1. Introduction

In human research, there is clear evidence that high levels of perceived stress and anxiety during pregnancy are associated with several negative health consequences, like gestational complications, spontaneous abortion, preterm labor, low infant birth weight, post-partum depression and negative developmental outcome in infancy (Goland et al., 1993; Hedegaard, Henriksen, Sabroe, & Secher, 1993; Huizink, Robles de Medina, Mulder, Visser, & Buitelaar, 2003; Killingsworth, Dunkel-Schetter, Wadhwa, & Sandman, 1997; Mancuso, Schetter, Rini, Roesch, & Hobel, 2004; Robertson, Grace, Wallington, & Stewart, 2004; Sieber, Germann, Barbir, & Ehlert, submitted; Van den Bergh, Mulder, Mennes, & Glover, 2005; Wadhwa, Culhane et al., 2001; Wadhwa, Sandman, Porto, Dunkel-Schetter, & Garite, 1993; Zaers, Waschke, & Ehlert, submitted). Even though these studies showed, that stress is a significant risk factor, it has to be taken into account that psychosocial stress during pregnancy is as common as during non-pregnant states and not all pregnant women who report high levels of stress, proceed to deliver preterm. This raises the question of the psychological and physiological determinants of vulnerability in the context of psychosocial stress and pregnancy complications.

Clinical studies report that levels of the stress related hormone corticotropine-releasing hormone (CRH) are increased in plasma and in the placenta in pregnancies with preterm labor and/or fetal growth restriction (Erickson et al., 2001; Goland et al.,

1993; C. J. Hobel, Dunkel-Schetter, Roesch, Castro, & Arora, 1999; Holzman, Jetton, Siler-Khodr, Fisher, & Rip, 2001; Inder et al., 2001; Ruiz, Fullerton, Brown, & Dudley, 2002; Wadhwa et al., 2004). Further, following the results of two other studies, consistently higher basal blood concentrations of another stress related hormone, norepinephrine (NE), have been found in women with preeclampsia than in matched healthy pregnant women (Kaaja et al., 1999; Manyonda et al., 1998). These findings suggest that biological dysregulations in pregnant women play a mediating role with regard to stress related complications during pregnancy and negative birth outcome.

Animal experiments have already convincingly demonstrated large causal effects of prenatal stress on permanent changes in biological systems in association with behaviour and adverse outcomes (Braastad, 1998). However, in human research, there seems to be a compelling need for studies, focusing on the association of stress with biological dysregulations and pregnancy complications (de Weerth & Buitelaar, 2005). Recent research on pharmacological or physical provocation procedures in pregnant women has resulted in inhomogeneous findings regarding the extent of alterations of the hypothalamic pituitary adrenal (HPA) axis and the autonomic nervous system (ANS) with respect to the progression of pregnancy and the type of stressor. The variety of experimental designs, the lack of adequate control groups, and different forms and low reliability of hormonal assessment make it difficult to draw conclusions (Bonen, Campagna, Gilchrist, & Beresford, 1995; Eneroth-Grimfors, Bevegard,

Nilsson, & Satterstrom, 1988; Kammerer, Adams, Castelberg, & Glover, 2002; McMurray, Hackney, Guion, & Katz, 1996; Petraglia et al., 2001; Rauramo, Andersson, Laatikainen, & Pettersson, 1982; Schulte, Weisner, & Allolio, 1990; Suda et al., 1989; Vaha-Eskeli, Erkkola, Scheinin, & Seppanen, 1992). This underlines the assumption that before stress prevention during pregnancy can effectively be undertaken, first of all more and particularly reliable basic information must be gathered.

Moreover, the majority of the aforementioned studies with pregnant women focus on chronic stress, major life events and anxiety related to complications or negative development outcome of the fetus and/or the child. However, there seems to be a lack of studies integrating a salutogenic point of view, by taking into considerations factors, which might play an important role in *protecting* the pregnant woman and her unborn for harmful consequences of heightened stress levels. Basic knowledge about stress buffering factors might effectively advance future studies focusing on stress prevention and intervention. Regarding this issue, one first recent pilot study of Urizar and colleagues showed buffering effects of favorable coping strategies on psychological and physiological stress responses during pregnancy (Urizar et al., 2004).

With regard to the fact that research in this field is still in its infancy, it was our aim to obtain reliable basic information about psychological, neuroendocrine and autonomic

responses following standardized psychosocial stress at different stages of pregnancy in healthy women. The presented research project was the first one designed to investigate psychological, endocrine and autonomic responses to standardized psychosocial stress in second- and third- trimester pregnant women. A total of ninety women, including sixty healthy nulliparous women, with a singleton intrauterine pregnancy and a group of thirty non-pregnant healthy women, participated in the study. Psychosocial stress was induced by the Trier Social Stress Test, TSST (Kirschbaum, Pirke, & Hellhammer, 1993), which consists of an unprepared speech and a mental arithmetic task in front of an audience.

The first part of this dissertation provides a theoretical background of psychological constructs, biological processes and systems, as well as of the state of research in this field onto which specific hypotheses have been developed for the two experimental studies in the second part of this work. In the first study changes of the HPA axis and the autonomic nervous system due to psychosocial stress were investigated, whereas the second study examined the relation of potential buffering effects in pregnancy on biological and psychological laboratory stress responses. The results and the clinical relevance of the studies will be generally discussed in the last part of this volume.

PART I THEORETICAL BACKGROUND

The aim of this chapter is to provide a theoretical background of psychological constructs, biological processes and systems, as well as of the state of research in this field onto which specific hypotheses have been developed for the two empirical studies in the second part of this work.

2. Stress

The term stress is a common and often used term in modern times and describes a variety of negative situations, feelings and reactions. To elucidate the impact and the coverage of this broad concept, the history of main stress theories and in addition, psychological and physiological stress response will be elucidated in the following sections.

2.1 History of the stress concept

On his failed search for a new hormone in rats, Hans Selye stumbled upon the idea of a stress syndrome and gave the phenomenon "stress" its name (Selye, 1936, 1950). By "stress", he meant the *nonspecific* response of the body to any demand, theorizing that all individuals respond to all types of threatening situations in the same manner. He noted that someone who is subjected to a stressor goes through three phases: alarm reaction, stage of resistance and exhaustion, and termed this set of responses as the General Adaptation Syndrome (GAS). The first phase, the *alarm reaction* includes primarily the various biological responses of the autonomic nervous system when

confronted with a stressor, i.e. an increase of heart rate. The stage of *resistence* is a continued state of arousal, and the organism tries to regain its inner balance. If the stressful situation is prolonged, the high levels of hormones during the resistance may upset this balance and harm internal organs leaving the organism vulnerable to disease. The *exhaustion* stage occurs after prolonged resistance. During this phase the body's energy reserves are finally exhausted and the balance breaks down. Notably, Selye identified the stress-processing mechanism, which came to be known as the hypothalamus-pituitary-adrenal (HPA) system (Selye, 1974). Furthermore, his ideas about stress helped to forge an entirely new research field: the study of biological stress and its effects. It is a science that continues to make advances today by connecting stress to health problems and discovering new ways to help the body efficiently deal with harmful stressors.

Walter Cannon's research led him to describe the *fight or flight* response of the sympathetic nervous system (SNS) to threats. He found that SNS arousal (i.e. increase of heart rate and blood pressure) in response to a perceived threat involves several elements which prepare the body physiologically either to fight off an attacker or to flee from the danger (Cannon, 1929, 1932). Even if no action is taken, the body remains in a state of maintained arousal for a period of time following the time it experiences the stimuli that set of the reaction in the first place. Over time, *homeostasis* is achieved. Cannon defined homeostasis by the tendency of the body to return to the pre-stress physiological status.

John Mason contradicted the argument of Selye's *non specific response* that all stressors, whether psychological or physical would elicit the same physiological reactions (Mason, 1975). He revised Selye's theory by placing emotion, such as anxiety, as a mediator between stressor and stress responses. Mason suggested that the emotional reaction to a stressor activates the HPA axis and not the stressor itself and explained that differences in individual neuroendocrine stress responses occur because of *psychological* influences (Mason, 1975).

Lazarus and colleagues introduced a cognitive theory of stress. His theory places on the *meaning* that an event has for the individual. The psychological stress response will be focused on in the next section, by elucidating Lazarus theory (Lazarus, Deese J., & Osler, 1952).

2.2 Lazarus transaction theory of stress

The aforementioned concepts of Selye and Cannon were based on a "behavioristic" input-output perspective, considering the stressor as an input, and stress reaction as the output of stress. However, these paradigms could not explain, why not all persons react the same way to identical stressors. Therefore Lazarus and colleagues proposed defining stress as a *transaction of stressor, interpretation and reaction*, indicating that one's view of a situation determines whether an event is experienced stressful or not (Lazarus & Cohen, 1977; Lazarus & Launier, 1978). According to his Transaction

Theory of Stress, the variability of how individuals *appraise* stress, explain why people react differently under the same stress conditions. Furthermore, following his theory, stress is a *process* that involves the interaction of the individual with the environment, whereby the cognitive appraisal of stress includes a two-part process, which involves a primary and a secondary appraisal.

During *primary appraisal*, a person assesses the nature and severity of the event, evaluating whether a particular stressor is irrelevant, benign, or stressful. If the event is appraised as stressful (which implicates that the stressor is relevant) the situation is then evaluated as harm or loss, threat, or challenge. Harm or loss refers to an injury or damage that already has happened. Threat refers to something that *could* produce harm or loss, and challenge refers to the potential for growth, mastery, or some form of gain. During *secondary appraisal* a person considers alternative approaches to stress and evaluates his or her *coping* resources and options, including past history with that specific stressor, various expectations about one's self and environment, and the availability of resources. All possible coping strategies can be divided into two categories. *Problem-focused* coping strategies are used when one is actively seeking to solve a problem, whereas *emotion-oriented* coping is marked by passive and avoiding coping strategies. Overall, the more stressful the stressor is assessed to be and the lower one's ability to cope with that particular stressor, the more severe the experience of stress will be for that person (Lazarus, 1986). Folkman's model (Folkman, 1997) extends Lazarus model by integrating reappraisal, the creation of positive

psychological states, as well as renewed problem and emotion-focused coping efforts (see figure 1).

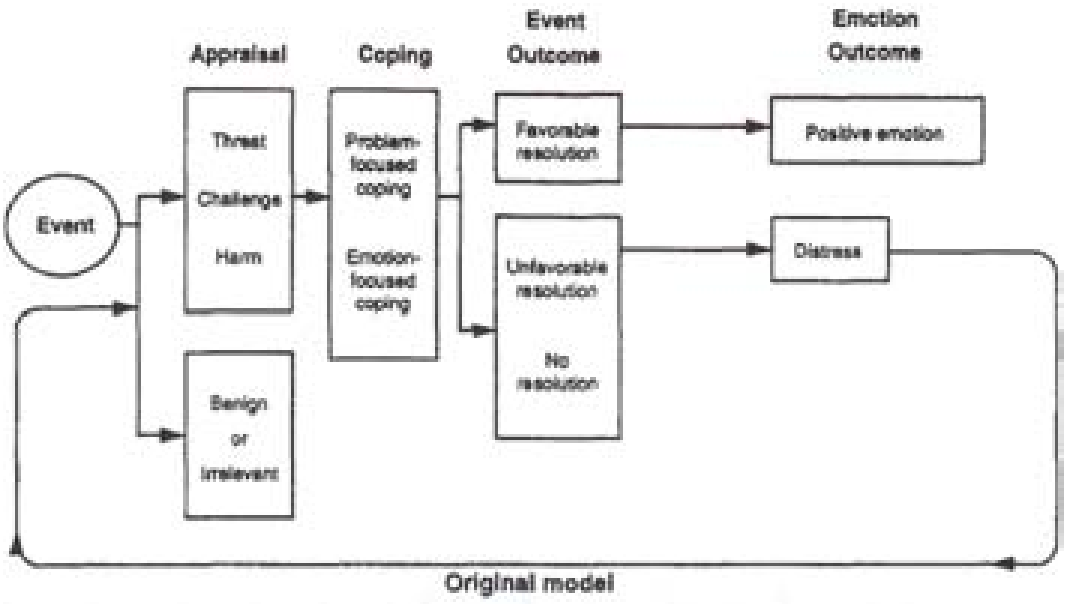

Figure 1 Lazaraus and Folkman's appraisal model (Folkman, 1997)

Mason collected more than 200 studies which examined the influence of psychological stress on the biological system. He concluded from his summary that psychological influences were among the most potent natural stimuli for activation of the hypothalamic pituitary adrenal (HPA) axis, and that psychological stress response has a physiological correlate (Folkman, 1997; Mason, 1968). In the following sections this physiological correlate of stress will be elucidated.