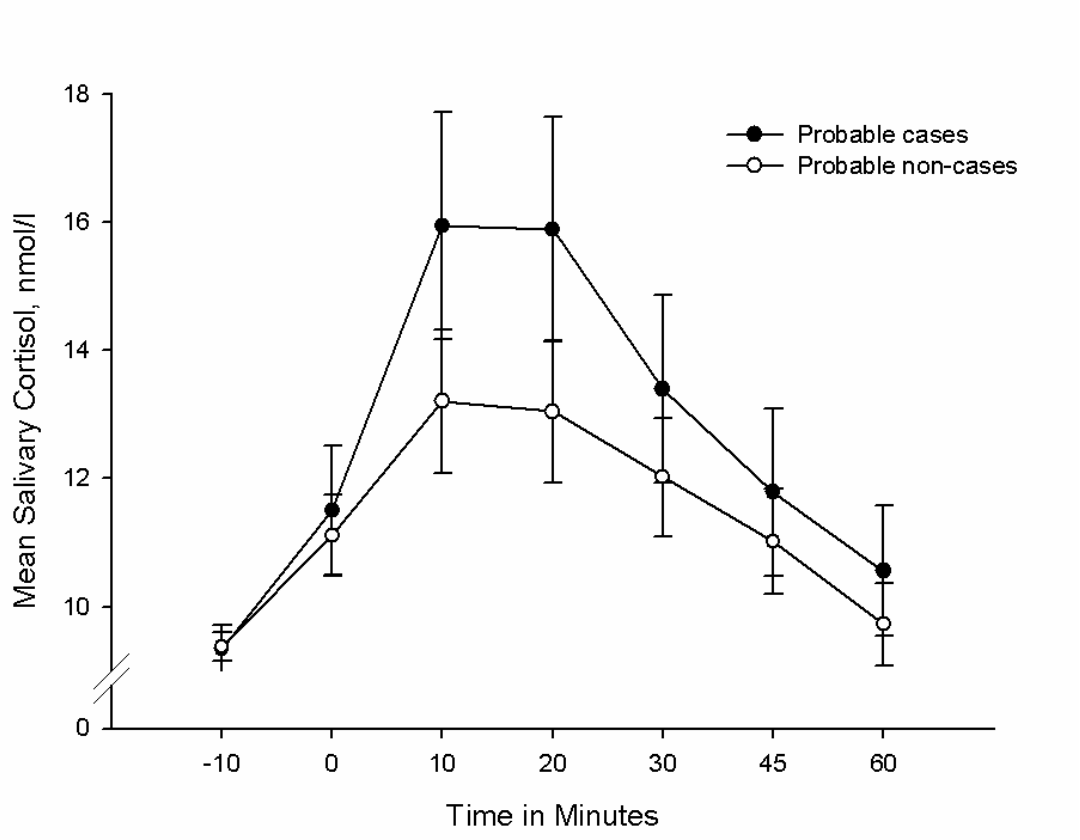

Figure 4.2 Mean salivary cortisol levels in the course of the experiment ± SEM

One-way ANOVA did not indicate significant salivary cortisol baseline differences (in nmol/l) between groups (F (1.00, 20.01 = 1.74; P = 0.19), or for the very first cortisol measure after stress exposure (F (1.00, 0.90) = 0.33; P = 0.86). Due to the known difference in cortisol stress reactivity between women in the second and third trimesters (Nierop et al., in revision), gestational age was controlled by ANCOVA with repeated measures and did not differ between the two groups. Similarly, as a past history of depressive illness is known to be a risk factor for postpartum depressive symptoms (Robertson et al., 2004), known depressive episodes in the women's past were also controlled by ANCOVA and did not differ between the two groups. Furthermore, results obtained by one-way ANOVA with the calculated area under the response curve of salivary cortisol over the aforementioned seven measures with respect to increase (AUCi) did not show significant differences between groups (F (1.00, 2379.67) = 1.82; P = 0.18), or for the AUCg (F (1.00, 305.21) = 0.18; P = 0.67).

4.3.3 Psychological responses

The TSST resulted in a significant decrease in mood (MDBF) ($F(3.30, 60.35) = 17.88$; $P < 0.000$). Two-way ANOVA with repeated measures indicated a significant interaction of time and group ($F(3.30, 10.93) = 3.24$; $P = 0.02$) and a significant group effect ($F(1.00, 163.31) = 9.83$; $P < 0.01$), with the lowest values in the probable case group and the highest values in the probable non-case group (see figure 4.3).

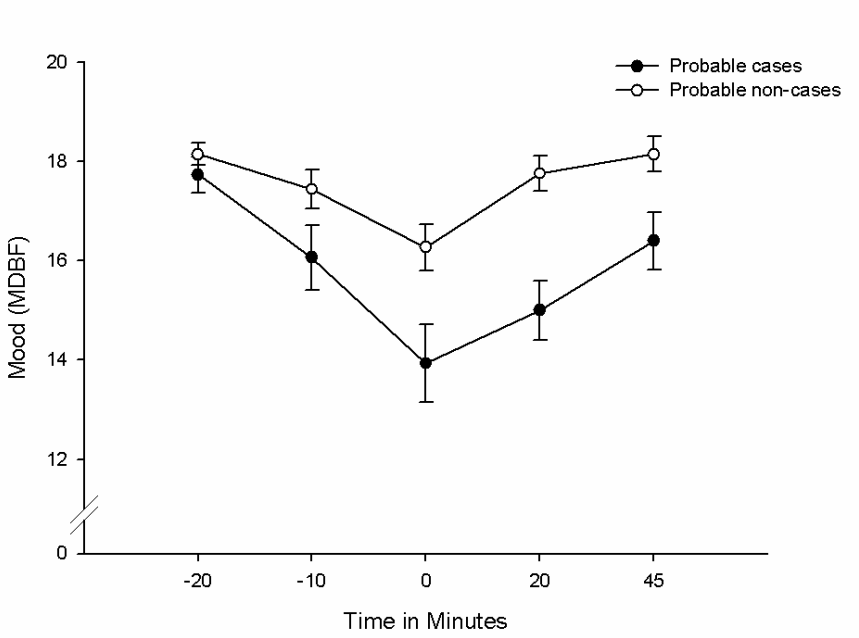

Figure 4.3 Mood (MDBF) in the course of the experiment of women having postpartum depressive symptoms (probable cases) vs. women without depressive symptoms in the puerperium (probable non-cases)

Furthermore, statistical analyses revealed that the probable case group showed significantly higher levels of state anxiety (STAI) than the probable non-case group throughout the entire period of the experiment (group effect: $F(1.00, 3.06) = 6.32$; $P = 0.02$) and a significant interaction of time and group ($F(2.93, 0.18) = 3.33$; $P = 0.02$) (see figure 4.4). Changes over time revealed by two-way ANOVA with repeated measures

showed a significant increase in state anxiety in response to stress (F (2.93, 1.57) = 29.10; P < 0.000).

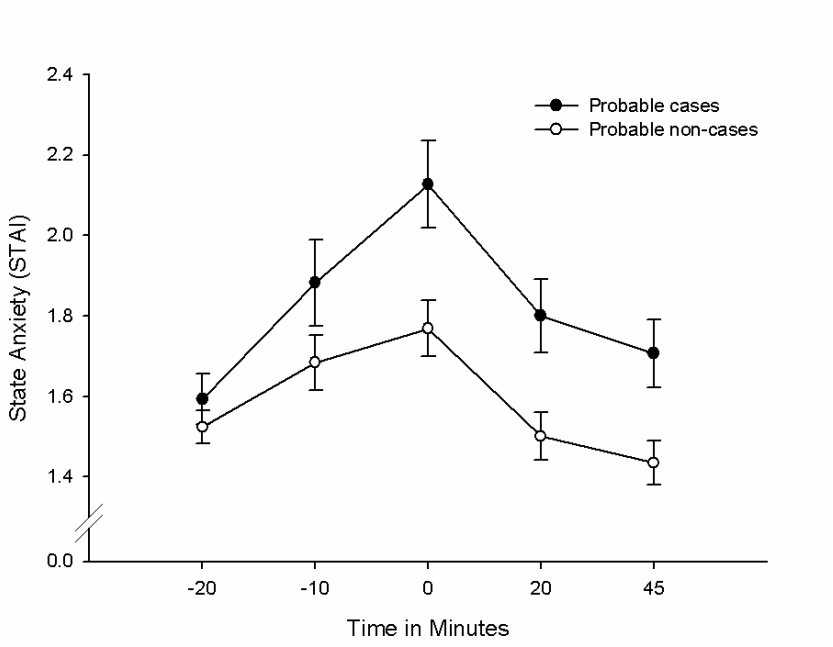

Figure 4.4 State-anxiety (STAI) in the course of the experiment of women having postpartum depressive symptoms (probable cases) vs. women without depressive symptoms in the puerperium (probable non-cases)

Results obtained from one-way ANOVA indicated that the two groups differed significantly in trait anxiety (STAI: F (1.00, 0.38) = 4.14; P = 0.05) (see figure 4.5) as well as in stress susceptibility (MESA: F (1.00, 574.17) = 9.37; P < 0.01), (see figure 4.6).

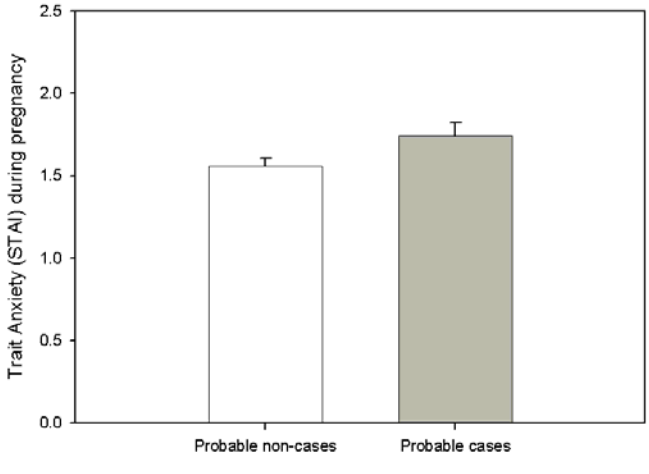

Figure 4.5 Trait-anxiety (STAI) differences between women having postpartum depressive symptoms (probable cases) vs. women without depressive symptoms in the puerperium (probable non-cases)

In addition, one-way ANOVA revealed significant differences in the subscale "additional items" of the SCL90-R (SCL90-R: $F\ (1.00, 2.36) = 7.48$; $P < 0.01$), shown in figure 4.7. No significant differences between groups were found for the VAS.

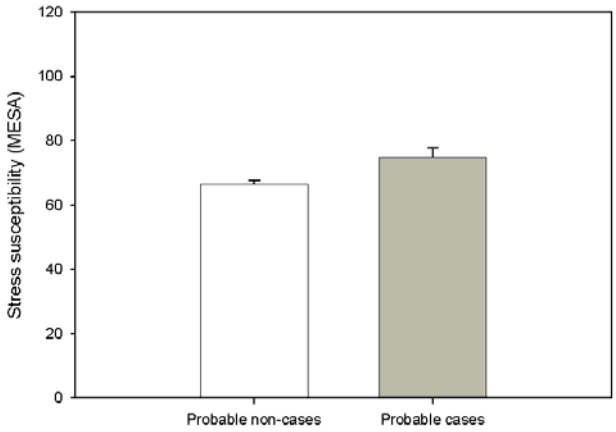

Figure 4.6 Stress susceptibility (MESA): Differences between women having postpartum depressive symptoms (probable cases) vs. women without depressive symptoms in the puerperium (probable non-cases)

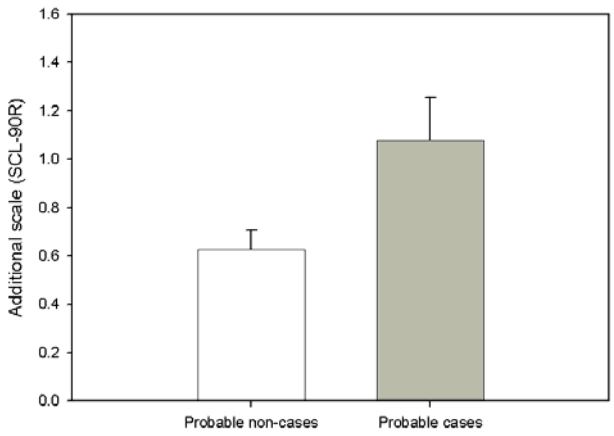

Figure 4.7 “Additional scale” of the SCL90-R: Differences between women having postpartum depressive symptoms (probable cases) vs. women without depressive symptoms in the puerperium (probable non-cases)

4.4 Discussion

This is the first study to prospectively compare healthy women with high and low risk for postpartum depressive symptoms in terms of their psychological and physiological reactivity to a standardized psychosocial stressor during pregnancy. High and low-risk groups were formed on the basis of a postpartum EPDS cut-off score of nine. The EPDS was applied within an average of 13 days postpartum. Women in the probable case group, with an EPDS score greater than nine after delivery, showed an increased hormonal response to psychosocial stress during pregnancy. According to this, women in the probable case group responded with a heightened increase in state anxiety and with a stronger decrease in mood to the psychosocial stressor. These data provide evidence that healthy pregnant women developing depressive symptoms postpartum might be identified during the time of pregnancy by means of their physiological and psychological coping with psychosocial stress.

As mentioned above, the probable case group showed an increased hormonal response to the stress test. With regard to the *baseline* cortisol levels, measured at the beginning of the experimental procedure during pregnancy, no significant differences were found between the two groups. This is in contrast to the findings of Handley et al. (1980), who revealed significantly elevated baseline levels of cortisol during the time of pregnancy in women with more severe blues on the fifth day postpartum compared to women without the experience of postpartum mood changes. These contradictory findings might be due to the different point in time of cortisol measurement during pregnancy. Handley et al. (1980) took baseline cortisol measurements at 38 weeks' gestation, whereas in the present study baseline cortisol measurements were taken in the second trimester (probable cases: 21.06, SD = 6.84 and probable non-cases: 22.45, SD = 6.53, respectively). Hence, it might be assumed that possible gestational cortisol baseline differences between women with and without the development of depressive symptoms in the early puerperium become

detectable at the end of pregnancy rather than in the second trimester. However, further investigations regarding unprovoked baseline cortisol levels measured during pregnancy, associated with postpartum mood states, should bear in mind that the point in time of baseline cortisol measurement during the period of pregnancy might play a decisive role.

The different endocrine stress *response* found in the probable case group is represented by an increased cortisol reactivity, while gestational age was controlled. The cortisol response to the TSST during pregnancy was significantly higher in the probable case group compared to the probable non-case group without depressive symptoms during early puerperium. Considering this finding of higher cortisol reactivity in the probable case group in the light of reports of HPA reactivity in *non*-pregnant and *non*-puerperal depressive patients, how can our results be explained? As previously reported, non-pregnant and non-puerperal depressive patients show a significantly blunted pattern of cortisol release in response to psychosocial stress (H. M. Burke, Davis et al., 2005), whereas healthy individuals show a more dynamic pattern. The fact that the pregnant women in the present study were healthy at the time of the experiment may corroborate the assumption that this differing hormonal stress response might be seen as a biological prodromal symptom, preceding postpartum depressive mood changes. This premorbid pattern observed in the probable case group of the present study might be interpreted as an allostatic load (McEwen, 2001). The higher HPA axis responsiveness may represent an inadequate response of the HPA axis as an allostatic system to potentially stressful challenges such as the TSST. Thus, if the long-term pattern of increased HPA reactivity persists, one might imagine that this may lead to damage in the long run, resulting in a blunted HPA reactivity, as observed in patients with melancholic depression (H. M. Burke, Fernald et al., 2005). This hypothesis is appropriate, since animal studies showed that there is an initial increase of corticosterone secretion to stress, which is followed by a reduced responsiveness over time (Heim, Ehlert, & Hellhammer, 2000).

Similar findings of biological premorbid patterns associated with subsequent non-pregnant and non-puerperal major depressive disorders are only found for cortisol activity, but not for cortisol reactivity. One such longitudinal study conducted by Harris and colleagues (T. O. Harris et al., 2000) examined a total sample of 116 women who were not currently depressed, but were comprised of 83 women who were known to be vulnerable to onset of major depression due to psychosocial reasons and 33 women who were not. At entry, unprovoked salivary cortisol was measured on four consecutive days at 8.00 and again at 20.00, while onset of major depression was measured during the 13-months follow-up period. Unprovoked morning cortisol levels at entry turned out to be significantly associated with a subsequent onset of major depression, providing evidence that premorbid elevated morning cortisol levels might represent an independent risk factor for the development of non-pregnant and non-puerperal depression. Another finding was revealed in a sample of 180 adolescents at high risk for psychopathology, where the occurrence of peaks in morning cortisol emerged as predictive for subsequent non-puerperal major depression at a 12-months follow-up (Goodyer, Herbert, Tamplin, & Altham, 2000). Hence, there is evidence for a specific premorbid pattern of psychoendocrine factors predicting the onset of non-pregnant and non-puerperal major depressive disorder. According to these findings, there might also be a similar biological premorbid pattern for puerperal depressive symptoms.

However, future research into unprovoked cortisol baseline levels as well as HPA responsiveness to psychosocial stress during pregnancy is needed to illuminate gestational HPA dysregulations in terms of postpartum depressive symptoms in pregnant samples.

With regard to psychological changes to stress, we found a significant change in mood and state anxiety due to the TSST. Analyses of variance with repeated measures revealed that women with postpartum depressive symptoms showed increased state anxiety ($p < 0.05$) and had a significantly lower mood state throughout the experiment ($p < 0.05$). Our

findings might be the result of different coping strategies of women who showed postpartum depressive symptoms. However, Murata and colleagues (Murata et al., 1998) found elevated trait anxiety during pregnancy associated with postpartum blues, which is extended by our results in showing that the probable case group showed higher trait anxiety compared to the probable non-case group ($p < 0.05$). Another study also showed that trait anxiety during late pregnancy was a significant predictor for depressive symptoms six months after delivery (Zaers, Waschke, & Ehlert, submitted).

Furthermore, we found differences in the susceptibility to stress between high and low-risk pregnant women for postpartum depressive symptoms in terms of a higher stress susceptibility found in the probable case group. This finding might indicate a general vulnerability to stress for women at high risk for postpartum mood changes.

No differences were found for obstetrical factors, as obstetrical complications and mode of delivery did not differ between the two groups. This result is in line with findings from several studies regarding postpartum depressive symptoms associated with obstetric complications (Johnstone et al., 2001; Josefsson et al., 2002; Saisto et al., 2001b) and mode of delivery (Patel et al., 2005), respectively. In contrast, there are some studies that provide an association between birth outcomes and postpartum mood disorders (Boyce & Todd, 1992; Koo, Lynch, & Cooper, 2003). These conflicting findings may be due to methodological problems, as, for instance, definitions of complications may differ between physicians or hospitals (Robertson et al., 2004).

In summary, our data provide evidence that women developing depressive symptoms in the puerperium already show increased reactivity in physiological and psychological measurements in response to a standardized psychosocial stressor during their pregnancy. Our results may lead to the conclusion that the increased cortisol response to psychosocial stress shown in healthy pregnant women with a potential risk for the development of postpartum depressive symptoms could play a part in terms of a prodromal symptom in the

biological basis of postpartum depression. However, healthy pregnant women with an increased cortisol reactivity, high levels of general anxiety, and high stress susceptibility are at increased risk for postpartum depression. In conclusion, women at high risk for depression after delivery might already be identified during pregnancy through their higher stress reactivity. The health and well-being of the mother and child call for early diagnosis and can be facilitated through an awareness of the psychobiological mechanisms and the risk factors for postpartum mood changes and disorders.

5 General discussion

This research focused on the assessment of psychobiological well-being during pregnancy and its relation to postpartum mood states. It consisted of two empirical parts (empirical studies part I and II), of which the first is divided into three sub-studies. Sub-study one is exploratory, while the other two sub-studies represent validation studies. Empirical studies part II has a prospective design.

In this last section the findings of the empirical studies will be summarized in short, followed by the discussion of the reported data and comments on methodological issues. Finally, the chapter ends with conclusions and an outlook.

5.1 Summary of the results

5.1.1 The Zurich Inventory of Psychosocial Well-being in Pregnancy (ZIPP): Development and empirical findings

The goal of the first empirical part was the development and validation of a questionnaire assessing psychosocial well-being in pregnancy. It consists of the following three sub-studies.

The first one comprised the explorative compilation of an item pool, based upon fourteen interviews with pregnant women, who suffered from idiopathic premature labour and were therefore hospitalized. Additionally, a comprehensive literature research about possible risk factors related to adverse pregnancy and birth outcome was taken into account in adapting items of existing questionnaires measuring psychosocial risk factors for adverse birth outcomes. This resulted in an item pool of 127 items, which was reduced in the subsequent study.

In a second step, the draft of the questionnaire derived in sub-study one was applied in a sample of 154 pregnant women. Then, principal component factor analysis with varimax rotation was conducted in order to test the internal factorial structure and internal consistency by the evaluation of Cronbach's Alpha. The abbreviation of the item pool was conducted through statistical analyses. Items with insufficient factor loadings in the factor analyses or unsatisfactory Cronbach's Alpha coefficients were excluded from the questionnaire. This resulted in the ZIPP consisting of the following five sub-scales of ten items each: "job strain", "marital discord", "general strain", "pregnancy and birth related strain" and "lack of resources".

In a third step, the ZIPP was applied to a sample of 60 healthy primiparous pregnant women. Factor analyses revealed the same factors found in the antecedent sub-study, whereas internal consistency showed reasonable to very good results. The ZIPP scales collectively explained a total variance of 49.96%. Intercorrelations were shown to be good, albeit they had been negligibly higher compared to the intercorrelations in the foregoing study.

In addition to the assessment of factorial structure and internal consistency, we tested the predictive as well as the convergent validity. Therefore we calculated correlations between the ZIPP scales and other questionnaires measuring prenatal stress (convergent validity) and correlations between the ZIPP and birth outcomes (predictive validity). As anticipated, high correlations in the logical and expected directions between ZIPP scales and other questionnaires indicated good convergent validity.

Regarding the predictive validity we found significant correlations in the expected direction between ZIPP scales and the outcome variables gestational length, pregnancy complications, birth complications such as secondary caesarean section, birth initiation

and perineal rupture of second and third grade. No associations were found for birth weight. The predictive validity for the other questionnaires measuring prenatal stress was only given by few significant correlations for the two birth outcomes gestational length and pregnancy complications (both correlated to the PSEQ).

5.1.2 Are stress-induced cortisol changes during pregnancy associated with postpartum depressive symptoms?

Besides the assessment of prenatal stress and its adverse effects on the course of pregnancy and birth outcomes, it was intended to identify psychobiological factors which may be associated with the development of depressive mood changes in the puerperium.

In a prospective design, a sample of 57 women who took part in the TSST during their pregnancy ("time 1 experiment") were visited on average 13 days after they had given birth ("time 2 assessment"). Postpartum depressive symptoms had been assessed using the well validated German version of the EPDS, using a cut-off point of nine. Allocation relating to this EPDS score postpartum resulted in two groups: 41 participants (71.93%) had a score of less or equal than nine (probable non-case group), whereas 16 participants (28.07%) showed a score of ten or more (probable case group). Significant differences in the psychological as well as in the physiological stress response were found between the two groups.

Regarding the physiological stress reactivity to the standardized psychosocial stress test during pregnancy, our investigations revealed an increased response in the hormone cortisol in women developing puerperal depressive symptoms. The cortisol response was significantly higher in the probable case group, while cortisol baseline levels did not differ between the two groups.

Significant differences were also shown for several psychological factors. Notably, those participants who showed postpartum depressive symptoms had significantly lower mood state and increased anxiety throughout the whole experimental procedure (time 1

experiment). Furthermore, the group of women with postpartum depressive symptoms was significantly more anxious (state anxiety) and showed higher stress susceptibility. Moreover, the same group had significant higher scores in the additional scale of the SCL90-R, whose items refer to sleep and appetite disturbances, as well as thoughts about dying.

However, no differences were found for obstetrical factors such as gestational or intrapartal complications or for mode of delivery. Further, the two groups did neither differ in their gestational length and birth weight, nor for prior episodes of psychiatric illness.

The results of this longitudinal analysis indicate that women at high risk for adverse postpartum mood changes might already be identified during the time of pregnancy by their higher physiological as well as psychological stress reactivity to psychosocial stress.

5.2 Methodological considerations

Based on the first empirical part we found a five-factor solution in the first sub-study consisting of a principal component analysis with varimax rotation. This finding was successfully replicated in the subsequent sub-study, indicating the stability of these five factors. Instead of that structural equation models (e.g. Lisrel) could have been used to verify stability on the base of a confirmatory factor analysis (Bollen & Long, 1993).

Another methodological consideration affects the point in time of assessing women with postpartum depressive symptoms. As the average of days of the assessment of women with depressive symptoms amounts to 13, it is not clear, whether the end of postpartum blues period, or rather the beginning of a postpartum depression was measured. Further measurements would have been necessary to answer this question, e.g. by means of a four month follow-up.

As reported, we found no differences in regard to the AUCg or the AUCi for cortisol measurement. One possible explanation might be the great variability in the group's response to the TSST, leading to greater standard errors and standard error of means, respectively. It is noticeable that the variability seems to be higher for the probable case group compared to the probable non-case group. Similar findings are observable in the study of Young, Lopez, Murphy-Weinberg, Watson and Akil (2000) , who investigated the psychobiological stress response to psychosocial stress (TSST) of depressed subjects in comparison to healthy controls, and found greater variability for the depressed group, too. The different variability might be explained by the different types of HPA dysregulation observable in depressed women (H. M. Burke, Davis et al., 2005). For instance, only 50% of the patients with non-pregnant and non-puerperal major depression show elevated plasma levels at rest (Young et al., 2000). According to H. M. Burke, Davis et al. (2005) potential sources of variation are individual characteristics such as age, depression characteristics like subtypes and severity of depressive symptoms or early life stress (H. M. Burke, Davis et al., 2005). However, the great variability found in this study might be due to similar reasons.

In the second empirical part women with low educational level were excluded because of its possible effect of a limited ability to do a free speech within the course of the TSST. Further research including women with various educational levels is needed in the future in order to draw general conclusions.

As far as physiological parameters are concerned, we only measured salivary free cortisol as an indicator of the HPA axis reactivity to psychosocial stress, which has been shown to be a reliable and valid indicator for the activity and reactivity of the HPA axis, respectively. Next to cortisol, the assessment of other endocrine parameters such as

plasma cortisol or ACTH might be helpful to illuminate the association of HPA reactivity as a prodromal symptom preceding postpartum depressive symptomatology.

5.3 Discussion of the results

The aim of the present thesis "Assessment of psychobiological well-being during pregnancy and its relation to postpartum mood states" was to measure psychological as well as physiological parameters during pregnancy and to relate them to postpartum mood states. In order to evaluate the *psychosocial* aspect of well-being during pregnancy a new questionnaire was developed and statistically evaluated. This resulted in the "Zurich Inventory of Psychosocial Well-being during Pregnancy", the ZIPP.

The questionnaire consisted of five scales of ten items each. Psychometric results suggested internally consistent items indicating relatively little measurement error. Further, intercorrelations (divergent validity) of the subscales and correlations with other instruments (convergent validity) assessing similar constructs turned out to be as expected, indicating a valid and reliable assessment of psychosocial well-being of pregnant women.

It is noteworthy, that the level of significant correlations (0.31 to 0.41 range) between the ZIPP scales and the outcome variables are equivalent to, if not better than, correlations between the birth outcome variables and the questionnaires assessing similar constructs. The ZIPP scales were significantly associated with multiple outcome variables such as gestational length, pregnancy complications, secondary caesarean section (emergency section), birth initiation and perineal rupture of second and third grade, whereas other inventories also measuring psychosocial well-being failed to show the same associations, despite their high correlations (construct validity) between the ZIPP scales and those inventories (0.31 to 0.68). An exception is the PSEQ, whose subscale identification of

motherhood was logically and significantly related to the occurrence of pregnancy complications.

The ZIPP disposes of the following strengths: To our knowledge, this is the first questionnaire assessing perceived stress (general strain), pregnancy and birth related stress, lack of resources (daily uplifts), job strain and marital discord in one single questionnaire. Furthermore, cognitive factors such as general and pregnancy/birth related locus of control, reflecting the secondary appraisal of the transactional stress theory of Lazarus, were also included. Up to now, several separate scales or inventories were required in order to assess all of the above mentioned scales. Thus, the time and effort needed for the completion of such batteries is far too high and its application therefore questionable.

Additionally to the measurement of the psychological well-being of pregnant women, it was intended to assess psychobiologic stress reactivity during pregnancy and to relate stress response to the subsequent occurrence of depressive symptoms in the postpartum period. As reported above, we found significant group differences in cortisol reactivity, whereas baseline levels did not differ.

The lack of differences between gestational cortisol *baselines* in women with and without the development of depressive symptoms in the puerperium is contrary to the findings of Handley et al. (1980). The authors revealed that women, who experienced severe baby blues on the fifth day postpartum showed elevated cortisol baseline levels during the time of pregnancy. The contradicting findings might be due to different time of cortisol measurements in these studies. Handley and his colleagues (1980) measured cortisol baselines two times, at 36th and 38th week of pregnancy, whereas cortisol measurements in the present study took place in the second trimester (22.05, SD = 6.59). Thus, it might be hypothesized that potential gestational baseline differences in cortisol between women

with and without the development of depressive symptoms after delivery, are detectable rather at the end than in the middle of the course of pregnancy. Another point is that Handley et al. (1980) found significant differences only for the measurement in the 38th week, but not in the 36th week of gestation. However, up to now little attention has been paid to the association of gestational baseline cortisol levels and the subsequent development of depressive symptoms in the puerperium. Further investigations should take the point in time of cortisol measurements, as it might play a decisive role into account.

As far as the endocrine stress *reactivity* is concerned, significant group differences were found. This is the first study to show that women, who develop depressive symptoms in the early puerperium, show higher cortisol reactivity during pregnancy, compared to those without puerperal depressive symptoms. Referring to reports of the dysfunctional HPA reactivity in samples of non-pregnant and non-puerperal depressive patients, what does our finding indicate?

There is great evidence that non-pregnant and non-puerperal depressive patients show a characteristic pattern of cortisol response to psychosocial stress, consisting of a significant blunted cortisol release, whereas healthy individuals show a more dynamic pattern (H. M. Burke, Davis et al., 2005). As the pregnant women in the present study were healthy at the time of the experimental procedure, it may be hypothesized that the observed increase of cortisol response is a biological prodromal symptom which precedes postpartum mood changes. This premorbid pattern might be interpreted as a so-called “allostatic state”. Sterling and Eyer (1988) described the neuroendocrine system, such as the HPA axis, as a mediator of adaptation to challenges of daily life, the allostasis. If there is increased activity of such a mediator, as for instance the result of chronic stress, this state is described as an “allostatic state” (McEwen, 2003). The costs and consequences of such a state are manifested in a number of adverse health outcomes, the “allostatic load”.

McEwen (2003) describes a number of patterns of allostatic states in major depression as for example the known increased evening levels of cortisol or the distorted diurnal rhythm found in patients with major depression. Allostatic states represent a pathway for the development of allostatic load and produce cumulative changes in both brain and other organs. Consequently, higher HPA axis responsiveness during pregnancy in women with the development of postpartum symptoms in the puerperium, might represent an allostatic state and lead, if continued, to an allostatic load, manifested in a blunted HPA reactivity, similar to patients with melancholic depression.

Looking at the psychological stress reactivity to the TSST, women developing depressive mood changes in the early puerperium, showed significant lower mood state and increased state anxiety throughout the experimental procedure. This indicated a specific pattern of coping with psychosocial stress, which resulted in being more anxious and thus, feeling worse during the experimental procedure.

Further manifestations of adverse well-being of this group are shown in the observed higher stress susceptibility, higher trait anxiety and higher levels in the “additional scale” of the SCL90-R, which refers to sleep and appetite disturbances, thoughts about dying and death. In regard to the latter, Chaudron et al. (2001) found similar results showing that thoughts of death and dying and difficulties falling asleep were strong predictors for postpartum depression in the forth month after delivery. Predictors were measured in the first month postpartum, while in the present study they were measured during pregnancy.

As far as anxiety is concerned, the present findings are in line with Saisto et al. (2001), who revealed that general anxiety, measured once before and once after the 30th week of gestation, was a significant predictor of puerperal depression. Robertson et al. (2004) derive in their review that higher levels of anxiety during gestation predict not only the

occurrence but also the intensity of postpartum depressive symptoms. In their view, general anxiety might function as a moderator variable for depression in the puerperium. Further, the higher stress vulnerability during pregnancy found in women with high risk of puerperal depressive symptoms might indicate a general susceptibility of stress in these women.

5.4 Conclusions and Outlook

The findings of the empirical part I of the present work indicate that the ZIPP is a reliable and valid instrument for the assessment of the psychosocial well-being of pregnant women. The findings regarding the predictive validity of the ZIPP, lead to the conclusion that the questionnaire can serve as a screening tool helping to identify women at risk for several adverse birth outcomes. The possibility for early preventive interventions is therefore given.

The study presented in the empirical part II is the first to examine the association of psychobiological stress reactivity during pregnancy and its association with postpartum depressive symptoms. The results indicate that women at high risk for the development of postpartum depressive symptoms in the early puerperium might be identified by means of their specific psychobiological stress reactivity to psychosocial stress during pregnancy. The fact of finding higher cortisol reactivity in women, vulnerable for postpartum depressive symptoms, might contribute to a deeper understanding of the underlying physiological mechanisms of postpartum mood disturbances.

Through this work a number of new questions arose, which could be answered in the future. The reported results regarding the first empirical part of this thesis strongly support the reliability and validity of the ZIPP. However, psychometric questions such as

factor structure or predictive validity have to be further explored by means of greater sample sizes.

In order to investigate the association of cortisol baseline differences during pregnancy between women with high and low risk for the development of depressive symptoms postpartum, several baseline levels should be measured systematically from the beginning of the second trimester until the end of pregnancy, as the time measurement of cortisol baselines might play a role in the ability to identify women at high risk for postpartum depressive mood changes.

Considering the fact that higher gestational cortisol reactivity was found in women who developed depressive symptoms in the puerperium, further studies should be conducted in order to explore whether the heightened cortisol reactivity will persist in the puerperium, and whether cortisol reactivity is directly associated with postpartum depressive symptomatology.

The endocrine findings of the present study gain importance considering the possibility, that intrauterine environment might have an influence on the development of the HPA axis of the unborn child. As for instance Maccari, Darnaudery, Morley-Fletcher, Zuena, Cinque and Van Reeth (2003) showed in their animal study, stress-induced maternal increase of glucocorticoids of adult rats influenced fetal brain development by means of HPA axis dysfunctions. In addition, Halligan et al. (Halligan, Herbert, Goodyer, & Murray, 2004) showed that postpartum depression in humans is significantly associated with higher and more variable morning cortisol levels in offsprings 13 years later. Current depressive symptoms in the mother and the adolescent, maternal marital discord, overall duration of maternal depression and the experience of undesirable life events by the adolescent were controlled. According to Halligan et al. (2004) perturbations in morning cortisol levels

might represent a risk factor for depressive disorder, which is in turn one strong risk factor for postpartum depression.

As a consequence, it would be of great interest to investigate whether the children of women with higher cortisol reactivity during pregnancy and postpartum depressive symptoms show similar patterns of HPA axis dysfunction in the TSST.

It remains unclear whether the endocrine finding of higher cortisol reactivity in pregnancy, found in the present research project, may contribute to the identification of women at high risk for postpartum depressive symptoms in respect of a *clinical setting*. However, our findings might lead to an awareness, that aspects of psychosocial well-being (e.g. anxiety, stress susceptibility, marital discord) during pregnancy are associated with endocrine factors, which in turn asks for more support from the clinical psychologists in consiliary and liaison services for the clinics.

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Items of the “Zurich Inventory of Psychosocial Well-being in Pregnancy” (ZIPP):

First factor: Berufsbezogene Belastung

1. Mein Arbeitgeber verlangt zuviel.
2. Wir haben Kommunikationsprobleme.
3. An meinem Arbeitsplatz gibt es Ärger oder angespannte Beziehungen.
4. Ich komme mit einigen meiner Kollegen/-innen nicht aus.
5. Ich habe Probleme mit meinem Vorgesetzten.
6. An meinem Arbeitsplatz herrscht oft eine angespannte Atmosphäre.
7. Ich werde von meinem Vorgesetzten nicht unterstützt.
8. Die Arbeitsatmosphäre ist kalt und unfreundlich.
9. Die Leute im Team sind distanziert und unfreundlich.
10. Ich habe das Gefühl, dass ich für das, was ich leiste, nicht angemessen bezahlt werde.

Second factor: Generelle Belastung

1. Ich fühle mich oft überfordert.
2. Ich fühle mich „gestresst“.
3. Ich habe das Gefühl, zu viele Dinge bewältigen zu müssen.
4. Oft habe ich zu wenig Zeit für mich selbst.
5. Ich habe noch so viele Dinge zu regeln, bevor das Kind auf die Welt kommt.
6. Ich setze oft zu hohe Erwartungen an mich.
7. In meiner Freizeit bin ich durch Pflichten zu stark eingebunden.
8. Ich müsste mich eigentlich schon lange schonen, habe es aber nicht getan.
9. Ich leide unter Verspanntheit.
10. Ich habe Schwierigkeiten, mich zu entspannen.

Third factor: Partnerschaftsbezogene Belastung

1. Ich fühle mich von meinem Partner verstanden.
2. Nach einer Auseinandersetzung verlasse ich mich mehr auf die Unterstützung von Freunden als auf die des Partners.
3. Ich fühle mich von meinem Partner im Stich gelassen.
4. Manchmal habe ich das Gefühl, dass mein Partner nicht voll hinter mir steht.
5. Manchmal glaube ich, dass mir mein Partner nicht die volle Wahrheit sagt.
6. Ich bin mit meiner Partnerschaft im Grossen und Ganzen zufrieden.
7. Nach einem Streit haben wir Schwierigkeiten, Lösungen für unsere Probleme zu finden.
8. Mein Partner hat zu einigen Themen sehr unterschiedliche Lebensvorstellungen.
9. Ich habe das Gefühl, dass mir mein P. nicht richtig zuhört, wenn ich etwas erzähle
10. Ich finde es schwierig mit meinem Partner über Gefühle zu sprechen.

Fourth factor: Mangel an Ressourcen

1. Besuche erhalten.
2. Sich etwas Gutes tun.
3. Ich habe das Gefühl, an meinen freien Tagen so richtig Energie tanken zu können.
4. Sich sicher fühlen.
5. Musik hören.
6. Lachen.
7. Komplimente erhalten.
8. Ich verbringe meine Freizeit so, dass sie für mich Entspannung bringt.
9. Geschlechtsverkehr haben.
10. Ein Geschenk erhalten.

Fifth factor: Schwangerschaftsspezifische Belastung

1. Wie sehr sich eine Frau ein Baby wünschen mag, eine Schwangerschaft ist immer ein unangenehmes Erlebnis.
2. Ich fühle mich den Ärzten und Hebammen ausgeliefert.
3. Wenige Frauen empfinden die Schwangerschaft als eine angenehme Zeit.
4. Ich stelle mir vor, während der Geburt den Wehenschmerzen hilflos ausgeliefert zu sein.
5. Jede Mutter hat grosse Angst vor der Geburt.
6. Flaschenernährung ist für das Kind gesünder als Stillen.
7. Komplizierte Geburten sind häufiger, als man denkt.
8. Ich habe die Sorge, bei der Geburt nicht mitbestimmen zu können.
9. Es ist ganz normal, wenn sich eine Frau die grössten Sorgen über Komplikationen bei der Geburt macht.
10. Ich glaube, dass ich wenig Kontrolle über das habe, was mit mir geschieht.