



Prenatal stress and children's cortisol reaction to the first day of school

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Summary Maternal prenatal stress has been found to be related to over-activity and/or dysregulation of the HPA-system in the offspring. These effects are more readily apparent in response to novel situations. The aim of the present report was to examine whether pregnancy stress predicted HPA-axis reactions of children to the first day of school after the summer break. Children of mothers with more prenatal stress were compared to those of mothers with less stress. Habituation was studied by comparisons between the first school day and a second school day a week later. Finally, cortisol levels at school were compared to those of a weekend day. The participants were 29 mother-child pairs (20 girls and nine boys, mean age 5.31 years, SD=0.50). The children's cortisol levels were determined in saliva. Multilevel analysis (hierarchical linear modelling) was used to analyze the data. Both prenatal cortisol and pregnancy anxiety were related to the children's cortisol levels as a reaction to the first school day. Children whose mothers had higher levels of morning cortisol during pregnancy, and more fear of bearing a handicapped child showed higher levels of cortisol on school days. In addition, the circadian rhythm of cortisol on school days appeared to have a steeper slope as compared to that of the circadian curve on a weekend day.

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1. Introduction

Children can react very differently to novel situations: while one child approaches a novel situation with interest and curiosity, another hesitates or finds the situation threatening. The perceptions and strategies for dealing with novel situations, which are often appraised as stressful, are influenced by

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several factors (Lazarus and Folkman, 1984), such as children's temperament, social competence (Gunnar et al., 1997), and personality characteristics (Mulder et al., 2002). Also, the manner in which children deal with novel or stressful situations is expected to be reflected in their physiological responses (Gunnar et al., 1997).

Reactions to stressful situations in mammals are regulated by the mobilization of energy stores in preparation for a brief surge of enhanced activity. Stress leads to activation of the hypothalamus, which secretes the corticotropin-releasing hormone (CRH). This hormone stimulates the anterior pituitary lobe to release the adrenocorticotropic hormone (ACTH), which in turn activates the release of glucocorticoids from the adrenal glands. The major glucocorticoid in rodents is corticosterone and in humans cortisol. This stress system is known as the hypothalamus-pituitary-adrenal (HPA)-system.

Several studies in mammals have shown that maternal prenatal stress may induce over-activity and/or dysregulation of the HPA-system in the offspring, and that these changes are often apparent in response to novel situations (Fride and Weinstock, 1984; Fride et al., 1986; Weinstock et al., 1992; McCormick et al., 1995; Barbazanges et al., 1996; Mulder et al., 2002; Huizink et al., 2004a).

Human studies on the effects of maternal stress indicate that prenatal maternal stress increases rates of low birth weight, premature delivery and a small head circumference (Lou et al., 1994).

Behavioral development following prenatal stress in humans is also compromised, as indicated by more difficult temperament at 10 weeks and 7 months after birth (Van den Bergh, 1990). Furthermore, more behavioral and emotional problems in children are found in prenatally stressed children as compared to prenatally non-stressed children (O'Connor et al., 2002; Van den Bergh and Marcoen, 2004). Though the neurobiological underpinnings of these adverse consequences of prenatal stress have not been fully clarified, impairment or hyperactivity of the HPA-system to stress in the offspring seems to be an important component (Barbazanges et al., 1996). Three possible mechanisms, which may act in concert, have been hypothesized to be the cause of the negative effects on the HPA-axis (Huizink et al., 2004a). One possible mechanism is transplacental transport of maternal stress hormones to the fetus. A second possibility is the stress-induced release of placental hormones into the fetal circulation. In both these cases, the excessive levels of stress hormones would be detrimental for fetal brain development.

Finally, the blood flow to the placenta may be decreased by maternal stress, causing restriction in fetal growth and abnormalities in development.

In order to investigate possible influences of prenatal stress on the development of children we started a prospective longitudinal multidimensional study. Prenatal stress was measured by self-report and levels of hormones in three periods of pregnancy (Huizink, 2000; Huizink et al., 2002; Buitelaar et al., 2003; Huizink et al., 2004a; Gutteling et al., *in press-a*; Barbazanges et al., 1996). A multidimensional concept of stress was used according to the model of Lazarus and Folkman (1984). This model describes three types of stress factors. The first ones are the stress-provoking factors (daily hassles and life events). The second ones are the stress-mediating factors, which may interact with or modify the effect of the stress-provoking factors (coping and social support, for example). The third factors are the stress resulting factors (anxiety and perceived stress).

In this study, higher levels of maternal prenatal stress and anxiety were found to predict less test-affectivity and goal-directedness in 8 month-old children, whereas perceived stress predicted more unadaptability at 3 months. Higher levels of ACTH during mid pregnancy (24 weeks of gestation) were associated with more unadaptability at 8 months (Huizink et al., 2002). At 2 years of age, higher levels of prenatal perceived stress were associated with more behavioral problems, and higher levels of pregnancy related fear was related to more temperamental problems (Gutteling et al., *in press-a*). Finally, higher levels of morning cortisol, more daily hassles and a higher level of anxiety during pregnancy were associated with higher levels of cortisol in children at age 4-6 years (Gutteling et al., 2005b).

The start of a new school year is a challenging event (Davis et al., 1999) that can be described as a situation with an important degree of novelty. Kirschbaum and Hellhammer (1989) have shown that cortisol rises in response to threatening, challenging or novel events.

The present report presents the results of a follow-up of our longitudinal study on the effects of maternal prenatal stress, in which prenatal stress is related to the cortisol reactions of children to a situation with a high degree of novelty, namely the first school day after the summer break. The reaction to the first school day will be compared to the reaction to a second school day, 1 week later. In addition, the reaction on the school days will be compared to the cortisol levels on a weekend day a few months earlier. Based upon the literature and previous results there are five expectations concerning the results. First, stress-resulting factors

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