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Tied to mommy's womb? Prenatal maternal stress, postnatal parental interaction style and child development

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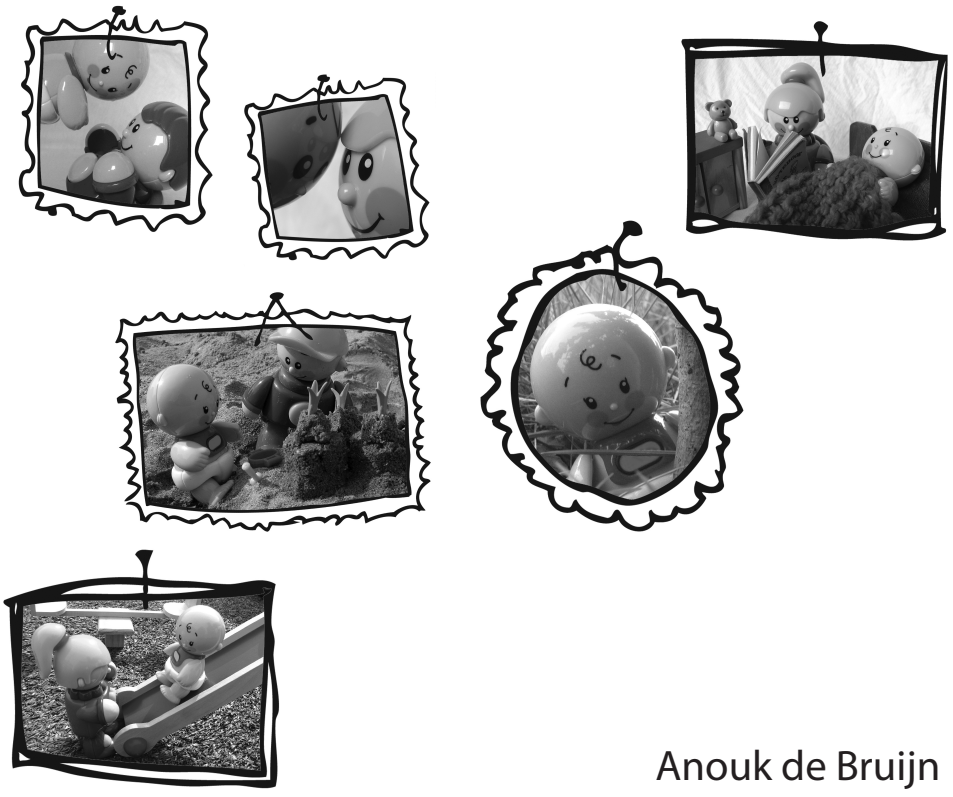

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Tied to mommy's womb?

Prenatal maternal stress, postnatal parental interaction style and child development

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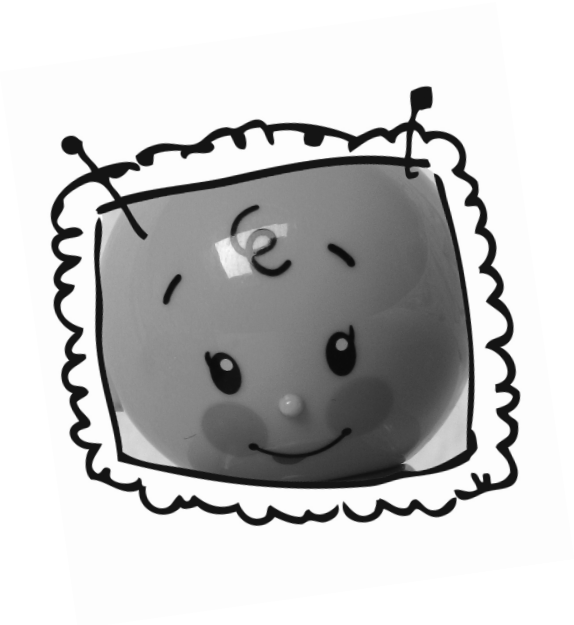
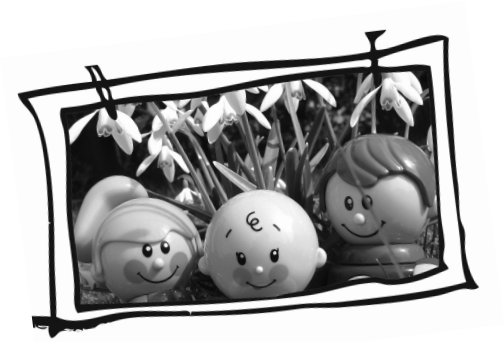
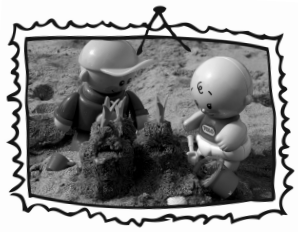


Contents





1

General introduction

> ***"And surely we are all out of the computation of our age, and every man is some months elder than he bethinks him; for we live, move, have a being, and are subject to the actions of the elements and the malices of diseases, in that other World, the truest Microcosm, the Womb of our mother"*** (Religio Medici; Sir Thomas Browne, 1642).

It is known for centuries that the physical condition of a woman during her pregnancy can influence her developing child. Diseases of the mother like diabetes or high blood pressure, or life style characteristics like smoking or alcohol intake can have detrimental effects for the unborn child. However, not only the mother's physical condition during pregnancy is important, but also her psychological wellbeing when she raises her child. In the past decades, many studies have reported negative effects of maternal depression and anxiety on child development, from infancy to adolescence. Infants of mothers with postpartum depression have been found to be more fussy and to have more difficult temperaments, obtain lower mental and motor developmental scores and have less secure attachments to their mothers (Field, 1998). Toddlers of depressed mothers have been found to react more negatively to stress and are delayed in their development of effective self-regulation strategies. Furthermore at school age, these children show more school problems, are less socially competent and have lower levels of self esteem and higher levels of behavioural problems (Goodman & Gotlib, 1999).

Moreover, not only postnatally but also maternal emotional complaints during pregnancy, e.g. maternal stress, feelings of depression and anxiety, pregnancy related anxiety, daily hassles, and positive or negative life events, have been found to be associated with negative effects on neonatal outcome (for a review see Mulder et al., 2002). Studies showed that pregnant women with high levels of stress and anxiety are at increased risk to have a spontaneous abortion (Neugebauer et al., 1996) or to develop preeclampsia in a later phase of the pregnancy (Kurki, Hiilesmaa, Raitasalo, Mattila, & Ylikorkala, 2000). Among the most replicated findings are the associations between high prenatal anxiety/stress and preterm delivery or low birth weight for gestational age (Copper et al., 1996; Dole et al., 2003; Glynn, Dunkel-Schetter, Hobel, & Sandman, 2008).

The long term outcome of children after exposure to prenatal maternal emotional complaints also gradually gains more scientific attention. Davis et al. (2004) found that higher levels of depressive and anxious symptoms during pregnancy were related to negative behavioural reactivity to novelty in 4-month old infants. Huizink, Robles de Medina, Mulder, Visser, and Buitelaar (2003) concluded that prenatal stress (such as

daily hassles and pregnancy specific anxiety) might be one of the causes for a delay in motor and mental development in infants at 8 months of age and a risk factor for later developmental problems. Gutteling et al. (2005) found that perceived stress during pregnancy was a predictor of more (externalizing) behavioural problems in 2-year olds. Fear of bearing a handicapped child was a predictor of higher levels of restless, disruptive temperament and more attention regulation problems in toddlers. Brouwers, Van Baar, and Pop (2001) found that high maternal (state) anxiety at 32 weeks gestation was associated with lower mental developmental scores at the age of 2 years. O' Connor, Heron, Golding, Beveridge, and Glover (2002) found strong associations between prenatal anxiety and children's behavioural and emotional problems at 4 years of age, which were maintained after controlling for maternal anxiety and depression in the postnatal period. This link between antenatal anxiety and behavioural and emotional problems in children remained significant in children of almost 7 years old (O'Connor, Heron, Golding, & Glover, 2003). Martin, Noyes, Wisenbaker, and Huttunen (1999) found a significant relation between maternal distress in the first trimester of pregnancy and ratings of negative emotionality at age 5. Niederhofer and Reiter (2004) reported that an accumulation of risk factors (e.g. financial problems) during pregnancy was associated with lower school grades and more negative behaviour in school at 6 years. Van den Bergh and Marcoen (2004) showed that high levels of maternal state anxiety at 12 to 22 weeks gestational age enhances the offspring's susceptibility for developing Attention Deficit Hyperactivity Disorder (ADHD) symptoms, externalizing problems, and anxiety during childhood. Rodriguez and Bohlin (2005) found an association between high levels of prenatal stress and ADHD symptoms in 7-year-old children. Van den Bergh et al. (2005) found a negative relationship between maternal anxiety at 12–22 weeks of pregnancy and cognitive functioning at age 14–15. To summarize, from infancy to adolescence, children are found to show more difficulties in motor, cognitive, and especially socio-emotional development, when their mothers had prenatal complaints reflecting distress, anxiety or depression (O'Donnell, O'Connor, & Glover, 2009).

Explanations for the relationship between prenatal maternal emotional complaints and outcome in child development

A potentially important underlying mechanism to explain the associations between prenatal maternal emotional complaints and child outcome is fetal programming of the Hypothalamic – Pituitary – Adrenal (HPA) axis (van den Bergh, Mulder, Mennes, & Glover, 2005; van den Bergh, van Calster, Smits, van Huffel, & Lagae, 2008). The HPA-axis is the stress-response system of mammals. During exposure to a stressor, the HPA-axis is activated. The stressor activates the hypothalamus, which secretes the corticotropin-releasing hormone (CHR). 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 (Figure 1.1). The major glucocorticoid in humans is cortisol (Gutteling, de Weerth, & Buitelaar, 2005). Cortisol responses to stress serve an important function in adaptation to novel and stressful

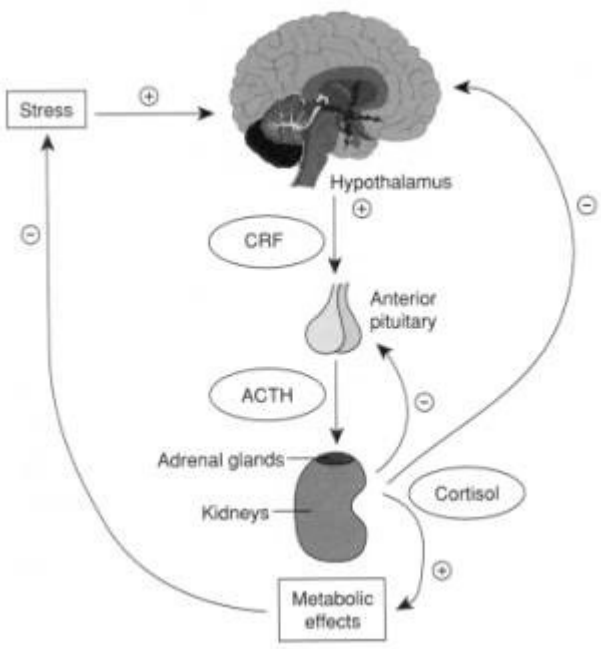


Figure 1.1 The Hypothalamic-Pituitary-Adrenal (HPA) axis.

circumstances. Effective reactivity of the HPA system is thus adaptive, but hyperactivity of the system has been found to have negative effects on immune system activity (Coe, Rosenberg, & Levine, 1988), child health (Flinn & England, 1995) and cognitive and memory functioning (de Kloet, Oitzl, & Joëls, 1999; Heffelfinger & Newcomer, 2001). Maternal prenatal stress may induce overactivity and/or dysregulation of the HPA-system in offspring, due to the fetal programming processes.

The concept of fetal programming originated from Barker's (1995) "fetal origins of adult disease hypothesis". This theory states that the fetus physiologically adapts to the characteristics of the intrauterine environment within which it is developing. As such the environment in utero can alter the development of the fetus during particular sensitive periods. This adaptation may subsequently affect the physiological systems of the body that undergo rapid structural and functional changes. Especially the set point when the organism starts to respond to specific neurobiological input may be affected. Consequently variation in the prenatal environment may influence the physiological responses of the offspring for life. In support of this theory Barker (1995) found that undernutrition in utero changes the body's structure, physiology, and metabolism and predicts the susceptibility to hypertension, diabetes, coronary heart disease, and stroke in adult life. The principle that the endocrine and metabolic environment afforded by the mother has lasting or lifelong significance has been called 'fetal programming' (Lucas, 1998).

In animal studies it is found that the fetal HPA-axis is especially vulnerable to environmental input, such as prenatal stress. Physiological changes in the offspring after exposure to prenatal maternal stress have been found, including overactivity and impaired negative feedback regulation of the HPA-axis (Huizink, Mulder, & Buitelaar, 2004). For example, rats that were prenatally exposed to stress, produced faster, stronger, and / or more prolonged glucocorticoid responses than controls, when exposed to novel or challenging situations (Weinstock, Matlina, Maor, Rosen, & McEwen, 1992).

In human studies was found that maternal cortisol is not fully metabolized by the placenta and crosses to the fetus (Gitau, Cameron, Fisk, & Glover, 1998), where it may influence the developing fetal HPA-axis. Prenatal anxiety and stress stimulate activation of the maternal HPA-axis that leads in turn to release of cortisol (O'Connor et al., 2005). The HPA-axis of the offspring might then be "programmed", indicating that as a result of the adaptation to a specific environment, the set point of the stress response system of the fetus may become affected and the system becomes easily overactivated or dysregulated.

Quality of maternal interaction style

An alternative explanation for the consequences of maternal prenatal emotional complaints for the development of the children can be found in the influence of postnatal parent-child interaction processes. Prenatal mood disturbance predicts postpartum depression (Heron, O'Connor, Evans, Golding, & Glover, 2004) and 80% of depression is recurrent (Goodman & Gotlib, 2002). As a consequence, it is possible that depressive or anxious complaints in prenatally stressed women persist or recur after birth. Several studies have shown that postnatal maternal depression and anxiety are related to disturbances in the quality of parenting, specifically in parental sensitivity (Field, 1995; Lovejoy, Graczyk, O'Hare, & Neuman, 2000). Depressed parents have been found to be more negative, guilt-inducing, critical, unsupportive and intrusive with their children. They also demonstrate more negative affect (Cummings & Davies, 1999; Lovejoy et al., 2000). Such negative emotions and interaction processes are associated with behavioural problems in the children (Elgar, McGrath, Waschbusch, Stewart, & Curtis, 2004; Leckman-Westin, Cohen, & Stueve, 2009). If the mothers are (also) suffering from emotional complaints after giving birth, they might interact more negatively and less sensitively with their child, which subsequently might lead to more behavioural problems in their children. As a result, the quality of the maternal interaction style might mediate or moderate the association between prenatal maternal emotional complaints and child outcome. Kaplan, Evans, and Monk (2008) indeed found in a group of mothers who had been given a psychiatric diagnosis during pregnancy that the infants who received insensitive care showed higher cortisol levels at 4 months compared to the children who received sensitive care of these mothers. However, no study investigated the influence of the quality of the maternal interaction style on the association between prenatal maternal emotional complaints and child behavioural problems in humans.

Quality of paternal interaction style

Not only the quality of the mother-child interaction style needs attention in the association between prenatal maternal emotional complaints and child development. The role of the fathers might also be important. Up until now, research on the influences of prenatal maternal stress on child outcome has only focused on the mothers and neglected the influences of fathers. However, mental health problems tend to co-occur in mothers and fathers (Merikangas & Brunetto, 1996). When mothers are depressed or anxious, fathers may also experience emotional complaints. These complaints may negatively affect their interaction quality and consequently, paternal interactive behaviour may become an *additional risk factor* for the development of their children (Goodman, 2008). On the other hand, an emotionally healthy father may also constitute a *protective factor* against the negative effects of maternal emotional complaints on child behavioural problems. Fathers may increase their role as a caretaker of the child and interact in a positive way with their children, or they may provide support to the child's mother, which indirectly could form a protective factor for the development of the children (Edhborg, Lundh, Seimyr, and Widström, 2003; Hossain et al.,1994). The possible moderating role of the quality of father-child interaction style in the association between prenatal maternal stress and child outcome has not yet been examined.

Sex differences

HPA-axis functioning might be different for boys and girls. Animal studies showed that regulation of the HPA-axis can be affected by sex hormones in the offspring (McCormick & Mathews, 2007). Numerous animal studies have shown that glucocorticoid levels are higher in females than in males after HPA-axis stimulation (for a review see Kudielka & Kirschbaum, 2005). Furthermore, greater glucocorticoid transfer occurs across the placenta of female compared to male fetuses and this could account for the increased effect of prenatal stress in female offspring (Montano, Wang, & vom Saal, 1993; Matthews, 2002). In humans, sex differences in the associations between prenatal maternal emotional complaints and child outcome have not been studied in detail. However, sex differences in HPA-axis functioning in relation to prenatal maternal emotional complaints deserve further study, as these may show important moderations in fetal programming processes.

Furthermore, also from a parent-child relationship point of view, sex differences may be important for child development. Parents tend to differ in their interaction with their sons and daughters. Both mothers and fathers are found to be more sensitive with daughters than with sons. Daughters are more responsive to both mothers and fathers than sons and they actively involve their parents more in interaction (Lovas, 2005). Analyses of sex differences in relation to prenatal maternal emotional complaints might clarify the processes whereby risk factors operate to influence children's development (Rutter, Caspi, & Moffitt, 2003).

Aims of the study

The aim of this thesis is to study the relationship between maternal emotional complaints during pregnancy and developmental outcome of the children from a psychological, behavioural and neurobiological perspective. First, associations between prenatal maternal emotional complaints and child behavioural problems are studied. Second, stress responses and neurobiological functioning of the children are examined in relation to high or low levels of prenatal maternal emotional complaints. Next, the core aims of this thesis are addressed and the effect of the quality of the mother-child and father-child interaction on the association between prenatal maternal emotional complaints and child development is investigated. For every research topic potential sex differences are studied as well.

Research design

Participants

This thesis is part of a large prospective follow-up study that started in 2002 (Wijnen, 2005) in which 1500 mothers were extensively followed during pregnancy and the first week after birth of the child. Between July 2002 and May 2005, twenty midwives working in seven community midwifery practices in the Netherlands, invited healthy Dutch Caucasian pregnant women to participate in the study at their first antenatal check-up at 10-12 weeks' gestation. During the three trimesters of pregnancy, the mothers answered several questionnaires about their own medical history (e.g. smoking, alcohol intake) and their emotional complaints. Furthermore, demographic features were obtained. Complete information was available for 1093 women.

After pregnancy, the parents of 700 term born children were asked to give informed consent to participate in future follow-up studies. In total 444 mothers and their partners agreed to participate and returned questionnaires about their current emotional complaints and behavioural problems of their children. From this first wave, two groups, with or without exposure to prenatal emotional complaints were selected to examine the families in more detail during a home visit. Selection criteria for the groups were as follows. Children whose mothers scored above a standardized cut off, or higher than one standard deviation above the mean, on one of the three prenatal measurements of anxiety or depression at 12, 24 or 36 weeks in pregnancy were selected for the target (prenatally exposed) group. This applied to 25% of the total group. For the comparison group (prenatally non-exposed), children were selected whose mothers had at least given information in two separate periods during pregnancy and did not report high scores for any of the prenatal depression or anxiety questionnaires.

All families with maternal prenatal emotional complaints were asked for participation in the second wave of the study. The families with comparison children were matched to the target cases regarding month of birth and sex, before they were invited for the second wave of the study. In total 222 families were asked for participation with the

home visits and 132 (59.5%) agreed, $N = 66$ (59%) in the exposed group and $N = 66$ (60%) in the non exposed group. Most important reasons for non-participation were lack of time (43%), personal difficulties (16%, e.g. illness or death of family member), problems with being videotaped (12%) and inability to contact some families because they had moved (8.9%).

Procedure of data collection for the second wave

Two separate home visits were done, one with the mother and child and one with father and child. During the mother-child visit, the mothers and children were instructed to perform several tasks together to observe the mother-child interaction. Moreover, saliva of the children was collected to analyze their cortisol levels. At the start of the home visit, the child was asked to build a tower of wooden blocks. After five minutes, the child received the first cotton roll used for saliva collection. Next, mother and child were asked to play together for five minutes with clay, followed by a five minute puzzle task. Then mother and child were given a marble allay to play with for five minutes. Approximately 22 minutes after the first mother-child interaction task (clay episode), the child received the second cotton roll to suck on for saliva collection. Next a potentially frustrating task was administered to assess the stress response of the children. The children were confronted with a large plexiglas box (see Figure 1.2), in which an attractive plastic Mickey Mouse puppet was seated. The researcher promised the children that they were allowed to keep the puppet, if they were able to open the box. Two small holes were at both sides of the box and the child was handed two wooden sticks. The sticks could be put into the holes, but were unable to reach the puppet. A lock with a key was also attached to the box, but the key did not fit into the lock. The mother was instructed to say as little as possible to her child and was asked not to

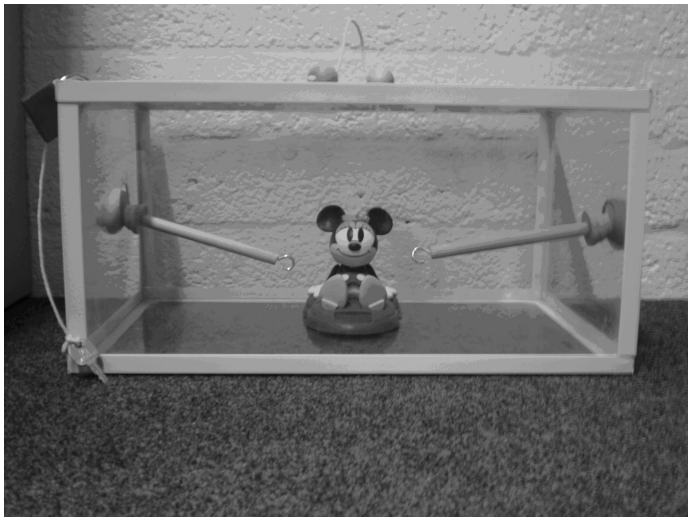


Figure 1.2 Frustration box.

help her child in opening the box. She was only allowed to encourage her child to try to open the box him/herself. After five minutes the researcher explained in a playful way ("Mickey wants to stay in his little house") to the child that it was impossible to get the puppet out of the box. Approximately 22 minutes after the frustration task, the child was handed the third and final cotton roll to suck on.

During the home visit with the fathers, to observe the quality of the father-child interaction style, the children and their fathers were instructed to play three games together: a building blocks game, a puzzle and a free play session. Table 1.1 presents an overview of the measures used.

Table 1.1 Research measures

	Parental measures	Child measures
Prenatal period (*N* = 1093)		
10–12 weeks	Smoking and drinking habits of mother Parity	
	Maternal emotional complaints: Edinburgh Depression Scale Anxiety subscale of the Symptom Checklist State anxiety scale of the State Trait Anxiety Inventory	
24 weeks	*Maternal emotional complaints:* Edinburgh Depression Scale Anxiety subscale of the Symptom Checklist State anxiety scale of the State Trait Anxiety Inventory	
36 weeks	*Maternal emotional complaints:* Edinburgh Depression Scale Anxiety subscale of the Symptom Checklist State anxiety scale of the State Trait Anxiety Inventory	
Birth		Birth weight Gestational age
Postnatal period		
First wave (*N* = 444)		
14–54 months	Background questionnaire	Maternal and paternal report of the Child Behaviour Checklist
	Current emotional complaints of both parents: Edinburgh Depression Scale Anxiety subscale of the Symptom Checklist	
Second wave (*N* = 132)		
23–60 months	Quality of the parent-child interaction style with the Emotional Availability Scales	Cortisol levels in saliva during a home visit
	Current emotional complaints of both parents: State anxiety scale of the State Trait Anxiety Inventory	

Outline of this thesis

The present thesis includes four empirical studies, which are described in four chapters. After the present introductory chapter, *Chapter 2* presents the results of the first wave of our study that describes the association between prenatal maternal emotional complaints and the children's behavioural outcome. Associations between prenatal maternal depressive and anxious complaints during different trimesters in pregnancy and externalizing and internalizing behavioural problems of the children were studied separately for boys and girls at toddler or preschool age. The second study, reported in *Chapter 3*, examines the stress responses and neurobiological functioning in relation to prenatal maternal emotional complaints. Cortisol response patterns of the children that were prenatally exposed to high levels of maternal emotional complaints were compared to the non-exposed group, separately for boys and girls. *Chapter 4* focuses on the role of the quality of the postnatal maternal interaction style in the association between prenatal maternal emotional complaints and child behavioural problems. In *Chapter 5* the role of the quality of the father-child interaction in the associations between prenatal maternal emotional complaints and child behaviour is studied, again for both sexes separately. Finally, a general discussion and a summary of the findings is presented in *Chapter 6*.

References

Barker, D. J. P. (1995). The fetal origins of adult disease. Proceedings of the Royal Society of London. Series B. *Biological Sciences*, *262*, 37–43.

Brouwers, E. P. M., Van Baar, A. L., & Pop, V. J. M. (2001). Maternal anxiety during pregnancy and subsequent infant development. *Infant Behavior & Development*, *24*, 95–106.

Coe, C. L., Rosenberg, L. T., & Levine, S. (1988). Immunological consequences of psychological disturbance and maternal loss in infancy. In C. Rovee-Collier & L. P. Lipsitt (Eds.), *Advances in Infancy Research: Vol. 5* (pp. 97–134). Norwood, NJ: Ablex.

Copper, R. L., Goldenberg, R. L., Das, A., Elder, N., Swain, M., Norman, G., et al., & the National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. (1996). The preterm prediction study: Maternal stress is associated with spontaneous preterm birth at less than thirty-five weeks' gestation. *American Journal of Obstetrics and Gynecology*, *175*, 1286–1292.

Cummings, E. M., & Davies, P. T. (1999). Depressed parents and family functioning: Interpersonal effects and children's functioning and development. In T. Joiner & J. C. Coyne (Eds.), *The interactional nature of depression* (pp. 299–327). Washington, DC: American Psychological Association.

Davis, E. P., Snidman, N., Wadhwa, P. D., Glynn, L. M., Dunkel Schetter, C., & Sandman, C. (2004) Prenatal maternal anxiety and depression predict negative behavioral reactivity in infancy. *Infancy*, *6*, 319–331.

De Kloet, E. R., Oitzl, M. S., & Joëls, M. (1999). Stress and cognition: Are corticosteroids good or bad guys? *Trends in Neurosciences*, *22*, 422–426.

Dole, N., Savitz, I., Hertz-Picciotto, I., Siega-Riz, A. M., McMahon, M. J., & Buekens, P. (2003). Maternal stress and preterm birth. *American Journal of Epidemiology*, *157*, 14–24.

Edhborg, M., Lundh, W., Seimyr, L., & Widström, A. M. (2003). The parent-child relationship in the context of maternal depressive mood. *Archives of Women's Mental Health*, *6*, 211–216.

Elgar, F. J., McGrath, P. J., Waschbusch, D. A., Stewart, S. H., & Curtis, L. J. (2004). Mutual influences on maternal depression and child adjustment problems. *Clinical Psychology Review*, *24*, 441–459.

Field, T. (1995). Infants of depressed mothers. *Infant Behavior and Development*, *18*, 1–13.

Field, T. (1998). Maternal depression effects on infants and early interventions. *Preventive Medicine*, *27*, 200–203.

Flinn, M. V., & England, B. G. (1995). Childhood stress and family environment. *Current Anthropology*, *36*(5), 854–866.

Gitau, R., Cameron, A., Fisk, N. M., & Glover, V. (1998). Fetal exposure to maternal cortisol. *Lancet*, *352*, 707–708.

Glynn, L. M., Dunkel Schetter, C., Hobel, C. J., & Sandman, C. A. (2008). Pattern of perceived stress and anxiety in pregnancy predicts preterm birth. *Health Psychology*, *27*, 43–51.

Goodman, J. H. (2008). Influences of maternal postpartum depression on fathers and on father-infant interaction. *Infant Mental Health Journal*, *29*, 624–643.

Goodman, S. H. & Gotlib, I. H. (2002). Introduction. In S. H. Goodman & I. H. Gotlib (Eds.), *Children of depressed parents: Mechanisms of risk and implications for treatment* (pp. 3–9). Washington, DC: American Psychological Association.

Goodman, S. H. & Gotlib, I. H. (1999). Risk for psychopathology in the children of depressed mothers: A developmental model for understanding mechanisms of transmission. *Psychological Review*, *106*, 458–490.

Gutteling, B. M., de Weerth, C., & Buitelaar, J. K. (2005). Prenatal stress and children's cortisol reaction to the first day of school. *Psychoneuroendocrinology*, *30*, 541–549.

Gutteling, B. M., De Weerth, C., Willemsen-Swinkels, S. H. N., Huizink, A. C., Mulder, E. J. H., Visser, G. H. A., & Buitelaar, J. K. (2005). The effects of prenatal stress temperament and problem behaviours of 27-month-old toddlers. *European Child and Adolescent Psychiatry*, *14*, 41–51.

Heffelfinger, A. K., & Newcomer, J. W. (2001). Glucocorticoid effects on memory function over the human life span. *Development and Psychopathology*, *13*, 491–513.

Heron, J., O'Connor, T. G., Evans, J., Golding, J., & Glover, V. (2004). The course of anxiety and depression through pregnancy and the postpartum in a community sample. *Journal of Affective Disorders*, *80*, 65–73.

Hossain, Z., Field, T., Gonzalez, J., Malphurs, J., Del Valle, C., & Pickens, J. (1994). Infants of "depressed" mothers interact better with their nondepressed fathers. *Infant Mental Health Journal*, *15*, 348–357.

Huizink, A. C., Mulder, E. J. H., & Buitelaar, J. K. (2004). Prenatal stress and risk for psychopathology: Specific effects or induction of general susceptibility? *Psychological Bulletin*, *130*, 115–142.

Huizink, A. C., Robles de Medina, P. G., Mulder, E. J. H., Visser, G. H. A., & Buitelaar, J. K. (2003). Stress during pregnancy is associated with developmental outcome in infancy. *Journal of Child Psychology and Psychiatry*, *44*, 810–818.

Kaplan, L. A., Evans, L., & Monk, C. (2008). Effects of mothers' prenatal psychiatric status and postnatal caregiving on infant biobehavioral regulation: can prenatal programming be modified? *Early Human Development*, *84*, 249–256.

Kudielka, N. M., & Kirschbaum, C. (2005). Sex differences in HPA axis response to stress: a review. *Biological Psychology*, *69*, 113–132.

Kurki, T., Hiilesmaa, V., Raitasalo, R., Mattila, H., & Ylikorkala, O. (2000). Depression and anxiety in early pregnancy and risk for preeclampsia. *Obstetrics and Gynecology*, *95*, 487–490.

Leckman-Westin, E., Cohen, P. R., & Stueve, A. (2009). Maternal depression and mother-child interaction patterns: association with toddler problems and continuity of effects to late childhood. *Journal of Child Psychology and Psychiatry*, *50*, 1176–1184.

Lovas, G. S. (2005). Gender and patterns of emotional availability in mother-toddler and father-toddler dyads. *Infant Mental Health Journal*, *26*, 327–353.

Lovejoy, M. C., Graczyk, P. A., O'Hare, E., & Neuman, G. (2000). Maternal depression and parenting behavior: A meta-analytic review. *Clinical Psychology Review*, *20*, 561–592.

Lucas, A. (1998). Programming by early nutrition: An experimental approach. *Journal of Nutrition*, *128*, 401S–406S.

Martin, R. P., Noyes, J. N., Wisenbaker, J., & Huttunen, M. O. (1999). Prediction of early childhood negative emotionality and inhibition from maternal distress during pregnancy. *Merrill-Palmer Quarterly*, *45*, 370–391.

Matthews, S. G. (2002). Early pogramming of the hypothalamo-pituitary-adrenal axis. *Trends in Endocrinology & Metabolism*, *13*, 373–380.

McCormick, C. M., & Mathews, I. Z. (2007). HPA function in adolescence: Role of sex hormones in its regulation and the enduring consequences of exposure to stressors. *Pharmacology, Biochemistry and Behavior*, *86*, 220–233.

Merikangas, K., & Brunetto, W. (1996). Assortative mating and psychiatric disorders. *Bailliere's Clinical Psychiatry*, *2*, 175–185.

Montano, M. M., Wang, M.-H., & vom Saal, F. S. (1993). Sex differences in plasma corticosterone in mouse fetuses are mediated by differential placental transport from the mother and eliminated by maternal adrenalectomy or stress. *Journal of Reproduction and Fertility*, *99*, 283–290.

Mulder, E. J. H., Robles de Medina, P. G., Huizink, A. C., Van den Bergh, B. R. H., Buitelaar, J. K., & Visser, G. H. A. (2002). Prenatal maternal stress: effects on pregnancy and the (unborn) child. *Early Human Development*, *70*, 3–14.

Neugebauer, R., Kline, J., Stein, Z., Shrout, P., Warburton, D., & Susser, M. (1996). Association of stressful life events with chromosomally normal spontaneous abortion. *American Journal of Epidemiology*, *143*, 588–596.

Niederhofer, H., & Reiter, A. (2004). Prenatal maternal stress, prenatal fetal movements and perinatal temperament factors influence behavior and school marks at the age of 6 years. *Fetal Diagnosis and Therapy*, *19*, 160–162.

O'Connor, T. G., Ben-Shlomo, Y., Heron, J., Golding, J., Adams, D., & Glover, V. (2005). Prenatal anxiety predicts individual differences in cortisol in pre-adolescent children. *Biological Psychiatry*, *58*, 211–217.

O'Connor, T. G., Heron, J., Golding, J., Beveridge, M., & Glover, V. (2002). Maternal antenatal anxiety and children's behavioural / emotional problems at 4 years. *British Journal of Psychiatry*, *180*, 502–508.

O'Connor, T. G., Heron, J., Golding, J., & Glover, V. (2003). Maternal antenatal anxiety and behavioural/ emotional problems in children: a test of a programming hypothesis. *Journal of Child Psychology and Psychiatry*, *44*, 1025–1036.

O'Donnell, K., O'Connor, T. G., & Glover, V. (2009). Prenatal stress and neurodevelopment of the child: Focus on the HPA axis and role of the placenta. *Developmental Neuroscience*, *31*, 285–292.

Rodriguez, A. & Bohlin, G. (2005). Are maternal smoking and stress during pregnancy related to ADHD symptoms in children? *Journal of Child Psychology and Psychiatry*, *46*, 246–254.

Rutter, M., Caspi, A., & Moffitt, T. E. (2003). Using sex differences in psychopathology to study causal mechanisms: unifying issues and research strategies. *Journal of Child Psychology and Psychiatry*, *44*, 1092–1115.

Van den Bergh, B. R. H. & Marcoen, A. (2004). High antenatal maternal anxiety is related to ADHD symptoms, externalising problems, and anxiety in 8- and 9-year olds. *Child Development*, *75*, 1085–1097.

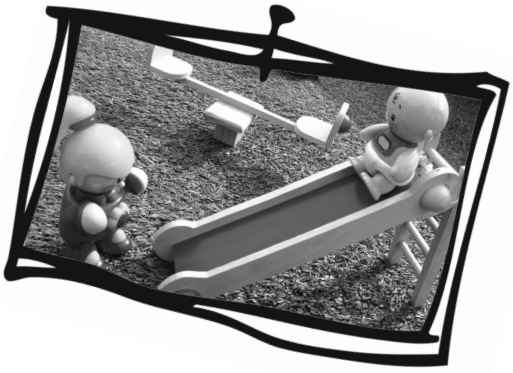
Van den Bergh, B. R. H., Mennes, M., Oosterlaan, J., Stevens, V., Stiers, P., Marcoen, A., & Lagae, L. (2005). High antenatal maternal anxiety is related to impulsivity during performance on cognitive tasks in 14- and 15-year-olds. *Neuroscience and Biobehavioral Reviews*, *29*, 259–269.

Van den Bergh, B. R. H., Mulder, E. J. H., Mennes, M. & Glover, V. (2005). Antenatal maternal anxiety and stress and the neurobehavioural development of the fetus and child: links and possible mechanisms. A review. *Neuroscience and Biobehavioral Reviews*, *29*, 237–258.

Van den Bergh, B. R. H., van Calster, B., Smits, T., van Huffel, S., & Lagae, L. (2008). Antenatal maternal anxiety is related to HPA-Axis dysregulation and self-reported depressive symptoms in adolescence: A prospective study on the fetal origins of depressed mood. *Neuropsychopharmacology*, *33*, 536–545.

Weinstock, M., Matlina, E., Maor, G. I., Rosen, H., & McEwen, B. S. (1992). Prenatal stress selectivley alters the reactivity of the hypothalamic-pituitary-adrenal system in the female rat. *Brain Research*, *595*, 195–200.

Wijnen, H. (2005). *The Kempen study: Aspects of maternal well-being and obstetrical outcome in relation to gestational thyroid function*. PhD Thesis, Tilburg University, The Netherlands.



2

Sex differences in the relation between prenatal maternal emotional complaints and child outcome

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Abstract

Background: Sex differences are found in animal studies concerning the relationship between prenatal maternal stress and outcome of the offspring. Most human studies in this field have not addressed sex differences, although differences between boys and girls may elucidate the biochemical as well as psychological processes involved. Associations between prenatal maternal emotional complaints and behavioural problems of toddlers and preschoolers as assessed by both mothers and fathers are studied separately for boys and girls.

Methods: Healthy Dutch Caucasian singleton, pregnant women (N = 444) answered questionnaires about anxiety and depression in every trimester of pregnancy. When their children (227 boys, 217 girls) were between 14–54 months old, both parents reported on their current feelings of depression and anxiety and on the behavioural problems of their children.

Results: Prenatal maternal emotional complaints were found to be associated with child behavioural problems both in boys and in girls, but in different ways. Prenatal maternal emotional complaints during the first trimester were associated with total and internalizing behavioural problems for boys. Emotional complaints during the third trimester were associated with total, internalizing, as well as externalizing behavioural problems for girls.

Conclusions: Differentiation according to sex and information on timing of emotional complaints during pregnancy is needed in studies concerning the relation between prenatal maternal emotional complaints and child outcome.

Introduction

Children of women with complaints reflecting distress, anxiety or depression during pregnancy, show more difficulties in motor, cognitive, and especially socio-emotional development from infancy to adolescence (Talge, Neal, & Glover, 2007; van den Bergh, Mulder, Mennes, & Glover, 2005). Several mechanisms have been proposed to explain these relations. First, the function of the hypothalamic-pituitary-adrenal (HPA) system may have been affected by prenatal maternal distress (Talge et al., 2007). In addition, genetic factors or sex hormones may also be important in the processes that affect the developing fetus as a result from maternal distress (Sarkar, Bergman, Fisk, O'Connor, & Glover, 2007; van den Bergh & Marcoen, 2004). The Developmental Origins of Health and Disease (DOHaD) approach states that the fetus will adapt and develop by shaping and structuring the organs for optimal performance in the fetal environment and maternal distress may elicit such biological programming processes (Swanson & Wadhwa, 2008).

Animal studies have shown different effects of prenatal stress on postnatal outcomes for male and female offspring. Several animal studies indicated an effect of prenatal stress on the hypothalamic-pituitary-adrenal (HPA) function, specifically for females and showed more prominent, mainly externalizing behaviour of the female offspring (Kaiser & Sachser, 2005; McCormick, Smythe, Sharma, & Meaney, 1995). Only a few studies have addressed sex differences in humans. Van den Bergh, van Calster, Smits, van Huffel, and Lagae (2008) reported that antenatal exposure to maternal anxiety at 12–22 weeks pregnancy was associated with a high and more flattened cortisol day-

time profile in both sexes and, in female adolescents only, with depressive symptoms. Rodriguez and Bohlin (2005) found a significant association between prenatal stress experienced around the 10th week of pregnancy and ADHD symptoms in boys only. Martin, Noyes, Wisenbaker, and Huttunen (1999) found a stronger correlation for 5-year-old boys between maternal distress during the first trimester of pregnancy and ratings of negative emotionality. O'Connor, Heron, Golding, Beveridge, and Glover (2002) however, found that high levels of anxiety at 32 weeks gestation were associated significantly with hyperactivity and inattention in 4-year-old boys, and with behavioural and emotional problems in boys as well as girls. They also found that high levels of anxiety at 18 weeks gestation were associated with more behavioural and emotional problems in girls at 81 months (O'Connor, Heron, Golding, & Glover, 2003). Hence, the available results are inconsistent for the nature of sex differences, the timing of distress during pregnancy and the nature of the maternal complaints involved. In this study, the association between prenatal maternal depressive and anxious complaints during different trimesters in pregnancy and externalizing and internalizing behavioural problems of the children is studied separately for boys and girls at toddler or preschool age, with both mothers and fathers as informants.

Methods

Participants

Between July 2002 and May 2005, midwives working in seven community midwifery practices in the southern regions of the Netherlands, invited healthy Dutch Caucasian singleton pregnant women (complete information was available for 1093 women) to participate in the study at their first antenatal check-up, at 10–12 weeks' gestation (Pop et al., 2006). After pregnancy, the women were asked to give informed consent to participate in future follow-up studies. In total 444 (response rate of 41%) mothers agreed to participate in the follow-up study and returned questionnaires about their current emotional complaints and behavioural problems of their children. The participating mothers did not differ from the non-participants in prenatal emotional complaints, maternal age at birth and marital status. However, the mothers who participated did have a higher educational level than non-participants (5.3% vs. 10.2% for low education; 55.2% vs. 54.9% for middle education; 39.5% vs. 34.8% for higher education, $p < .01$). Participating mothers smoked less during pregnancy than non-participating mothers. Furthermore, the children of mothers who participated had a 107 grams higher mean birth weight and 0.45 week longer mean gestation duration compared to the children of non-participating mothers.

At delivery, the 444 participating women ranged in age from 19 to 42 years ($M = 30.7$, $SD = 3.7$) and 98% were married or living together with the father of their children. Their partners ranged in age from 23 to 47 years ($M = 33.0$, $SD = 3.9$). Half of the women were primiparous ($N = 219$, 50.3%). 5.9% of the women finished primary education, 51.2% attended secondary education and 42.9% completed higher education

or university. Almost ten percent (9.6%) of their partners completed primary education, 45.6% attended secondary education and 44.9% finished higher education or university. The majority of the women (87.3%) did not smoke during pregnancy, 11.5% smoked less then 10 cigarettes a day and 1.2% smoked more than 10 cigarettes a day. Alcohol intake during pregnancy was rare. The infants (227 boys, 51.1%; 217 girls, 48.9%) were assessed between the ages of 14–54 months (age range boys 14–53 months, $M = 29.4$, $SD = 10.3$; age range girls 15–54 months, $M = 29.8$, $SD = 10.6$). All of the infants were born at term with a mean gestational age of 39.8 weeks ($SD = 1.3$ weeks) and a mean birth weight of 3527 g ($SD = 479$ g). 110 women (24.8%) gave birth to another baby after the target child was born.

Measures

Depression

Prenatal depression of the mothers was assessed using the Dutch version of the Edinburgh Depression Scale (EDS; Cox, Holden, & Sagovsky, 1987; Pop, Komproe, & van Son, 1992). The EDS is a widely used 10-item self-report scale designed as a screening instrument for depression and has been shown valid in and outside the postnatal period. Items are scored on four-point rating scales. Total scores range between 0 and 30, with a cut-off score of 12 and higher (Becht et al., 2001) to indicate mild to severe depressive symptoms ($M = 5.89$, $SD = 4.03$) (Pop et al., 1992). Current depressive complaints of both parents were also assessed with the EDS.

Anxiety

Prenatal anxiety of the mothers was assessed with the state version of the State-Trait Anxiety Inventory (STAI; Spielberger, Gorsuch, & Lushene, 1970). The STAI consists of two subscales each containing 20 items. The state anxiety subscale measures transient anxiety or anxiety at the moment of scoring. Trait anxiety measures dispositional anxiety or anxiety in general. The State version was used to assess the feelings of anxiety of the women during a specific period in their pregnancy. Total scores on the State subscale range between 20 and 80. The Dutch version of the STAI has been validated previously (normal population mean for women < 40 years = 38.0, $SD = 12.8$) (van der Ploeg, 2000).

Prenatal as well as current anxiety was assessed with the anxiety scale of the Symptom Check List (SCL-90; Derogatis, Lipman, & Covi, 1973). The SCL-90 has been validated before in the Netherlands and its use as well as the use of several subscales only, has revealed appropriate psychometric properties (Arrindell & Ettema, 2005). Total scores of the anxiety scale range between 10 and 50 (normal population mean for women = 13.43, $SD = 4.91$; for men: 12.23, $SD = 3.80$) (Arrindell & Ettema, 2005).

Child assessment

When the children were between 14 and 54 months old, both parents completed the Child Behaviour Check List (CBCL 1½–5) to evaluate the behaviour of their children (Achenbach & Rescorla, 2000). The CBCL 1½–5 is a parent-completed questionnaire

that contains 100 behavioural and emotional problem items, for which is indicated if a problem is seen sometimes (1), frequently (2) or not (0). Next to a total scale score, the results are differentiated according to *internalizing* (anxiety, depression, withdrawn behavior) or *externalizing* (attention difficulties, aggressive behaviour) problems. Raw scores are converted, based on the age and gender of the child, into standardized *T*-scores. The standardized *T*-scores can be compared for boys and girls from 1½ to 5 years. A norm referenced *T*-score of >70 is considered to be in the clinical range. Norm referenced *T*-scores of 65–70 are considered to be in the borderline-clinical range (Achenbach & Rescorla, 2000).

Procedures

Most studies concerning prenatal maternal emotional complaints and developmental outcome of the children use data based on maternal (self-) reports. However it is most likely that emotional complaints of mothers continue or recur after birth and possibly affect the mothers' ratings or perceptions of their children's behaviour. This may result in a reporter bias, as anxious or depressed mothers might be more likely to misinterpret disturbances in their children (Mednick, Hocevar, Baker, & Schulsinger, 1996; O'Connor et al., 2002). It is also found that 80% of depressive symptoms are recurrent (Goodman & Gotlib, 1999). Therefore, to obtain information from multiple informants, also fathers' report of the behaviour of their daughters and sons were included.

When the children were between 1 and 5 years of age both parents were also asked to answer questionnaires about their own current emotional complaints. Current sociodemographic information was obtained through a background questionnaire for both parents. Maternal emotional complaints (depression and anxiety) had been assessed at three time points during pregnancy, at 12, 24 and 36 weeks of gestation. Prenatal medical, sociodemographic and life style information was collected as part of the Kempen studies on obstetric outcome (Pop et al., 2006).

The Medical Ethical Committee of the St. Elisabeth Hospital in Tilburg approved the follow up study.

Results

The intensity and kind of prenatal maternal emotional complaints during each trimester and current complaints of both parents are presented in Table 2.1. The table shows only small differences between the prenatal emotional complaints during each trimester. The anxious complaints of women pregnant of a boy do not differ from the women pregnant of a girl, but the first group had slightly more depressive complaints during the third trimester (t (1) = 2.70, $p < .001$).

Table 2.2 shows weak to moderate correlations between current maternal EDS scores and prenatal EDS, SCL, and STAI scores in each trimester, which range between .26 and .50. Correlations between current maternal SCL scores and prenatal emotional complaints range between .16 and .51.

Table 2.1 Descriptive information for maternal prenatal EDS, STAI, and SCL scores and both parents' scores on EDS and SCL at time of child assessment (current emotional complaints) (*N* between 194 and 227)

	EDS		STAI		SCL	
	Boys	Girls	Boys	Girls	Boys	Girls
12 wk GA						
M (*SD*)	5.0 (4.01)	4.7 (3.93)	29.6 (8.05)	29.4 (8.24)	12.2 (2.78)	12.3 (3.77)
Range	0–18	0–22	20–60	20–63	10–22	10–38
24 wk GA						
M (*SD*)	4.5 (4.21)	3.8 (3.93)	30.0 (8.61)	29.3 (8.41)	12.5 (3.20)	12.0 (3.11)
Range	0–25	0–17	20–61	20–64	10–33	10–29
36 wk GA						
M (*SD*)	4.8 (4.18)	3.7 (3.75)*	31.9 (9.48)	31.4 (9.23)	12.9 (3.55)	12.5 (3.39)
Range	0–21	0–17	20–69	20–64	10–30	10–30
Current maternal scores						
M (*SD*)	4.6 (4.32)	4.6 (4.58)			11.9 (3.71)	12.0 (4.97)
Range	0–22	0–20			10–34	10–39
Current paternal scores						
M (*SD*)	2.9 (3.07)	3.3 (3.48)			11.1 (3.05)	11.2 (3.64)
Range	0–13	0–18			10–34	10–45

wk GA, weeks gestation; EDS, Edinburgh Depression Scale; STAI, State Trait Anxiety Inventory; SCL, Symptom Check List. * $p < .05$ (difference between boys and girls on EDS at 36 wk GA).

Furthermore, Table 2.2 shows several possibilities for data reduction. First, strong correlations between the three emotional complaints measures during each trimester (*r* ranges between .57 and .75) are found. Therefore, the three measures were standardized and summed, to create a total emotional complaints score of each trimester, Emo12, Emo24 and Emo36. These total scores of each trimester were used in subsequent analyses to measure potential timing effects of prenatal emotional complaints.

Second, strong correlations are also found between the results of the same questionnaire answered at different weeks in pregnancy, for example correlations between the EDS sores at 12, 24, and 36 weeks of pregnancy range between .55 and .70. A sum score was computed by averaging the scores on the three prenatal maternal EDS measures to create a mean prenatal EDS score (MEDS) during the total course of pregnancy. Identically, sum scores on the prenatal maternal SCL and STAI measures were also created to obtain a mean prenatal SCL score (MSCL) and a mean prenatal STAI score (MSTAI). These mean prenatal scores were used in subsequent analyses to study the associations between different kinds of emotional complaints and behavioural outcome of the boys and girls.

Results of the current (postnatal) SCL and EDS questionnaires were also found to

be strongly correlated for both mothers, as well as fathers. Therefore the scores of these two questionnaires were standardized to compute a total sum score for current emotional complaints for mothers and for fathers separately (i.e., current Emo mother and current Emo father). These summed scores of current emotional complaints are used in all subsequent analyses.

Results of the maternal and paternal assessments of the behavioural problems of their sons and daughters on the CBCL are presented in Table 2.3. The means of the CBCL scores are close to the population norms (Achenbach & Rescorla, 2000). CBCL scores by mothers and fathers are strongly correlated: for total problems in boys $r = .62$, in girls $r = .64$, for externalizing problems in boys $r = .59$, in girls $r = .66$, and for internalizing problems in boys $r = .55$, and in girls $r = .61$.

Main results

The associations between prenatal maternal emotional complaints and total, externalizing and internalizing behavioural problems are assessed for boys and girls and for maternal and paternal report separately (Table 2.4). Overall, significant, weak to moderate correlations are found between outcome and maternal prenatal complaints, both for the summary scores of emotional complaints per trimester, as well as for the mean results of the EDS, the STAI and the SCL measured over the whole pregnancy period.

To evaluate to what extent prenatal maternal emotional complaints account for the variance in the behavioural problems of the children independent of potential confounders, hierarchical regression analyses were performed.

First, to assess the relationship with the timing of emotional complaints in pregnancy, the total prenatal emotional complaints scores (Emo12, Emo24, Emo36) during each trimester were used as predictors and the assessments of behavioural problems as dependent variables (Table 2.5). Separate regression analyses were performed for maternal and paternal reports and for boys and girls. Preliminary analyses indicated that potentially confounding variables, maternal and paternal age at time of birth, birth weight and gestational age of the child at birth and the occurrence of a new pregnancy between delivery and child assessment, were not associated with both predictor and dependent variables. However, current emotional complaints and educational level of both parents, prenatal maternal smoking, women's parity and child's age were associated with both predictor and dependent variables. These variables were included in the regression analyses as confounders.

After controlling for the confounding variables, a significant effect of emotional complaints during the first trimester was found for internalizing problems in boys, as reported by the mothers ($R^2 = .13$, F model = 6.14, $p < .01$; $\beta = .18$, $p < .05$). Also a significant effect of emotional complaints during the first trimester on total behavioural problems in boys was found, as reported by the fathers ($R^2 = .09$, F model = 5.51, $p < .01$; $\beta = .21$, $p < .05$). Moreover, significant effects are found for emotional complaints during the third trimester on total ($R^2 = .18$, F model = 8.19, $p < .001$; $\beta = .28$, $p < .01$), externalizing ($R^2 = .14$, F model = 6.37, $p < .001$; $\beta = .26$, $p < .05$) and internalizing

Table 2.2 Intra-correlations between prenatal maternal emotional complaints and between prenatal maternal emotional complaints and current emotional complaints of both parents (*N* between 194 and 227)

Girls	EDS			STAI			SCL			Current mothers			Current fathers		
	12	24	36	12	24	36	12	24	36	EDS	SCL	Total	EDS	SCL	Total
EDS 12	1														
EDS 24	**.55**	1													
EDS 36	**.62**	**.59**	1												
STAI 12	**.65**	**.42**	**.48**	1											
STAI 24	**.49**	**.69**	**.52**	**.55**	1										
STAI 36	**.57**	**.54**	**.75**	**.57**	**.64**	1									
SCL 12	**.69**	**.48**	**.51**	**.60**	**.48**	**.54**	1								
SCL 24	**.54**	**.70**	**.53**	**.36**	**.61**	**.64**	**.59**	1							
SCL 36	**.52**	**.45**	**.68**	**.44**	**.48**	**.68**	**.55**	**.65**	1						
Current mothers															
EDS	**.35**	**.35**	**.48**	**.29**	**.44**	**.49**	**.32**	**.41**	**.50**	1					
SCL	**.32**	**.42**	**.39**	**.27**	**.40**	**.38**	**.38**	**.51**	**.44**	**.68**	–				
Total	**.36**	**.42**	**.47**	**.31**	**.46**	**.47**	**.38**	**.51**	**.51**	–	–	–			
Current fathers															
EDS	**.27**	**.19**	**.22**	**.31**	**.26**	**.35**	**.27**	**.25**	**.25**	**.37**	**.27**	**.35**	1		
SCL	.09	.03	.05	.15*	.08	.17*	.04	.16*	.18*	.14*	.13	.15*	**.43**	–	
Total	**.21**	.13	.16	**.27**	**.20**	**.30**	.18*	**.24**	**.26**	**.30**	**.24**	**.29**	–	–	–

Boys	EDS			STAI			SCL			Current mothers			Current fathers		
	12	24	36	12	24	36	12	24	36	EDS	SCL	Total	EDS	SCL	Total
EDS 12	1														
EDS 24	**.58**	1													
EDS 36	**.55**	**.70**	1												
STAI 12	**.66**	**.52**	**.45**	1											
STAI 24	**.52**	**.74**	**.57**	**.64**	1										
STAI 36	**.48**	**.60**	**.75**	**.52**	**.64**	1									
SCL 12	**.57**	**.43**	**.42**	**.62**	**.47**	**.44**	1								
SCL 24	**.43**	**.70**	**.57**	**.50**	**.70**	**.56**	**.56**	1							
SCL 36	**.39**	**.53**	**.65**	**.38**	**.51**	**.76**	**.45**	**.61**	1						
Current mothers															
EDS	**.49**	**.35**	**.31**	**.35**	**.34**	**.31**	**.30**	**.26**	**.28**	1					
SCL	**.35**	**.20**	.16*	**.33**	**.25**	**.21**	**.38**	**.25**	**.23**	**.61**	–				
Total	**.48**	**.31**	**.27**	**.38**	**.33**	**.30**	**.38**	**.28**	**.29**	–	–	–			
Current fathers															
EDS	.13	.05	.13	.15*	.10	.17*	.15*	-.04	.16*	**.22**	**.24**	**.25**	1		
SCL	.17*	.12	.09	.11	.12	.09	**.22**	.04	.09	.15*	**.19**	**.19**	**.43**	–	
Total	**.18**	.10	.13	.16*	.13	.15*	**.22**	.00	.15*	**.22**	**.26**	**.26**	–	–	–

Bold indicates $p < .01$, * $p < .05$.

(R^2 = .22, F model = 7.88, $p < .001$; $\beta = .25$, $p < .05$) behavioural problems in girls, as reported by the fathers.

Second, to measure the effect of the kind of emotional complaints during pregnancy, regression analyses were performed with the mean prenatal emotional complaints scores as predictor variables (Table 2.6). After controlling for confounding factors,

Table 2.3 CBCL *T*-scores for boys and girls as assessed by mothers and fathers

	Maternal report		Paternal report	
CBCL	Boys (*N* = 227)	Girls (*N* = 217)	Boys (*N* = 192)	Girls (*N* = 183)
Total *M* (*SD*)	47.93 (9.06)	46.06 (8.98)*	46.03 (8.06)	44.78 (9.14)
Range	28–74	28–71	28–69	28–70
Externalizing *M (SD)*	50.51 (9.18)	47.94 (9.36)*	48.70 (7.96)	46.98 (9.17)
Range	28–82	28–71	28–68	28–71
Internalizing *M (SD)*	46.52 (9.61)	45.51 (9.41)	44.41 (9.03)	44.25 (9.81)
Range	29–76	29–73	29–71	29–69

* $p < .05$, boys had somewhat more problems than girls, as reported by the mothers.

Table 2.4 Correlations between prenatal maternal emotional complaints and behavioural problems in boys and girls, as assessed by both parents

Maternal report	Girls (*N* = 192–196)			Boys (*N* = 185–191)		
CBCL	Total	Ext	Int	Total	Ext	Int
Emo 12	.25**	.23**	.17*	.24**	.21**	.26**
Emo 24	.30**	.26**	.28**	.19**	.24**	.18*
Emo 36	.26**	.23**	.22**	.26**	.28**	.26**
M EDS	.30**	.28**	.25**	.23**	.24**	.26**
M STAI	.32**	.30**	.25**	.20**	.21**	.20**
M SCL	.29**	.28**	.23**	.29**	.30**	.26**
Paternal report	Girls (*N* = 162–165)			Boys (*N* = 160–163)		
CBCL	Total	Ext	Int	Total	Ext	Int
Emo 12	.17*	.13	.16*	.25**	.22**	.18*
Emo 24	.25**	.21**	.25**	.17*	.17*	.05
Emo 36	.22**	.23**	.21**	.14	.14	.06
M EDS	.26**	.22**	.25**	.18*	.16*	.09
M STAI	.31**	.27**	.29**	.21**	.19*	.11
M SCL	.26**	.23**	.24**	.20*	.20*	.09

Total, CBCL total problems; Ext, CBCL externalizing problems; Int, CBCL internalizing problems; Emo 12, Total prenatal emotional complaints in first trimester; Emo 24, Total prenatal emotional complaints in second trimester; Emo 36, Total prenatal emotional complaints in third trimester; *M* EDS, mean level prenatal EDS scores; *M* STAI, mean level prenatal STAI scores; *M* SCL, mean level prenatal SCL scores. * $p < .05$, ** $p < .01$.

significant effects are found for mean prenatal STAI scores on total (R^2 = .23, F model = 3.19, p < .01; β = .36, p < .05), externalizing (R^2 =.19, F model = 2.45, p < .05; β = .33, p < .05), and internalizing (R^2 = .25, F model = 3.50, p < .05; β = .32, p < .05) behavioural problems in girls, as reported by the fathers. No significant effects are found for mean prenatal EDS or SCL scores. Regression analyses using the mothers' reports of their sons' and daughters' behavioural problems as dependent variable, while controlling for confounding factors, showed no significant effects.

Table 2.5 Summary of standardized beta coefficients of the hierarchical regression analyses with total emotional complaints in each trimester as predictors

Maternal report	Girls (N = 130)			Boys (N = 127)		
	Total	Ext	Int	Total	Ext	Int
Step 1: Covariates						
Current emo mother	.37**	.33**	.36**	.20*	.23**	.15
Current emo father	.07	.06	.02	.11	.07	.03
Education mother	-.08	-.02	-.10	-.17	-.15	-.09
Education father	-.20*	-.04	-.20*	-.15	-.20*	-.07
Smoking	.12	.17*	.06	.12	.10	.09
Child's age	.01	-.12	.16*	.09	-.06	.21*
Para	.00	.07	-.13	-.08	-.01	-.15
Step 2: Predictors						
Emo 12	.14	.17	.02	.16	.11	.18*
Emo 24	.01	.05	-.06	.06	.08	-.08
Emo 36	.12	.13	.12	.15	.15	.10
Paternal report	**Girls (N = 119)**			**Boys (N = 117)**		
	Total	Ext	Int	Total	Ext	Int
Step 1: Covariates						
Current emo mother	.12	.06	.14	.06	.14	.08
Current emo father	.10	.10	.02	.18*	.12	.24**
Education mother	-.06	-.05	.01	-.15	-.09	-.07
Education father	-.18*	-.08	-.16	-.18	-.24**	-.09
Smoking	.13	.18*	.01	.10	.01	.06
Child's age	.07	-.11	.22**	.07	-.02	.22*
Para	-.01	-.03	-.09	-.01	.04	-.02
Step 2: Predictors						
Emo 12	.11	.03	.11	.21*	.17	.13
Emo 24	-.02	-.07	.03	-.16	.06	-.02
Emo 36	.28**	.26*	.25*	-.11	.03	-.03

Total, CBCL total problems; Ext, CBCL externalizing problems; Int, CBCL internalizing problems; Para, women's parity; Emo 12, Total prenatal emotional complaints in first trimester; Emo 24, Total emotional complaints in second trimester; Emo 36, Total emotional complaints in third trimester; Current Emo, Current emotional complaints. * p < .05, ** p < .01.

Table 2.6 Summary of standardized beta coefficients of the hierarchical regression analyses with mean prenatal complaints as predictors

Maternal report	Girls (*N* = 130)			Boys (*N* = 127)		
	Total	Ext	Int	Total	Ext	Int
Step 1: Covariates						
Current emo mother	.32**	.30**	.33**	.18*	.23*	.22*
Current emo father	.07	.08	.01	.09	.05	.07
Education mother	-.07	-.01	-.12	-.15	-.14	-.09
Education father	-.15	-.03	-.16	-.08	-.12	-.00
Smoking	.12	.17	.05	.09	.08	.09
Child's age	-.02	-.14	.17*	.14	-.04	.25**
Para	.00	.09	-.14	-.11	-.03	-.17
Step 2: Predictors						
M EDS	.03	.04	.06	-.01	-.01	.05
M STAI	.09	.09	.04	-.06	-.02	-.04
M SCL	-.03	-.01	-.09	.19	.15	.15
Paternal report	**Girls (*N* = 119)**			**Boys (*N* = 117)**		
	Total	Ext	Int	Total	Ext	Int
Step 1: Covariates						
Current emo mother	.19	.13	.24*	.12	.14	.08
Current emo father	.13	.14	.04	.17	.10	.21*
Education mother	-.10	-.10	-.05	-.11	-.09	-.06
Education father	-.12	-.06	-.16	-.14	-.21*	-.07
Smoking	.15	.19*	.03	.06	-.02	.03
Child's age	.04	-.14	.22*	.10	-.02	.23*
Para	-.03	-.03	-.11	-.03	.01	-.04
Step 2: Predictors						
M EDS	-.06	-.06	.00	-.22	-.22	-.19
M STAI	.36*	.33*	.32*	.19	.14	.14
M SCL	-.05	-.09	-.04	.09	.11	.00

Total, CBCL total problems; Ext, CBCL externalizing problems; Int, CBCL internalizing problems; Para, women's parity; *M* EDS, mean level prenatal EDS scores; *M* STAI, mean level prenatal STAI scores; *M* SCL, mean level prenatal SCL scores; Current Emo, Current emotional complaints. * $p < .05$, ** $p < .01$.

Discussion

A clear difference in the association between prenatal maternal emotional complaints and behavioural problems of the children is found for boys and girls. For boys, emotional complaints during the first trimester show a significant effect on total and specifically internalizing behavioural problems. For girls, emotional complaints during the third trimester show significant effects on total, internalizing as well as externalizing behavioural problems.

An explanation for the differences in the effects of timing in boys and girls may be based on the differences in the amount of sex hormones in the developing fetus. A high level of prenatal maternal emotional complaints may result in a high level of cortisol secretion. Sarkar et al. (2007) have found a positive relation between cortisol and testosterone levels in amniotic fluid, in both male and female fetuses. Testosterone may mediate the relationship between prenatal stress and behavioural outcome (Sarkar et al., 2004). In genetically male fetuses, testosterone secretion is highest between week 10 and week 20 of gestation (Knickmeyer & Baron-Cohen, 2006). Testosterone levels in female fetuses increases significantly with gestational age (Gitau, Adams, Fisk, & Glover, 2005). Hence, time of prenatal maternal emotional complaints may have a different effect for boys and girls because of the differential rate in increase of testosterone during gestation.

The finding that girls, in contrast to boys, show more externalizing problems after exposure to prenatal emotional complaints might also be related to the levels of the sex hormone testosterone. Several animal studies indicated also more externalizing problems in female offspring compared to male offspring after exposure to prenatal distress (Kaiser & Sachser, 2005). It was assumed that prenatal stress induces a permanent behavioural masculinization in female offspring that is accompanied by changes in the endocrine and autonomic system, as well as by changes in the distribution of sex hormone receptors in the limbic system. Sarkar et al. (2004) concluded that the positive association between cortisol and testosterone in amniotic fluid, might also suggest a possible mechanism for masculinization of human offspring associated with increased exposure to prenatal stress. More physiological and behavioural research in humans is needed to study if this increase in externalizing behaviour of girls can be corroborated further.

Furthermore, in the regression analyses with the mean prenatal emotional complaints scores as predictors, only significant effects are found for maternal mean prenatal STAI scores on behavioural problems in girls, as reported by the fathers. No significant results are found for the mean prenatal EDS or SCL scores. Prenatal anxiety as measured with the STAI might be a more important predictor for child behavioural problems compared to scores on the EDS and SCL.

It is important to realize that our analyses concern the whole continuum of the amount of emotional complaints and behavioural scores (that showed normal distributions) and did not particularly focus upon the extremes, e.g. mothers with clinical levels of anxiety or depression or children with clinical levels of behavioural problems. Nevertheless a clear relationship is found between prenatal maternal emotional complaints and behavioural problems within this population of pregnant women with a normal variation in emotional complaints. Our sample had somewhat lower mean results on the STAI state anxiety questionnaires than the population norm indicated, but these results resembled those of an earlier study in the same geographical region and also on pregnant women (Brouwers, van Baar, & Pop, 2001).

Several difficulties arise concerning the attempts to disentangle pre- and postnatal influences. When controlling for the current level of emotional complaints of the

mothers, the association between prenatal emotional complaints and child behavioural problems as assessed by mothers was only found in one regression analysis. A significant effect was found for emotional complaints during the first trimester on internalizing behavioural problems in boys as assessed by the mothers. Mothers may rate their children more negatively when they are currently suffering from feelings of depression or anxiety, which reflects a reporter bias (O'Connor et al., 2002). However another possibility is that children indeed react to current maternal emotional complaints that are related to earlier complaints, and show more behavioural problems in response, which are then also statistically controlled. The possible effect of the prenatal complaints on behavioural problems of the children, as assessed by mothers, can also be statistically diminished as confounding factors such as smoking and low education are all already associated with prenatal feelings of depression or anxiety of the mothers. Perceived stress increases the likelihood of continued smoking during pregnancy (Rodriguez & Bohlin, 2000). Furthermore, depressed pregnant women tend to have lower educational levels (Field, Hernandez-Reif, & Diego, 2006). Smoking, low education and current feelings of depression and anxiety can be considered as a behavioural cluster or a lifestyle that form an inherent part of (prenatal) emotional complaints. If this cluster is controlled in the regression analyses, a form of over-control might be exerted, which also extracts a part of the effect of prenatal depressive or anxious functioning from the analyses.

Furthermore, another important factor may be the interaction style and behaviour of the mother towards the child postnatally. Kaplan, Evans, and Monk (2008) recently found, in 4-month-old infants, a significant interaction effect between prenatal maternal psychiatric status and postnatal maternal sensitivity on infant cortisol levels. Compared to prenatally stressed infants with sensitive mothers only prenatally stressed infants who postnatally received insensitive care, showed higher cortisol levels at 4 months. Maternal interactive behaviour might be a possible moderator or mediator in the relation between prenatal measures and child outcome. If the mother is currently suffering from emotional complaints, she might interact more negatively and less sensitively with her child, which subsequently might lead to more behavioural problems in the children (Elgar, McGrath, Waschbusch, Stewart, & Curtis, 2004). Girls, compared to boys, are better at interpreting non-verbal cues (Lindahl & Heimann, 1997) and therefore might react with an increase in behavioural problems to these less optimal interaction processes. Research including observations of parent-child interaction in order to disentangle the weight of prenatal influences from that of the postnatal interaction experiences is currently undertaken at toddler and preschool age. Early biological programming processes as well as psychological processes as evidenced in interaction experiences might shape children's emotional and behavioural development.

To conclude: in studies concerning the relation between prenatal maternal emotional complaints and child outcome, differentiation according to sex, timing and kind of prenatal complaints is needed. The relationship of prenatal maternal emotional complaints and behavioural outcome in the children differs for boys and girls.

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References

Achenbach, T. M., & Rescorla, L. A. (2000). *Manual for the ASEBA Preschool Forms & Profiles*. Burlington, VT: University of Vermont, Research Center for Children, Youth, & Families.

Arrindell, W. A., & Ettema, J. H. M. (2005). *SCL-90. Handleiding bij een multidimensionele psychopathologie-indicator*. Amsterdam, The Netherlands: Harcourt Test Publishers.

Becht, M. C., Van Erp, C. F., Teeuwisse, T. M., Van Heck, G. L., Van Son, M. J., & Pop, V. J. (2001). Measuring depression in women around menopausal age towards a validation on the Edinburgh Depression Scale. *Journal of Affective Disorders*, *63*, 209–213.

Brouwers, E. P. M., van Baar, A. L., & Pop, V. J. M. (2001). Does the Edinburgh Postnatal Depression Scale measure anxiety? *Journal of Psychosomatic Research*, *51*, 659–663.

Cox, J. L., Holden, J. M., & Sagovsky, R. (1987). Detection of postnatal depression. *British Journal of Psychiatry*, *150*, 782–786.

Derogatis, L. R., Lipman, R. S., Covi, L. (1973). SCL-90: an outpatient psychiatric rating scale – preliminary report. *Psychopharmacology Bulletin*, *9*, 13–28.

Elgar, F. J., McGrath, P. J., Waschbusch, D. A., Stewart, S. H., & Curtis L. J. (2004). Mutual influences on maternal depression and child adjustment problems. *Clinical Psychology Reviews*, *24*, 441–459.

Field, T., Hernandez-Reif, M., & Diego, M. (2006). Risk factors and stress variables that differentiate depressed from nondepressed pregnant women. *Infant Behavior and Development*, *29*, 169–174.

Gitau, R., Adams, D., Fisk, N. M., & Glover, V. (2005). Fetal plasma testosterone correlates positively with cortisol. *Archives of Disease in Childhood. Fetal and Neonatal Edition*, *90*, F166–F169.

Goodman, S. H., & Gotlib, I. H. (1999). Risk for psychopathology in the children of depressed mothers: A developmental model for understanding mechanisms of transmission. *Psychological Reviews*, *106*, 458–490.

Kaiser, S., & Sachser, N. (2005). The effects of prenatal social stress on behaviour: mechanisms and function. *Neuroscience and Biobehavioral Reviews*, *29*, 283–294.

Kaplan, L. A., Evans, L., & Monk, C. (2008). Effects of mothers' prenatal psychiatric status and postnatal caregiving on infant biobehavioral regulation: Can prenatal programming be modified? *Early Human Development*, *84*, 249–256.

Knickmeyer, R. C, & Baron-Cohen, S. (2006). Fetal testosterone and sex differences. *Early Human Development*, *82*, 755–760.

Lindahl, L. B., & Heimann, M. (1997). Research report: Social proximity in early mother-infant interactions: implications for gender differences? *Early Development and Parenting*, *6*, 83–88.

Martin, R. P., Noyes, J. N., Wisenbaker, J., & Huttunen, M. O. (1999). Prediction of early childhood negative emotionality and inhibition from maternal distress during pregnancy. *Merrill-Palmer Quarterly*, *45*, 370–391.

McCormick, C. M., Smythe, J. W., Sharma, S., & Meaney, M. J. (1995). Sex-specifc effects of prenatal stress on hypothalamic-pituitary-adrenal responses to stress and brain glucocorticoid receptor density. *Developmental Brain Research*, *84*, 55–61.

Mednick, B. R., Hocevar, D., Baker, R. L., & Schulsinger, C. (1996). Personality and demographic characteristics of mothers and their ratings of child difficultness. *International Journal of Behavioral Development*, *19*, 121–140.

O'Connor, T. G., Heron, J., Golding, J., Beveridge, M., & Glover, V. (2002). Maternal antenatal anxiety and children's behavioural/emotional problems at 4 years. *British Journal of Psychiatry*, *180*, 502–508.

O'Connor, T. G., Heron, J., Golding, J., & Glover, V. (2003). Maternal antenatal anxiety and behavioural/emotional problems in children: a test of a programming hypothesis. *Journal of Child Psychology and Psychiatry*, *44*, 1025–1036.

Pop, V. J., Komproe, I. H., & van Son, M. J. (1992). Characteristics of the Edinburgh Post Natal Depression Scale in the Netherlands. *Journal of Affective Disorders*, *26*, 105–110.

Pop, V. J., Wijnen, H. A., Lapkienne, L., Bunivicius, R., Vader, H. L., & Essed, G. G. (2006). The relation between thyroid parameters and depression: A reflection of the downregulation of the immune system during pregnancy? *Thyroid*, *16*, 485–492.

Rodriguez, A., & Bohlin, G. (2005). Are maternal smoking and stress during pregnancy related to ADHD symptoms in children? *Journal of Child Psychology and Psychiatry*, *46*, 246–254.

Rodriguez, A., Bohlin, G., & Lindmark, G. (2000). Psychosocial predictors of smoking and exercise during pregnancy. *Journal of Reproductive and Infant Psychology*, *18*, 203–223.

Sarkar, P., Bergman, K., Fisk, N. M., O'Connor, T. G., & Glover, V. (2007). Amniotic fluid testosterone: relationship with cortisol and gestational age. *Clinical Endocrinology*, *67*, 743–747.

Spielberger, C. D., Gorsuch, R. L., & Lushene, R. E. (1970). *STAI Manual for the State-trait Anxiety Inventory*. Palo Alto, California: Consulting Psychologists Press.

Swanson, J. D., & Wadhwa, P. M. (2008). Developmental origins of child mental health disorders. *Journal of Child Psychology and Psychiatry*, *49*, 1009–1019.

Talge, N. M., Neal, C., & Glover, V. (2007). Antenatal maternal stress and long-term effects on child neurodevelopment: How and why? *Journal of Child Psychology and Psychiatry*, *48*, 245–261.

Van den Bergh, B. R. H., & Marcoen, A. (2004). High antenatal maternal anxiety is related to ADHD symptoms, externalizing problems, and anxiety in 8- and 9-year-olds. *Child Development*, *75*, 1085–1097.

Van den Bergh, B. R. H., Mulder, E. J. H., Mennes, M., & Glover, V. (2005). Antenatal maternal anxiety and stress and the neurobehavioural development of the fetus and child: links and possible mechanisms. A review. *Neuroscience and Biobehavioral Reviews*, *29*, 237–258.

Van den Bergh, B. R. H., van Calster, B., Smits, T., van Huffel, S., & Lagae, L. (2008). Antenatal maternal anxiety in related to HPA-axis dysregulation and self-reported depressive symptoms in adolescence: A prospective study on the fetal origins of depressed mood. *Neuropsyhopharmacology*, *33*, 536–545.

Van der Ploeg, H. M. (2000). *Handleiding bij de Zelf-BeoordelingsVragenlijst ZBV*. Lisse, The Netherlands: Swets & Zeitlinger.

3

Prenatal maternal emotional complaints are associated with cortisol responses in toddler and preschool aged girls

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Abstract

Associations between prenatal maternal emotional complaints and child behavioural and cognitive problems have been reported, with different relations for boys and girls. Fetal programming hypotheses underline these associations and state that the early development of the HPA-axis of the children may have been affected. In the present study, differences in cortisol responses of prenatally exposed and non-exposed children are examined for both sexes separately.

Cortisol response patterns of a group preschool aged children that were prenatally exposed to high levels of maternal emotional complaints ($N = 51$) were compared to a non-exposed group ($N = 52$). Child saliva was collected at the start of a home visit (T1), 22 minutes after a mother-child interaction episode (T2), and 22 minutes after a potentially frustrating task (T3). Repeated measures analyses showed that prenatally exposed girls showed higher cortisol levels across the three episodes compared to non-exposed girls. No differences were found in boys. Maternal prenatal emotional complaints might be related to child HPA-axis functioning differently for boys and girls.

Introduction

Children of women who had complaints reflecting distress, anxiety or depression during pregnancy, show more difficulties in motor, cognitive, and especially socio-emotional development from infancy to adolescence (Talge, Neal, & Glover, 2007). We also found that prenatal maternal emotional complaints are associated with child behavioural problems (de Bruijn, van Bakel, & van Baar, 2009).

When a pregnant woman experiences such emotional complaints the developing fetus may be affected. A potentially important underlying mechanism, is fetal programming of the Hypothalamic – Pituitary – Adrenal (HPA) axis (van den Bergh, van Calster, Smits, van Huffel, & Lagae, 2008). In animal studies, physiological changes after exposure to prenatal maternal stress are found including overactivity and impaired negative feedback regulation of the HPA-axis (Huizink, Mulder, & Buitelaar, 2004). For example, rats that were prenatally exposed to stress produced faster, stronger, and / or more prolonged glucocorticoid responses than controls, when exposed to novel or challenging situations (Weinstock, Matlina, Maor, Rosen, & McEwen, 1992). Furthermore, rats and nonhuman primates show delays in neuromotor development, increased emotionality, decreased exploratory behavior, and impaired adaptation to conditions of conflict after exposure to prenatal stress (for an overview see Huizink et al., 2004). Three possible mechanisms, which may act in concert, have been hypothesized to cause the negative effects of prenatal maternal stress on the development of the HPA-axis functioning of the fetus (Gutteling, de Weerth, & Buitelaar, 2005; Huizink et al., 2004). First, prenatal anxiety and stress stimulate activation of the maternal HPA-axis, leading to a release of cortisol (O'Connor et al., 2005). Maternal cortisol crosses the placenta and reaches the fetus (Gitau, Cameron, Fisk, & Glover, 1998). Under normal circumstances, access to maternal cortisol by the fetus is low, because of the action of the placental enzyme, 11 β-hydroxysteroid dehydrogenase type 2 (11BHSD2) (Wadhwa, 2005; Weinstock, 2008). This enzyme metabolizes about 80 % of the cortisol into the inactive cortisone. The impact of maternal stress on placental 11BHSD2 synthesis is not known. It is possible

that as in animal studies prolonged stress may decrease the activity of 11BHSD2. Or a decrease in the activity of cortisol binding globulin may result in exposure of the fetus to excessive amounts of maternal cortisol (Weinstock, 2008). Second, under the influence of maternal stress, placental cells might also release more stress hormones into the fetal circulation. Subsequently, these excessive levels of stress hormones could be detrimental for fetal brain development. Finally, maternal stress might decrease blood flow to the placenta and cause restriction in fetal growth and abnormalities in development (Gutteling et al., 2005; Huizink et al., 2004). Moreover, in animals it is found that the fetal HPA-axis is especially vulnerable to environmental input. As a result of this increased sensitivity in early development, the HPA-axis of the offspring might be "programmed" (O'Connor et al., 2005), indicating that as a result of the adaptation to a specific environment, the set point of the stress response system may have been affected, or the developmental pattern of proliferation and differentiation within key fetal tissues and organ systems may have been permanently changed (Wadhwa, 2005).

Several studies found relationships between maternal and fetal or children's cortisol levels, as well as associations with prenatal maternal stress levels, that support the notion of the potential adaptation of the HPA-axis development. Gitau et al. (1998) found that during pregnancy, maternal cortisol levels in healthy women are directly related to fetal cortisol levels. Field et al. (2004) measured urinary cortisol in newborns of prenatally depressed women and found that their cortisol levels mimicked the higher prenatal cortisol levels of their mothers. This same pattern of elevated cortisol levels in newborns was already found in the retrospective study of Lundy et al. (1999). Keenan, Gunthorpe, and Grace (2007) found a significant positive association between prenatal negative life events and pre-stressor cortisol levels of neonates. In a study of Brennan et al. (2008) was reported that exposure to maternal depression and anxiety during pregnancy and the postpartum period may increase infant salivary cortisol levels. Gutteling et al. (2005) analyzed salivary cortisol in school aged children at their first day of school and found higher cortisol levels in children whose mothers had higher levels of morning cortisol during pregnancy and more fear of bearing a handicapped child. Maternal prenatal cortisol level was also positively associated with offspring cortisol in response to a vaccination during the preschool period (Gutteling, de Weerth, & Buitelaar, 2004). O'Connor et al. (2005) measured diurnal cortisol in 10 year olds and found that the anxiety of the mothers at 32 weeks gestation was significantly and positively associated with the children's cortisol levels at awaking, after controlling for multiple postnatal assessments of maternal anxiety and depression. Huizink et al. (2008) studied the associations between exposure to prenatal stress and saliva cortisol in 14 year old adolescents of Finnish women who where pregnant during the Chernobyl disaster of 1986. The suddenness of the disaster and the very broad media coverage in addition to the rumours (e.g. if milk was safe to drink) might have caused stress in the Finnish population, including women who were pregnant at that time (Huizink et al., 2008). Results were compared with the associations in adolescents of women who were pregnant one year after the disaster. The authors found that prenatal exposure to maternal stress in the second trimester of pregnancy was related to elevated cortisol levels in the adolescent children of the women.

Sex differences may be important in the development of the HPA-axis of the fetus and its sensitivity to maternal stress processes, as in our study the pattern of associations between prenatal maternal emotional complaints and child behavioural problems was found to differ for boys and girls (de Bruijn et al., 2009). In animal studies, regulation of the HPA-axis has been found to be affected by sex hormones in adolescent offspring (McCormick & Mathews, 2007). Numerous animal studies have shown that glucocorticoid levels are higher in females than in males after HPA-axis stimulation (for a review see Kudielka & Kirschbaum, 2005). Furthermore, greater glucocorticoid transfer occurs across the placenta of female compared to male fetuses and this could account for the increased effect of prenatal stress in female offspring (Montano, Wang, & vom Saal, 1993; Matthews, 2002). Findings in human studies are less consistent. Most studies revealed that there are (a) no significant sex differences in psychological stress responses, or (b) higher cortisol responses in young men than in young women (Kudielka & Kirschbaum, 2005). In children, controlled stress response studies are rare. The few data available, including responses to psychosocial laboratory stress and adjustment to a day care setting seem to point towards similar stress-related cortisol responses in younger and older children with no apparent sex differences (Kudielka & Kirschbaum, 2005).

Sex differences in relation to prenatal maternal complaints and the cortisol levels of the children are reported in only one human study. Van den Bergh et al. (2008) measured diurnal cortisol in 14/15 year olds and found a more flattened diurnal profile after exposure to high levels of prenatal maternal anxiety. This flattened profile was found to be associated with depressive symptoms in female adolescents only.

Sex differences in HPA-axis functioning in relation to prenatal maternal emotional complaints deserve further study, as these may show an important moderation in fetal programming processes. Analyses of sex differences might illuminate the processes whereby risk factors operate to influence children's development (Rutter, Caspi, & Moffitt, 2003). The two sexes may be differentially sensitive to early experiences in the womb (Hay, Pawlby, Waters, & Sharp, 2008). In view of the sex differences seen in the pattern of association between behavioural problems of preschool aged children and their mothers' prenatal emotional complaints (de Bruijn et al., 2009), we would also expect sex differences in cortisol responses of these children.

As the different types of maternal complaints, for example feelings of depression, general anxiety, pregnancy related anxiety, and indicators of stress all showed associations with developmental problems or delay of the children and different measures of depression and anxiety had intercorrelations between .57 and .75, we preferred to indicate these as emotional complaints (de Bruijn et al., 2009). Depression and anxiety may be related because they share many overlapping symptoms including fatigue, impaired concentration, irritability, sleep disturbance and somatisation in addition to subjective experience of nervousness, worry and restlessness (Ressler & Nemeroff, 2000). Such complaints may also share a common underlying physiology. Hughes, Watkins, Blumenthal, Kuhn, and Sherwood (2004) evaluated the relationship between women's levels of self-reported symptoms of depression and anxiety and 24-

hour urinary catecholamine excretion. They found that higher levels of depression and anxiety symptoms are both related to increased urinary norepinephrine and cortisol excretion. It is suggested that depression and anxiety may be both associated with increased sympathetic nervous system activity. Ressler and Nemeroff (2000) concluded that in both the depressed and anxious state the stress/fear pathway cannot easily be shut off or returned to normal, which leaves the individual in a chronic state of abnormal affective responsiveness.

Timing, intensity and duration of maternal stress are also considered to be important (Weinstock, 2008). It is possible that an overall gradual dose-response relationship is important for fetal programming. However it could also be that fetal programming processes only come about, when a strong or consistently higher dose is working (for instance a more frequent or higher cortisol excretion of the pregnant woman). Irrespective of the conditions under which programming processes might be operating, if cortisol reactivity of the children is affected through such processes, the effect should be seen in children of women with relatively high levels of emotional complaints and it should be different from the cortisol reactivity of children whose mothers had few or no complaints during pregnancy. Hence, when HPA-axis functioning of the children is indeed affected by maternal emotional processes, cortisol response patterns of children born to mothers *with* high levels of prenatal emotional complaints should differ from the patterns seen in children born to mothers without high levels of emotional complaints. This could be seen in baseline cortisol levels as well as in the cortisol responses after a stressful task. In the present study we measured cortisol levels of toddlers and preschool children between the age of 23 and 60 months during a home visit in which the children performed various tasks, including a potentially stressful task. We hypothesized that the cortisol response patterns of children who were prenatally exposed to emotional complaints of their mothers, differ from the patterns of non-exposed children and that the responses are different for boys and girls.

Methods

Participants

This study is part of a prospective ongoing research line, which investigates the influence of prenatal maternal emotional complaints on the self-regulation and socio-emotional adjustment of toddlers and preschoolers in relation to parental interaction styles. Between July 2002 and May 2005, midwives working in the southern regions of the Netherlands, invited healthy Dutch Caucasian singleton pregnant women (complete information was available for 1093 women) to participate in the study at their first antenatal check-up, at 10–12 weeks' gestation (Wijnen, 2005; Pop et al., 2006). After pregnancy, the women were asked to give informed consent to participate in future follow-up studies. A total of 444 parents actually gave information through questionnaires on their children's behavioural functioning (de Bruijn et al., 2009).

From this group the participants for the current study were selected. Cases that

had fathers who did not want to cooperate (N = 26), or single mothers (N = 3) were excluded, as were children with perinatal problems like prematurity (N = 8) and twins (N = 6).

Selection criteria for the groups with or without prenatal maternal emotional complaints were as follows. Children whose mothers scored above a standardized cut off, or higher than one standard deviation above the mean, on one of the three prenatal measurements of anxiety or depression at 12, 24 or 36 weeks in pregnancy were selected for the target (prenatally exposed) group. This applied to 25% of the total group. For the comparison group (prenatally non-exposed), children were selected whose mothers had at least given information in two separate periods during pregnancy and did not report high scores for any of the prenatal depression or anxiety questionnaires. The comparison children were matched to the target cases regarding month of birth and sex.

In total 222 families were asked for participation with the home visits and 132 (59.5%; 67 girls, 65 boys, M age = 38.61 months, SD = 9.4, range = 23–60 months) agreed. Most important reasons for non-participation were lack of time (43%), personal difficulties (16%, e.g. illness or death of family member), problems with being videotaped (12%) and inability to contact some families because they had moved (8.9%). No differences were found between participants and non-participants in scores on prenatal anxiety and / or depression measures. Equal numbers of families were included in the target group (N = 66) and the comparison group (N = 66). Cortisol data were collected for 103 children (78%), 51 in the exposed group and 52 in the non-exposed group. Lack of data was caused by insufficient saliva production of the child, or child's refusal to suck on the cotton rolls, with younger children showing more refusal compared to older children. However, lack of data was equally represented within the two groups. The Medical Ethical Committee of the St. Elisabeth Hospital in Tilburg approved this study.

Measures

Depression

Prenatal depression of the mothers was assessed using the Dutch version of the Edinburgh Depression Scale (EDS; Cox, Holden, & Sagovsky, 1987; Pop, Komproe, & van Son, 1992) at 12, 24 and 36 weeks' gestation. The EDS is a widely used 10-item self-report scale designed as a screening instrument for depression and has been shown valid in and outside the postnatal period. Items are scored on four-point rating scales. Total scores range between 0 and 30. A cut-off score of 12 and higher was used (Becht et al., 2001) to indicate major depression (normal population mean 5.89, SD = 4.03; Pop et al., 1992).

Anxiety

Prenatal anxiety of the mothers was assessed with the State version of the State-Trait Anxiety Inventory (STAI; Spielberger, Gorsuch, & Lushene, 1970) at 12, 24 and 36 weeks' gestation. The STAI consists of two subscales each containing 20 items. The state anxiety subscale measures transient anxiety or anxiety at the moment of scoring. Trait anxiety

measures dispositional anxiety or anxiety in general. The state and trait version were found to correlate highly (.74) in a study with 32 weeks' pregnant women (Brouwers et al., 2001). The State version was used to assess the feelings of anxiety of the women during a specific period in their pregnancy. Total scores on the State subscale range between 20 and 80. The Dutch version of the STAI has been validated previously (Cronbach's alpha = .95, normal population mean for non pregnant women < 40 years = 38.0, *SD* = 12.8; Van der Ploeg, 2000). In our study a score above 39 (that is > 1 *SD* above the mean in our sample of pregnant women) was used as cut off, reflecting a high level of complaints.

Prenatal anxiety was also assessed with the Dutch version of the Symptom Check List (SCL-90; Derogatis, Lipman, & Covi, 1973; Arrindell & Ettema, 2003), a 90 item self-report scale that measures several dimensions in psychopathology. The SCL-90 is composed of eight subscales, of which only the anxiety subscale was used in this study. The SCL-90 has been validated before in the Netherlands and its use as well as the use of several subscales only, has revealed appropriate psychometric properties (Cronbach's alpha of anxiety subscale = .87; Arrindell & Ettema, 2003). Total scores of the anxiety subscale range between 10 and 50 (normal population mean for women = 13.43, *SD* = 4.91; for men: 12.23, *SD* = 3.80; Arrindell & Ettema, 2003). In our study, a score above 17 (that is > 1 *SD* above the mean in our sample of pregnant women) was used as cut off, reflecting a high level of complaints.

Strong correlations are found between the results of the same questionnaire answered at different weeks in pregnancy (*r* EDS at 12, 24, and 36 weeks range between .55 and .70; *r* STAI range between .52 and .64, *r* SCL range between .45 and .65). A mean score was computed by averaging the scores on the three prenatal maternal EDS measures to create a mean prenatal EDS score (MEDS) during the total course of pregnancy. Identically, sum scores on the prenatal maternal SCL and STAI measures were also created to obtain a mean prenatal SCL score (MSCL) and a mean prenatal STAI score (MSTAI). These mean prenatal emotional complaints scores for the prenatally exposed and non-exposed groups are presented in Table 3.1.

Cortisol

To measure cortisol levels, child saliva was collected three times during a home visit, using Salivette cotton dental rolls (Sarstedt, Etten-Leur, the Netherlands). The child was asked to put the cotton roll into his/her mouth and to chew and suck on it for about one minute, until the cotton roll was saturated. After the home visits, the Salivettes were stored at -28°C until being assayed by radioimmunoassay at the Research Center for Psychobiology and Psychosomatic at the University of Trier. Cortisol was analyzed by a time-resolved immunoassay with fluorescence detection (Dressendörfer, Kirschbaum, Rohde, Stahl, & Strasburger, 1992). All samples from one child were analyzed in one assay to minimize the variability of the results. To guarantee validity of analysis, duplicate assays were performed. The intra-assay coefficient of variation was between 4.0% and 6.7%, and the corresponding inter-assay coefficients of variation were between 7.1% and 9.0%. First basal saliva collection (T1) was at the start of the home visit, within 10 minutes after arrival of the researcher, so this cortisol measured reflected

Table 3.1 Descriptive characteristics

	Prenatally exposed		Prenatally non-exposed	
	Boys (*N* = 24–25)	Girls (*N* = 23–26)	Boys (*N*= 19–22)	Girls (*N* = 26–30)
Age child, months *M* (*SD*)	43.7 (10.1)	38.4 (9.2)	35.5 (8.3)	41.2 (7.6)[b]
Birth weight child in grams *M* (*SD*)	3515 (451)	3433 (420)	3824 (467)	3425 (462)[c]
Gestational age *M* (*SD*)	39.6 (1.2)	39.9 (1.3)	40.3 (1.3)	39.9 (1.2)
Age mother at birth, years *M* (*SD*)	32.0 (3.6)	30.0 (3.5)[a]	31.3 (3.4)	30.3 (3.8)
Education mother				
% low	4.0	15.4	0.0	3.4
% middle	60.0	38.5	63.6	37.9
% high	36.0	46.2	36.4	58.6
Education father				
% low	8.3	19.2	13.6	3.3
% middle	50.0	46.2	40.9	46.7
% high	41.7	34.6	45.5	50.0
Prenatal complaints				
EDS *M* (*SD*)	7.2 (3.2)	8.4 (3.5)	2.7 (2.3)	2.4 (2.1)
STAI *M* (*SD*)	38.3 (6.3)	40.5 (6.0)	26.2 (4.1)	25.2 (4.3)
SCL *M* (*SD*)	14.4 (2.4)	15.8 (4.6)	11.4 (1.2)	11.0 (1.3)

[a] $p < .05$, sex difference within the prenatally exposed group; [b] $p < .05$, sex difference within the prenatally non-exposed group; [c] $p < .01$, sex difference within the prenatally non-exposed group. NB see text for exposed versus non-exposed group differences.

the situation prior to the arrival of the researcher. The second sample (T2) was taken approximately 22 minutes after the first mother-child interaction task. During this task, that lasted five minutes, child and mother were asked to play together with clay, considered as a normal play situation. The third sample (T3) was taken approximately 22 minutes after a potentially frustrating task. The time interval of 22 minutes between each task and cortisol measurement was chosen to capture the peak cortisol response (Ramsay & Lewis, 2003). The mean time between T1 and T2 was 31.2 min (*SD* = 2.4 min) and between T2 and T3 was 30.7 min (*SD* = 2.8 min).

Procedures

The first author visited the mother-child dyads at home. During this visit, the mothers and children were instructed to perform several tasks together to observe the mother-child interaction and the self-regulation capacities of the children as part of our larger research project. At the start of the home visit, the child was asked to build a tower of wooden blocks. This was an easy and enjoyable task for all children, so they could get used to the researcher. After five minutes, the child received the first cotton roll used for saliva collection. Next, mother and child were asked to play together for five minutes

with clay, followed by a five minute puzzle task. Then mother and child were given a marble allay to play with for five minutes. After these three mother-child interaction tasks, the mother was asked some questions about her child (as part of our larger research project) and the child was allowed to play by him/herself. Approximately 22 minutes after the first mother-child interaction task (clay episode), the child received the second cotton roll to suck on for saliva collection. Next, a self regulation task was administered. This was a potentially frustrating task and is based upon the plastic barrier task of Calkins and Johnson (1998) that was found to elicit distress in toddlers. The children were confronted with a large plexiglas box, in which an attractive plastic Mickey Mouse puppet was seated. The researcher promised the children that they were allowed to keep the puppet, if they were able to open the box. Two small holes were at both sides of the box and the child was handed two wooden sticks. The sticks could be put into the holes, but were unable to reach the puppet. A lock with a key was also attached to the box, but the key did not fit into the lock. The mother was instructed to say as little as possible to her child and was asked not to help her child in opening the box. She was only allowed to encourage her child to try to open the box him/herself. After five minutes the researcher explained in a playful way ("Mickey wants to stay in his little house") to the child that it was impossible to get the puppet out of the box. Next, the researcher complimented the child for his/her efforts during the tasks and gave the child a box of sweets (raisins or little chocolates). Finally, mother and child were asked to play their own favourite game together. Approximately 22 minutes after the frustration task, the child was handed the third and final cotton roll to suck on. Before the final saliva collection, the children were asked to rinse their mouth thoroughly with water and to clean their mouth after eating the sweets. However, food intake before saliva collection does not seem to have an influence on cortisol levels (Gröschl, Wagner, Rauh, & Dörr, 2001).

Results

Participants

Descriptive characteristics of prenatally exposed and non-exposed boys and girls are shown in Table 3.1. At the time of assessment the age of prenatally exposed boys was significantly higher compared to the age of the prenatally non-exposed boys (mean difference = 8.27 months, t (45) = 3.04, $p < .01$). Moreover, birth weight of prenatally non-exposed boys was significantly higher compared to the birth weight of prenatally exposed boys (mean difference = 311g, t (45) = -2.33, $p < .05$). Reduced birth weight after exposure to prenatal maternal emotional complaints is one of the most replicated findings (Mulder et al., 2002). As expected, in view of the selection criteria, the prenatally exposed and non-exposed groups differed significantly in prenatal maternal emotional complaints. No significant differences in prenatal emotional complaints were found between boys and girls within the prenatally exposed group, nor within the prenatally non-exposed group. No other significant differences were found between prenatally exposed and non-exposed boys and girls.

Preliminary analyses

As the cortisol distributions were positively skewed, the cortisol data were log 10 transformed prior to the analyses. No outliers were found. Next, potential confounding factors were analysed for significance. Time of cortisol sampling may be a confounding variable. Due to the cortisol circadian rhythm, samples taken later in the day contain lower levels of cortisol than samples taken earlier in the day (Gutteling et al., 2005). One Way Anova with time of home visit (divided into three groups: 10.00–12.00 am, 13.00–15.00 pm, 15.00–17.00 pm) as fixed factor and cortisol level at T1, T2, and T3 respectively as dependent variable, revealed significant differences for girls in the prenatally exposed group. Cortisol levels at T1 and T2 during the home visit in the morning were significantly higher compared to the cortisol levels during the home visit between 13.00–15.00 pm ($F(2,21)= 6.11$, $p < .01$; $F(2,21) = 4.07$, $p < .05$). No difference was found for cortisol levels at T3. Time of home visit was used as covariate in the final analyses.

As the participating children had a rather large age range, correlational analyses between age and cortisol levels were done; this was done separately for the prenatally exposed and non-exposed group, as well as for boys and girls. In the prenatally non-exposed group, the child's age was significantly correlated with basal cortisol levels for boys ($r = -.56$, $p < .01$). Therefore age was also used as a covariate in subsequent analyses.

Time of feeding might also affect the HPA-axis (de Weerth, Zijl, & Buitelaar, 2003). This variable was not included as confounder, as no significant differences were found in time interval of last feeding until first cortisol measurement, between the prenatally exposed and non-exposed group for both sexes (boys: mean difference = 17.07, t (25) = .87, $p = .40$; girls: mean difference = -32.63, t (32) = -1.52, $p = .14$).

Cortisol levels at T1, T2, and T3, for prenatally exposed and non-exposed boys and girls are displayed in Table 3.2. Correlations between T1, T2, and T3 are significant and range between .52 and .84.

Table 3.2 Cortisol levels (log scores) at T1 (basal), T2, and T3

	Exposed		Non-exposed	
	Boys ($N = 25$)	Girls ($N = 24$)	Boys ($N = 19–22$)	Girls ($N = 27–29$)
T1 *M* (*SD*)	.37 (.29)	.60 (.42)*	.45 (.27)	.39 (.26)
T2 *M* (*SD*)	.21 (.22)	.39 (.29)*	.34 (.23)	.24 (.23)
T3 *M* (*SD*)	.17 (.25)	.30 (.23)	.34 (.19)	.27 (.28)

* $p < .05$, sex differences within the prenatally exposed group. NB see text for differences between exposed versus non-exposed group.

Main results

A repeated measures analysis of variance was performed to examine the differences in the levels as well as the patterns of cortisol responses at T1, T2, and T3 between the prenatally exposed and non-exposed groups. Children's age and time of home visit were entered as covariates in the analyses. The analyses were performed separately for boys and girls.

Girls

In the analyses for girls a significant difference in cortisol levels is found between the groups ($F(1,44) = 5.685$, $p = .02$, partial eta squared = .11). Pairwise comparisons revealed that prenatally exposed girls show higher cortisol levels (mean difference = .158, se = .066, $p = .021$) compared to prenatally non-exposed girls. Furthermore, a significant within subjects effect for measurement time during the home visit was seen, $F(2,43) = 6.05$, $p = .005$, eta squared = .22. Figure 3.1 shows the decline in cortisol levels for both groups from the first to the third measurement, as well as the consistently higher cortisol levels in the exposed group. After the stressful task the exposed girls show a further decline in cortisol levels between T2 and T3, whereas the non-exposed girls show a slight increase. However, the response patterns of the groups, reflected in the interaction of group by cortisol levels, did not differ significantly ($F(2,43) = 1.57$, $p = .22$, partial eta squared = .07).

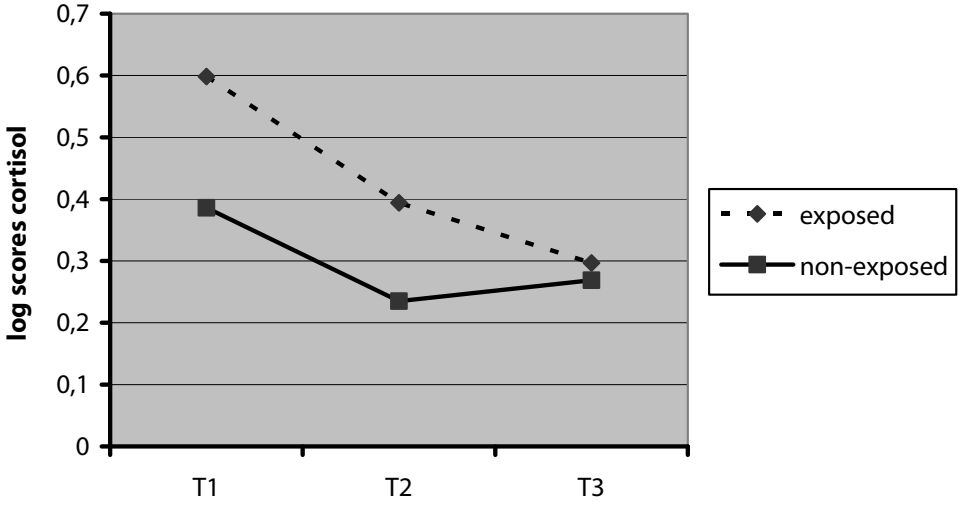

Figure 3.1 Cortisol response patterns of girls.

Boys

Analyses for boys controlling for age and time of day, show that the between subjects effect of group is not significant ($F(1,40) = 1.517$, $p = .23$, partial eta squared = .037). Figure 3.2 demonstrates a significant within subjects effect for time of cortisol measure during the home visit, $F(2,39) = 6.24$, $p = .004$, partial eta squared = .24, with both groups of boys showing a reduction in cortisol levels across the three measurements. The response patterns of the groups, reflected in the interaction of group by cortisol levels, did not differ significantly ($F(2,39) = 1.11$, $p = .34$, partial eta squared = .05).

Interestingly, as can be seen from Figures 3.1 and 3.2, boys and girls show the same cortisol response patterns in that they start with higher cortisol values than they have by the end of the home visit. These results led to additional exploratory analyses on gender differences within the exposed and non-exposed group. Using one-way analysis of variance, controlling for children's age and time of home-visit, cortisol levels between boys and girls were compared. Prenatally exposed girls show higher basal cortisol ($F(1,45) = 4.56$, $p = .038$) and cortisol levels at T2 ($F(1,45) = 5.84$, $p = .020$) compared to prenatally exposed boys. No significant differences were found for prenatally non-exposed boys and girls.

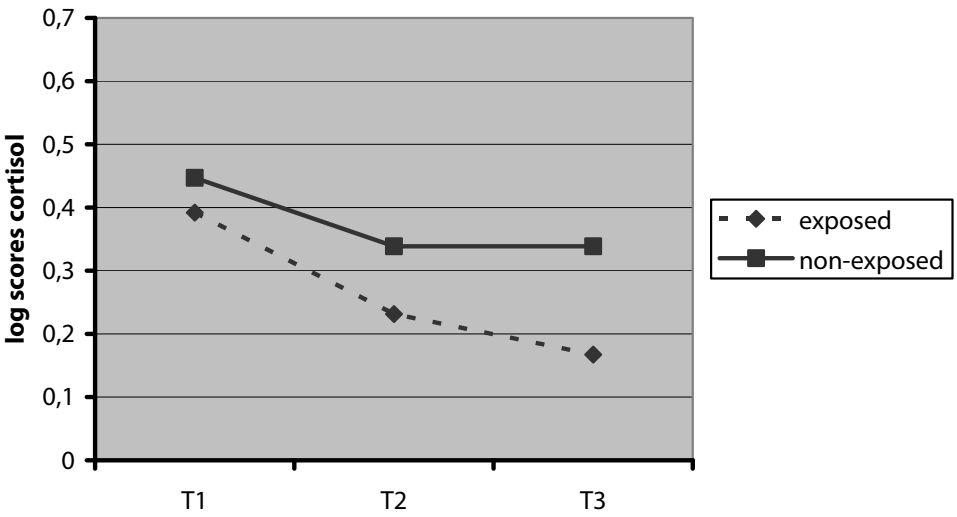

Figure 3.2 Cortisol response patterns of boys.

Discussion

During a home visit, different levels of cortisol responses are found between girls who were prenatally exposed to maternal emotional complaints and prenatally non-exposed girls. Prenatally exposed girls show higher cortisol levels compared to non-exposed girls. Contrary to the girls, the differences in cortisol levels between the exposed and non-exposed boys were not significant. Consequently prenatal maternal emotional complaints are related differently to the functioning and maybe programming of the HPA-axis for boys and girls. The current findings corroborate our results concerning sex differences in the association between prenatal exposure to maternal emotional complaints and outcome in the children measured by questionnaires on behavioural problems (de Bruijn et al., 2009). Gender seems to be influencing the processes involved, indicating that sex hormones, or sex related genetic factors play an important role. This finding corroborates results of van den Bergh et al. (2008), who concluded that prenatal maternal anxiety induces gender-specific changes in the HPA-axis functioning. Our design was not genetically sensitive. The women in the target group in our study might have a genetic predisposition for emotional complaints. As a consequence, their children might inherit this genetic risk for emotional problems. This may in part explain the results found in our study, at least for girls. Moreover, due to an interaction between genes and environment or a "nature-nurture interplay" (Silberg & Rutter, 2002), parents who pass on a genetic risk to their children tend also to create environments that may sensitize their children (Elgar et al., 2004). As we do not find differences in cortisol responses of exposed and non-exposed boys, neurobiological processes related to sex hormones are important next to genetic factors. Furthermore, the environment that elicits the emotional complaints of the mothers, is also likely the post-partum environment the child is experiencing, such as an environment with low income, social disadvantage and low social support (Elgar et al., 2004). Moreover, Hay et al. (2008) suggested that recurring episodes of maternal depression during the child's lifetime, often accompanied by disruption in family arrangements and the child's routines and activities, creates a gene-environment correlation that increases risk for both affective disorders and disruptive behaviour disorder.

In both prenatally exposed boys and girls, no significant increase in cortisol levels after the frustration task was found. This is not in line with the current view in animal research that maternal prenatal stress may induce overactivity of the HPA-axis (Weinstock et al., 1992). It may be that our frustration task was not an optimal stressor to elicit clear cortisol responses. Also in the non-exposed boys and girls no clear changes in cortisol responses were found after the stressful task. From the animal literature it appears that cortisol is not responsive to all types of stressors. In human adults it has been found that situations that are uncontrollable and contain social-evaluative elements are associated with the largest cortisol changes (Dickerson & Kemeny, 2004). The toddlers might not perceive our task as uncontrollable because different strategies to open the box could be used and therefore some control could be exerted over the situation. Our task was based upon the task used by Calkins and Johnson (1998) that elicited sufficient stress behaviours in toddlers. However, the children in their study

were 18 months old, whereas the age of the children in our sample ranged between 23 and 60 months.

Interestingly, higher cortisol levels are found at the start of the home visit for all children and decreased during the session. This is in accordance with earlier studies (for a review see Jessop & Turner-Cobb, 2007). The procedure of saliva sampling, as well as the location, has been found to have an effect on cortisol levels. In earlier studies, saliva was collected at home or in a laboratory setting. A laboratory, compared to the home, might be perceived as a stressful environment in itself, which may elevate basal cortisol levels (Jessop & Turner-Cobb, 2007). Basal cortisol levels were found to be higher in a laboratory setting compared to samples taken at home, in a sample of 7–9 year olds (Jones et al., 2006) and in a study of 9-year-old girls (Gunnar, 2003). However, Gunnar and Donzella (2002) have mentioned in their review contradictory effects when measuring cortisol in the laboratory in younger children of preschool age. Studies typically conducted in the morning hours, have revealed that cortisol levels upon arrival for testing in the laboratory were significantly lower than levels obtained at home at the same time of day (Gunnar & Donzella, 2002). In most studies where saliva is measured at home, saliva is collected with the aid of the parents. In our study saliva was collected by a researcher, an unknown person for the child. Perhaps the announced home visit and its social element in itself was a more important and uncontrollable stressor for the children in our study compared to the frustration task with the plexiglas box. The mothers may have informed the children before the home visit that a person is coming to play games with him/her. As a result, the potential stressful event likely started prior to the arrival of the researcher (Dozier, Peloso, Lewis, Laurenceau, & Levine, 2008; Gunnar & Donzella, 2002). This excitement or anticipatory stress may have resulted in higher cortisol baseline levels. Furthermore, girls prenatally exposed to high levels of emotional complaints may have shown the highest cortisol levels, because they have become more sensitive to potentially stressful situations. The exposure to prenatal stress of their mothers might have programmed the HPA-axis of girls and caused overactivity of their stress system. They might produce a stronger cortisol response when exposed in a novel, potential challenging situation, as was found in animal studies (Weinstock et al., 1992) and as a consequence produce higher baseline cortisol levels as a reaction to the home visit.

A meta-analysis of Alink et al. (2008) on cortisol reactivity and externalizing behaviour, reported on studies using different types of stressors that often did not result in a cortisol increase in the total group. Over the course of the first year, the HPA-axis does not respond as much to stressors as it does in older individuals. This stress hyporesponsive period might extend throughout childhood (Gunnar & Fisher, 2006). For children two through five years of age, hardly any stressor paradigm used has effectively elevated cortisol levels (Gunnar, Talge, & Herrera, 2009). In the study of Calkins and Johnson (1998) cortisol reactivity was not measured. They measured physiological arousal using baseline measures of vagal tone and heart period. They found no significant relation between the behavioural scoring of distress and physiological measures of heart period and vagal tone. The authors concluded that, by the age of 18 months, there might

not be a direct mapping of emotional and physiological reactivity. They propose that children may engage in emotion regulating behaviours during the frustration task that alter the behavioural display of distress, but nevertheless may remain physiologically aroused. Emotion and physiological reactivity may be two independent constructs. In our study, we have not coded behavioural stress reactivity of the children after the frustration task. It is possible that the children did show stress behaviours that were not reflected in their physiological, cortisol, reactivity.

Interestingly, higher cortisol levels are found at the start of the home visit and at T2 for prenatally exposed girls compared to prenatally exposed boys. These differences might reflect normal differences in HPA-axis function between boys and girls as reported in recent studies. For example, Rosmalen et al. (2005) found that the awakening cortisol response is significantly higher in 10–12 year old girls compared to boys. In a review on animal studies by McCormick and Mathews (2007) it is reported that, because of the influence of sex hormones on HPA-axis function, adult females have higher basal and stress levels of ACTH and corticosterone than males.

Another important variable that might have affected HPA-axis functioning in the children is maternal sensitivity during interaction. In a recent study of Blair, Douglas, Willoughby, and Kivlighan (2006) it was found that 6-month-old infants of more sensitive mothers had lower levels of baseline cortisol and increased cortisol reactivity and regulation in response to procedures designed to elicit negative affect. The non-exposed girls in our group also have lower cortisol baseline levels compared to the exposed girls. Because antenatal mood disturbance predicts postpartum depression (Heron, O 'Connor, Evans, Golding, & Glover, 2004), it is possible that the mothers of the prenatally exposed girls also were bothered by emotional complaints after birth. Maternal depression and anxiety are related to disturbances in the quality of parenting, specifically in parental sensitivity (Kaplan, Evans, & Monk, 2008). If the mothers are currently suffering from emotional complaints, they might interact more negatively and less sensitively with their child, which subsequently might lead to more behavioural problems in their children and higher cortisol levels (Elgar, McGrath, Waschbusch, Stewart, & Curtis, 2004; Blair et al., 2006). As a result, these prenatally exposed girls may show higher baseline cortisol levels and higher cortisol levels overall. Also in the study of Kaplan et al. (2008) a significant interaction effect between prenatal maternal psychiatric status and postnatal maternal sensitivity was found for cortisol levels in 4-month-old infants. Compared to prenatally stressed infants with sensitive mothers, only prenatally stressed infants who postnatally received insensitive care, showed higher cortisol levels at 4 months. The authors concluded that the association between prenatal maternal psychiatric status and infant HPA-axis programming appears to be modulated by maternal sensitivity. Sex differences are not addressed in the study of Kaplan et al. (2008). Girls, compared to boys, are better at interpreting non-verbal cues (Lindahl & Heimann, 1997) and might be more influenced by their mothers' insensitive caregiving. This might explain the higher cortisol levels found in prenatally exposed girls compared to boys. Further study on the relation between cortisol responses and the quality of mother-child interaction, is currently performed within our sample.

To conclude, prenatal maternal emotional complaints are found to be related to HPA-axis functioning, as prenatally exposed toddler or preschool aged girls show higher cortisol levels compared to non-exposed girls. Moreover, prenatally exposed girls were found to have higher cortisol levels compared to prenatally exposed toddler or preschool aged boys. This study was among the first, to study the influences of maternal prenatal emotional complaints on HPA-axis of toddlers and preschoolers separately for boys and girls. More research concerning sex differences is needed to illuminate the underlying mechanisms.

References

Alink, L. R. A., van IJzendoorn, M. H., Bakermans-Kranenburg, M. J., Mesman, J., Juffer, F., & Koot, H. M. (2008). Cortisol and externalizing behavior in children and adolescents: Mixed meta-analytic evidence for the inverse relation of basal cortisol and cortisol reactivity with externalizing behavior. *Developmental Psychobiology*, *50*, 427–450.

Arrindell, W. A. & Ettema, J. H. M. (2003). *SCL-90. Handleiding bij een multidimensionele psychopathologie-indicator*. Lisse, The Netherlands: Swets and Zeitlinger,

Becht, M.C., van Erp, C.F., Teeuwisse, T. M., van Heck, G. L., van Son, M. J, & Pop, V.J. (2001). Measuring depression in women around menopausal age towards a validation on the Edinburgh Depression Scale. *Journal of Affective Disorders*, *63*, 209–213.

Blair, C., Douglas, G., Willoughby, M., & Kivlighan, K. (2006). Maternal sensitivity is related to hypothalamic-pituitary- adrenal axis stress reactivity and regulation in response to emotion challenge in 6-month-old infants. *Annals of the New York Academy of Sciences*, *1094*, 263–267.

Brennan, P. A., Pargas, R., Walker, E. F., Green, P., Jeffrey Newport, D., & Stowe, Z. (2008). Maternal depression and infant cortisol: influences of timing, comorbidity and treatment. *Journal of Child Psychology and Psychiatry*, *49*, 1099–1107.

Brouwers, E. P. M., van Baar, A. L., & Pop, V. J. M. (2001). Maternal anxiety during pregnancy and subsequent infant development. *Infant Behavior and Development*, *24*, 95–106.

Calkins, S. D. & Johnson, M. C. (1998). Toddler regulation of distress to frustrating events: Temperamental and maternal correlates. *Infant Behavior and Development*, *21*, 379–395.

Cox, J. L., Holden, J. M., & Sagovsky, R. (1987). Detection of postnatal depression. *British Journal of Psychiatry*, *150*, 782–786.

De Bruijn, T. C. E., van Bakel, H. J. A., & van Baar, A. L. (2009). Sex differences in the relation between prenatal maternal emotional complaints and child outcome. *Early Human Development*, *85*, 319–324.

Derogatis, L. R., Lipman, R. S., & Covi, L. (1973). SCL-90: an outpatient psychiatric rating scale – preliminary report. *Psychopharmacological Bulletin*, *9*, 13–28.

De Weerth, C., Zijl, R. H., & Buitelaar, J. K. (2003). Development of cortisol circadian rhythm in infancy. *Early Human Development*, *73*, 39–52.

Dickerson, S. S., & Kemeny, M. E. (2004). Acute stressors and cortisol responses: A theoretical integration and synthesis of laboratory research. *Psychological Bulletin*, *130*, 355–391.

Dozier, M., Peloso, E., Lewis, E., Laurenceau, J. P., & Levine, S. (2008). Effects of an attachment-based intervention on the cortisol production of infants and toddlers in foster care. *Development and Psychopathology*, *20*, 845–859.

Dressendörfer, R. A., Kirschbaum, C., Rohde, W., Stahl, F., & Strasburger, C. J. (1992). Synthesis of a cortisol-biotin conjugate and evaluation as a tracer in an immunoassay for salivary cortisol measurement. *Journal of Steroid Biochemistry and Molecular Biology*, *43*, 683–692.

Elgar, F. J., McGrath, P. J., Waschbusch, D. A., Stewart, S. H., & Curtis, L. J. (2004). Mutual influences on maternal depression and child adjustment problems. *Clinical Psychology Review*, *24*, 441–459.

Field, T., Diego, M., Dieter, J., Hernandez-Reif, M., Schanberg, S., Kuhn, C., Yando, R., & Bendell, D. (2004). Prenatal depression effects on the fetus and the newborn. *Infant Behavior and Development*, *27*, 216–229.

Gitau, R., Cameron, A., Fisk, N. M., & Glover, V. (1998). Fetal exposure to maternal cortisol. *Lancet*, *352*, 707–708.

Gröschl, M., Wagner, R., Rauh, M., & Dörr, H. G. (2001). Stability of salivary steroids: the influences of storage, food, and dental care. *Steroids*, *66*, 737–741.

Gunnar, M. (2003). Integrating neuroscience and psychological approaches in the study of early experiences. *Annals of the New York Academy of Sciences*, *1008*, 238–247.

Gunnar, M. & Donzella, B. (2002). Social regulation of the cortisol levels in early human development. *Psychoneuroendocrinology*, *27*, 199–220.

Gunnar, M. & Fisher, P. A. (2006). Bringing basic research on early experience and stress neurobiology to bear on preventive interventions for neglected and maltreated children. *Development and Psychopathology*, *18*, 651–677.

Gunnar, M., Talge, N. M., & Herrera, A. (2009). Stressor paradigms in developmental studies: What does and does not work to produce mean increases in salivary cortisol. *Psychoneuroendocrinology*, *34*, 953–967.

Gutteling, B. M., de Weerth, C., & Buitelaar, J. K. (2004). Maternal prenatal stress and 4–6 year old children's salivary cortisol concentrations pre- and post-vaccination. *Stress*, *7*, 257–260.

Gutteling, B. M., de Weerth, C., & Buitelaar, J. K. (2005). Prenatal stress and children's cortisol reaction to the first day of school. *Psychoneuroendocrinology*, *30*, 541–549.

Hay, D. F., Pawlby, S., Waters, C. S., & Sharp, D. (2008). Antepartum and postpartum exposure to maternal depression: different effects on different adolescent outcomes. *Journal of Child Psychology and Psychiatry*, *49*, 1079–1088.

Heron, J., O'Connor, T. G., Evans, J., Golding, J., & Glover, V. (2004). The course of anxiety and depression through pregnancy and the postpartum in a community sample. *Journal of Affective Disorders*, *80*, 65–73.

Hughes, J. W., Watkins, L., Blumenthal, J. A., Kuhn, C., & Sherwood, A. (2004). Depression and anxiety symptoms are related to increased 24-hour urinary norepinephrine excretion among healthy middle-aged women. *Journal of Psychosomatic Research*, *57*, 353–358.

Huizink, A. C., Bartels, M., Rose, R. J., Pulkkinen, L., Eriksson, C. J. P., & Kaprio, J. (2008). Chernobyl exposure as stressor during pregnancy and hormone levels in adolescents offspring. *Journal of Epidemiology and Community Health*, *62*, e5.

Huizink, A. C., Mulder, E. J. H., & Buitelaar, J. K. (2004). Prenatal stress and risk for psychopathology: Specific effects or induction of general susceptibility? *Psychological Bulletin*, *130*, 115–142.

Jessop, D. S., & Turner-Cobb, J. M. (2007). Measurement and meaning of salivary cortisol: A focus on health and disease in children. *Stress*, *11*, 1–14.

Jones, A., & Godfrey, K. M., & Wood, P., Osmond, C., Goulden, P., & Philips, D. I. (2006). Fetal growth and the adrenocortical response to psychological stress. *Journal of Clinical Endocrinology and Metabolism*, *91*, 1868–1871.

Kaplan, L. A., Evans, L., & Monk, C. (2008). Effects of mothers' prenatal psychiatric status and postnatal caregiving on infant biobehavioral regulation: can prenatal programming be modified? *Early Human Development*, *84*, 249–256.

Keenan, K., Gunthorpe, D., & Grace, D. (2007). Parsing the relations between SES and stress reactivity: Examining individual differences in neonatal stress response. *Infant Behavior and Development*, *30*, 134–145.

Kudielka, N. M., & Kirschbaum, C. (2005). Sex differences in HPA axis response to stress: a review. *Biological Psychology*, *69*, 113–132.

Lindahl, L. B., & Heimann, M. (1997). Research report: Social proximity in early mother-infant interactions: Implications for gender differences? *Early Development and Parenting*, *6*, 83–88.

Lundy, B. L., Jones, N. A., Field, T., Nearing, G., Davalos, M., Pietro, P. A., Schanberg, & S., Kuhn, C. (1999). Prenatal depression effects on neonates. *Infant Behavior and Development*, *22*, 119–129.

Matthews, S. G. (2002). Early pogramming of the hypothalamo-pituitary-adrenal axis. *Trends in Endocrinology & Metabolism*, *13*, 373–380.

McCormick, C. M., & Mathews, I. Z. (2007). HPA function in adolescence: Role of sex hormones in its regulation and the enduring consequences of exposure to stressors. *Pharmacology, Biochemistry and Behavior*, *86*, 220–233.

Montano, M. M., Wang, M-H, & vom Saal, F. S. (1993). Sex differences in plasma corticosterone in mouse fetuses are mediated by differential placental transport from the mother and eliminated by maternal adrenalectomy or stress. *Journal of Reproduction and Fertility*, *99*, 283–290.

Mulder, E. J. H., Robles de Medina, P. G., Huizink, A. C., Van den Bergh, B. R. H., Buitelaar, J. K., & Visser, G. H. A. (2002). Prenatal maternal stress: effects on pregnancy and the (unborn) child. *Early Human Development*, *70*, 3–14.

O'Connor, T. G., Ben-Shlomo, Y., Heron, J., Golding, J., Adams, D., & Glover, V. (2005). Prenatal anxiety predicts individual differences in cortisol in pre-adolescent children. *Biological Psychiatry*, *58*, 211–217.

Pop, V. J., Komproe, I. H., & van Son, M. J. (1992). Characteristics of the Edinburgh Post Natal Depression Scale in the Netherlands. *Journal of Affective Disorders*, *26*, 105–110.

Pop, V. J., Wijnen, H. A., Lapkienne, L., Bunivicius, R., Vader, H. L., & Essed, G. G. (2006). The relation between thyroid parameters and depression: A reflection of the downregulation of the immune system during pregnancy? *Thyroid*, *16*, 485–492.

Ramsay, D. & Lewis, M. (2003). Reactivity and regulation in cortisol and behavioural responses to stress. *Child Development*, *74*, 456–464.

Ressler, K. J. & Nemeroff, C. B. (2000). Role of serotonergic and noradrenergic systems in the pathophysiology of depression and anxiety disorders. *Depression and Anxiety*, *12*, 2–19.

Rosmalen, J. G. M., Oldehinkel, A. J., Ormel, J., de Winter, A. F., Buitelaar, J. K., & Verhulst, F. C. (2005). Determinants of salivary cortisol in 10–12 year old children; a population-based study of individual differences. *Psychoneuroendocrinology*, *30*, 483–495.

Rutter, M., Caspi, A., & Moffitt, T. E. (2003). Using sex differences in psychopathology to study causal mechanisms: unifying issues and research strategies. *Journal of Child Psychology and Psychiatry*, *44*, 1092–1115.

Silberg, J., & Rutter, M. (2002). Nature-nurture interplay in the risk associated with parental depression. In S. H. Goodman, & I. H. Gotlib (Eds.), *Children of depressed parents: Mechanisms of risk and implications for treatment* (pp.13–36). Washington, DC: American Psychological Association.

Spielberger, C. D., Gorsuch, R. L., & Lushene, R. E. (1970). *STAI Manual for the State-trait Anxiety Inventory*. Palo Alto, California: Consulting Psychologists Press.

Talge, N. M., Neal, C., & Glover, V. (2007). Antenatal maternal stress and long-term effects on child neurodevelopment: How and why? *Journal of Child Psychology and Psychiatry*, *48*, 245–261.

Van den Bergh, B. R. H., van Calster, B., Smits, T., van Huffel, S., & Lagae, L. (2008). Antenatal maternal anxiety is related to HPA-Axis dysregulation and self-reported depressive symptoms in adolescence: A prospective study on the fetal origins of depressed mood. *Neuropsychopharmacology*, *33*, 536–545.

Van der Ploeg, H. M. (2000). *Handleiding bij de Zelf-Beoordelings Vragenlijst ZBV*. Lisse, The Netherlands: Swets and Zeitlinger.

Wadhwa, P. D. (2005). Psychoneuroendocrine processes in human pregnancy influence fetal development and health. *Psychoneuroendocrinology*, *30*, 724–743.

Weinstock, M. (2008). The long-term behavioural consequences of prenatal stress. *Neuroscience and Biobehavioral Reviews*, *32*, 1073–1086.

Weinstock, M., Matlina, E., Maor, G. I., Rosen, H., & McEwen, B. S. (1992). Prenatal stress selectivley alters the reactivity of the hypothalamic-pituitary-adrenal system in the female rat. *Brain Research*, *595*, 195–200.

Wijnen, H. (2005). *The Kempen study: Aspects of maternal well-being and obstetrical outcome in relation to gestational thyroid function*. PhD Thesis, Tilburg University, The Netherlands.

4

The influence of prenatal maternal emotional complaints on child behavioural problems is moderated by the quality of postnatal maternal interaction style

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Abstract

Background: Prenatal maternal emotional complaints are associated with increased difficulties in child motor, cognitive, and especially socio-emotional development. This study reports on the role of the mother-child interaction in the relationship between prenatal maternal emotional complaints and behavioural problems of toddlers and preschool aged children, for boys and girls separately.

Methods: Interaction processes and child behavioural problems are compared in two groups that differ according to prenatal maternal emotional complaints (N = 66), or not (N = 66). Healthy pregnant, Dutch Caucasian women (N = 132, M age = 30.9 years, SD = 3.8) completed questionnaires of anxiety and depression in week 12, 24, and 36 of gestation. When the children were between 23–60 months of age (M age = 38.6 months, SD = 9.4) both parents completed the Child Behaviour Check List (CBCL 1½–5). During a home visit, mothers and their children performed several tasks together, to assess the mother-child interaction using the Emotional Availability Scales (EAS).

Results: No significant differences were found in the quality of the mother-child interaction processes between the prenatally exposed and non-exposed group. Multiple hierarchical regression analyses showed a significant moderator effect of maternal interaction style on the relation between prenatal emotional complaints and internalizing problems of girls. Prenatally exposed girls showed more internalizing problems if the quality of their mothers' interaction behaviour was less optimal. More specifically, the quality of maternal structuring behaviour and non-hostility moderated the association between prenatal maternal emotional complaints and internalizing problems of girls. No significant effects were found for boys.

Conclusion: The early caregiving interaction processes modulate the association between prenatal maternal emotional complaints and child behavioural problems, especially for girls.

Introduction

Maternal emotional complaints during pregnancy are associated with more difficulties in children's motor, cognitive, and especially socio-emotional development from infancy to adolescence (O'Donnell, O'Connor, & Glover, 2009). For example, children prenatally exposed to maternal stress show more behavioural and emotional problems (Gutteling et al., 2005; O'Connor, Heron, Golding, Beveridge, & Glover, 2002), have a more negative temperament (Davis et al., 2007), and show more symptoms of ADHD (Van den Bergh & Marcoen, 2004; Rodriguez & Bohlin, 2005). A potentially underlying mechanism to explain these associations is fetal programming of the Hypothalamic – Pituitary – Adrenal (HPA) axis (van den Bergh, van Calster, Smits, van Huffel, & Lagae, 2008).

However, other factors could also explain the relationship between prenatal maternal emotional complaints and children's developmental outcome. The quality of the postnatal maternal interaction or parenting style might have an effect on children's behavioural problems. Maternal depression and anxiety are related to disturbances in the quality of parenting, specifically in parental sensitivity (Lovejoy, Graczyk, O'Hare, & Neuman, 2000). Depressed parents have been found to be more negative, guilt-inducing, critical, unsupportive and intrusive with their children and to demonstrate more negative affect (Cummings & Davies, 1999; Lovejoy et al., 2000). Such negative

interaction processes are associated with behavioural problems in the children (Elgar, McGrath, Waschbusch, Stewart, & Curtis, 2004; Leckman-Westin, Cohen, & Stueve, 2009). Because antenatal mood disturbance predicts postpartum depression (Heron, O'Connor, Evans, Golding, & Glover, 2004) and 80 % of depression is recurrent (Goodman & Gotlib, 2002) it is possible that depressive or anxious complaints in prenatally stressed women persist or recur after birth. If the mothers are (also) suffering from emotional complaints after giving birth, they might interact more negatively and less sensitively with their child, which subsequently might lead to more behavioural problems in their children.

However, no human studies have been reported yet on mother-child interaction processes in relation to prenatal maternal emotional complaints and children's behavioural problems. A few studies reported related information. Leckman-Westin et al. (2009) analyzed the moderating role of mother-child interactive patterns on the association between (postnatal) maternal depressive symptoms and behavioural problems in the children. They have found that depressive symptoms, together with problematic mother-child interaction behaviour, raise the risk of toddler behavioural problems. Kaplan, Evans, and Monk (2008) found a significant interaction effect between prenatal maternal psychiatric status and postnatal maternal sensitivity for baseline salivary cortisol levels in 4-month-old infants. Compared to prenatally stressed infants with sensitive mothers, only prenatally stressed infants who postnatally received insensitive care, showed higher cortisol levels at 4 months. The authors concluded that infant HPA-axis programming appears to be modulated by maternal sensitivity.

More research on the effects of maternal emotional complaints during pregnancy and developmental outcome of the children in relation to the quality of the mother-child interaction is needed. First, if mothers with or without prenatal emotional complaints differ in their interaction quality, these differences may completely mediate the associations between prenatal maternal emotional complaints and child behavioural problems. Prevention of (part) of the child behavioural problems then should be focused at the improvement of mother-child interaction processes. Second, if the postnatal interaction processes do not fully mediate the relationship between prenatal emotional complaints and child development, important moderation effects could still be present and prevention activities should be targeted at reduction of emotional complaints during pregnancy as well as at improvements of mother-child interaction processes. Finally, if mothers with or without prenatal emotional complaints do not differ clearly in the quality of their interaction with their children and no moderation effects are found, the role of the prenatal programming processes is most important and prevention should be targeted primarily at the emotional complaints of pregnant women.

We studied the quality of mother-child interaction processes in a group of mothers that reported prenatal emotional complaints compared to a group that did not report emotional complaints during pregnancy. In addition, the role of the quality of the maternal interaction style in the associations between prenatal maternal emotional complaints and internalizing and externalizing behavioural problems of toddlers and preschoolers was studied.

First, we hypothesize that women with prenatal emotional complaints show a less optimal interaction style compared to women with no emotional complaints during pregnancy. Second, we hypothesize that the quality of the postnatal maternal interaction style might act as a moderator in the association between prenatal maternal emotional complaints and child behavioural problems.

Furthermore, in our previous study the pattern of associations between prenatal maternal emotional complaints and child behavioural problems was found to differ for boys and girls (de Bruijn, van Bakel, & van Baar, 2009a). Hence we hypothesize a gender difference for the associations between prenatal emotional complaints, maternal interaction styles and behavioural outcome of the children.

Methods

Participants

This study is part of a prospective ongoing research line, which investigates the influence of prenatal maternal emotional complaints on the self-regulation and socio-emotional adjustment of toddlers and preschoolers in relation to parental interaction styles (de Bruijn et al., 2009a). For the current study, 222 families were asked for participation of which 132 agreed (59.5%; 67 girls, 65 boys, *M* age = 38.6 months, *SD* = 9.4, range = 23–60 months). No differences were found between participants and non-participants in scores on prenatal anxiety and / or depression measures. Children whose mothers scored above a standardized cut off, or higher than one standard deviation above the mean, on one of the three prenatal measurements of anxiety or depression at 12, 24 or 36 weeks in pregnancy were selected for the target (prenatally exposed, $N = 66$) group. For the comparison group (prenatally non-exposed, $N = 66$), children were selected whose mothers had at least given information in two of the three trimesters of pregnancy and did not report high scores for any of the prenatal depression or anxiety questionnaires. The comparison children were matched to the target cases regarding month of birth and sex (de Bruijn, van Bakel, Wijnen, Pop, & van Baar, 2009b). The Medical Ethical Committee of the St. Elisabeth Hospital in Tilburg approved this study.

Measures

Depression

Prenatal depression of the mothers was assessed using the Dutch version of the Edinburgh Depression Scale (EDS; Cox, Holden, & Sagovsky, 1987; Pop, Komproe, & van Son, 1992) at 12, 24 and 36 weeks' gestation. The EDS is a widely used 10-item self-report scale designed as a screening instrument for depression and has been shown valid in and outside the postnatal period. Items are scored on four-point rating scales. Total scores range between 0 and 30. A cut-off score of 12 and higher was used (Becht et al., 2001) to indicate major depression (normal population mean 5.89, *SD* = 4.03; Pop et al., 1992).

Anxiety

Prenatal anxiety of the mothers was assessed with the State version of the State-Trait Anxiety Inventory (STAI; Spielberger, Gorsuch, & Lushene, 1970) at 12, 24 and 36 weeks' gestation. The STAI consists of two subscales each containing 20 items. The state anxiety subscale measures transient anxiety or anxiety at the moment of scoring. Trait anxiety measures dispositional anxiety or anxiety in general. The State version was used to assess the feelings of anxiety of the women during a specific period in their pregnancy. Total scores on the State subscale range between 20 and 80. The Dutch version of the STAI has been validated previously (Cronbach's alpha = .95, normal population mean for non-pregnant women < 40 years = 38.0, *SD* = 12.8; Van der Ploeg, 2000). In our study a score above 39 (that is > 1 *SD* above the mean in our sample of pregnant women) was used as cut off, reflecting a high level of complaints.

Prenatal anxiety was also assessed with the anxiety subscale of the Dutch version of the Symptom Check List (SCL-90; Derogatis, Lipman, & Covi, 1973; Arrindell & Ettema, 2003) a 90 item self-report scale that measures several dimensions in psychopathology. The SCL-90 has been validated before in the Netherlands and its use as well as the use of several subscales only, has revealed appropriate psychometric properties (Cronbach's alpha of anxiety subscale = .87; Arrindell & Ettema, 2003). Total scores of the anxiety subscale range between 10 and 50 (normal population mean for women = 13.43, *SD* = 4.91; for men: 12.23, *SD* = 3.80; Arrindell & Ettema, 2003). In our study, a score above 17 (that is > 1 *SD* above the mean in our sample of pregnant women) was used as cut off, reflecting a high level of complaints.

Strong correlations were found between the results of the same questionnaire answered at different weeks in pregnancy (*r* EDS at 12, 24, and 36 weeks range between .55 and .70; *r* STAI range between .52 and .64, *r* SCL range between .45 and .65). A mean score was computed by averaging the scores on the three prenatal maternal EDS measures to create a mean prenatal EDS score (MEDS) during the total course of pregnancy. Identically, sum scores on the prenatal maternal SCL and STAI measures were also created to obtain a mean prenatal SCL score (MSCL) and a mean prenatal STAI score (MSTAI) (see Table 4.1).

Current emotional complaints

Postnatally, both parents answered the EDS, STAI, and SCL to measure their current emotional complaints. Because of high inter correlations between these measures (de Bruijn et al., 2009a) they were standardized and summed to create a total current emotional complaints score for mothers and for fathers separately. These total sum scores were used in subsequent analyses.

Mother-child interaction

The mother-child dyads were visited at home by one researcher (AdB) when the children were between 23 and 60 months old. During this home visit a semi-structured procedure was followed. The mothers and children were instructed to perform several tasks together to observe the mother-child interaction (for details of the procedure of

Table 4.1 Descriptive characteristics

	Prenatally exposed *N* = 66		Prenatally non-exposed *N* = 66	
	Boys (*N* = 25–36)	Girls (*N* = 24–30)	Boys (*N* = 19–29)	Girls (*N* = 27–37)
Age child, months *M* (*SD*)	40.6 (4.0)	37.6 (9.0)	35.1 (8.7)	40.2 (8.2)[b]
Birth weight child in grams *M* (*SD*)	3658 (562)	3408 (415)[a]	3827 (434)	3457 (429)[b]
Gestational age *M* (*SD*)	40.0 (1.3)	40.0 (1.2)	40.3 (1.2)	40.0 (1.1)
Age mother at birth, years *M* (*SD*)	31.9 (4.0)	30.4 (3.5)	30.6 (3.9)	30.6 (3.7)
Education mother				
% low	8.3	13.3	3.4	2.7
% middle	61.1	43.3	58.6	40.5
% high	30.6	43.3	37.9	54.1
Education father				
% low	8.3	16.7	10.3	2.7
% middle	44.4	46.7	41.4	54.1
% high	38.9	36.7	44.8	43.2
Prenatal complaints				
EDS *M* (*SD*)	7.4 (3.0)	8.2 (3.4)	3.1 (2.3)	2.6 (2.1)
STAI *M* (*SD*)	38.0 (6.0)	40.0 (5.8)	26.5 (4.3)	26.2 (4.3)
SCL *M* (*SD*)	14.7 (2.8)	15.8 (4.4)	11.3 (1.1)	11.1 (1.4)
Current emotional complaints *M* (*SD*)				
Maternal EDS	6.0 (4.6)	9.6 (5.4)	4.0 (4.3)	3.6 (4.1)
Maternal SCL	13.5 (5.5)	16.2 (8.6)	10.8 (1.9)	10.8 (2.4)
Maternal STAI	38.2 (10.0)	36.5 (10.7)	27.5 (5.5)	28.7 (7.3)
Paternal EDS	3.3 (3.6)	6.6 (5.0)	2.6 (3.2)	2.4 (2.9)
Paternal SCL	12.2 (5.4)	12.9 (4.3)	10.8 (2.2)	10.6 (2.3)
Paternal STAI	31.6 (9.9)	34.4 (6.8)	29.6 (7.1)	31.7 (6.1)

[a] sex difference within the prenatally exposed group. [b] sex difference within the prenatally non-exposed group. NB see text for exposed versus non-exposed group differences.

the home visit see de Bruijn et al., 2009b). During this visit, the quality of mother-child interaction processes was observed during three videotaped tasks. First, the mother and child were asked to play together with clay, followed by a puzzle task. Then mother and child were given a marble game to play with. The first five minutes of each interaction task were observed. Assessment of interaction behaviour was based on the total of 15 minutes of play observation during these different tasks. This was coded using the Emotional Availability Scales (EAS), Infancy to Early Childhood Version, 3rd Edition (Biringen, Robinson, & Emde, 1998; Biringen, 2000). The EAS is a global rating scale that emphasizes behavioural style rather than discrete behaviours. It consists of six subscales: parental sensitivity, structuring, non-intrusiveness, and non-hostility, child responsiveness, and child involvement. The sensitivity scale is a 9-point scale that refers to a variety of adult qualities, tapping the adult's ability to be warm and emotionally

connected with the child. A high score is given to a parent that displays much genuine, authentic, and congruent interest and pleasure with her/his child and accurately reads the child's signals. The structuring scale is a 5-point scale and assesses the degree to which the adult appropriately structures the child's play by taking care to follow the child's lead, and setting limits for appropriate child behaviour and/or misbehaviour. A high score on this scale is given to an adult that provides adequate structuring. The parental nonintrusiveness scale is a 5-point scale that reflects the parent's ability to provide autonomy for the child and to be available without being interfering. High scores are given to parents that support the child without interrupting the child by being over directive or interfering. The 5-point non-hostility scale reflects the absence of overt (e.g. hitting or threatening the child) and covert (e.g. a slightly raised voice, irritability, boredom, impatience) hostility to the child. The highest score is given to a parent that does not show any signs of hostility to the child. The child responsiveness scale is a 7-point scale and assesses the eagerness and willingness of a child to engage with the parent, following a suggestion as well as clear signs of pleasure in interaction. High scores are given to children that are optimally responsive to their parents. Finally, the 7-point child involvement scale assesses the degree to which the child attends to and engages the parent in play. High scores are given to children that show a balanced pattern between autonomous play and drawing the parent into interaction (Biringen et al., 1998). Two independent and blind raters, who had achieved reliability on the established coding construct with both the EAS developer Zeynep Biringen, and with each other, rated the videotaped interactions. Interrater reliability (Crohnbach's alpha) was above 0.87 for all EAS dimensions.

The four maternal interaction scales were standardized and subjected to principal components analysis. This analysis revealed the presence of one underlying component with an Eigen value exceeding 1, explaining 56.6% of the variance. Therefore, the standardized scores of the four maternal EAS subscales were summed to obtain an additional overall score for the quality of maternal interaction style (Crohnbach's alpha = .74), next to the scores on the separate subscales.

Child behavioural problems

Both parents completed the Child Behaviour Check List (CBCL 1½–5) to evaluate the behaviour of their children (Achenbach & Rescorla, 2000). The CBCL 1½–5 is a parent-completed questionnaire that contains 100 behavioural and emotional problem items, for which is indicated if a problem is seen sometimes (1), frequently (2) or not (0). Next to a total scale score, the results are differentiated according to internalizing (anxiety, depression, withdrawn behaviour) or externalizing (attention difficulties, aggressive behaviour) problems. Raw scores are converted into standardized *T*-scores. A norm referenced *T*-score of >70 is considered to be in the clinical range. Norm referenced *T*-scores of 65–70 are considered to be in the borderline-clinical range (Achenbach & Rescorla, 2000).

In the analyses, only the fathers' report of the behaviour of their sons and daughters is used as dependent variable, as the potential recurrence or continuation of the maternal

emotional complaints after birth, might affect the mothers' ratings or perceptions of their children's behaviour. This may result in a reporter bias, as anxious or depressed mothers might be more likely to misinterpret disturbances in their children (O'Connor et al., 2002).

Results

Participants

Descriptive characteristics of prenatally exposed and non-exposed boys and girls and postnatal data are shown in Tables 4.1 and 4.2. At the time of assessment, the age of prenatally exposed boys was significantly higher compared to the age of the prenatally non-exposed boys (mean difference = 5.48 months, t (63) = 2.22, $p < .05$), consequently age was used as a covariate in the analyses. As expected, in view of the selection criteria, the groups differed significantly in prenatal maternal emotional complaints ($p < .05$). Differences in current emotional complaints between the subgroups of exposed and non-exposed girls were also significant for all maternal measures and for the paternal EDS and STAI ($p < .01$). For boys, the current SCL and STAI scores of mothers differed significantly between the exposed and non-exposed group ($p < .01$), but no differences were found in the paternal results for all three questionnaires. Furthermore, the exposed girls showed significantly higher CBCL behavioural problems compared to the non-exposed girls ($p < .01$) which was not the case for boys.

Interaction quality

Multivariate analyses of covariance (MANCOVA) were done with child's age as covariate, to examine if the subscales of the EAS significantly differed between prenatally exposed and non-exposed children. Analyses were done separately for boys and girls. No significant differences were found for both sexes (for boys: Wilks' Lambda = .85, F (6,55) = 1.68, *ns*; for girls: Wilks' Lambda = .90, F (6,56) = 1.10, *ns*). The groups according to prenatal emotional complaints did not differ in the quality of the interaction style for both the maternal as well as the child scales (see Table 4.2).

The quality of interaction and child behavioural problems

Next, the associations between the quality of the maternal interaction style and externalizing and internalizing behavioural problems of the children – as reported by the fathers – were analyzed with Pearson correlations. Analyses were done separately for the exposed and non-exposed group and for boys and girls. For the prenatally exposed girls, significant correlations were found between the EAS subscale *structuring* and CBCL total (r = -.50, $p < .01$) and internalizing (r = -.53, $p < .01$) behavioural problems. For the prenatally non-exposed girls and for the prenatally exposed and non-exposed boys, no significant correlations were found between the subscales of the EAS and CBCL behavioural problems.

Table 4.2 Outcome data

	Prenatally exposed *N* = 66		Prenatally non-exposed *N* = 66	
	Boys (*N* = 31–36)	Girls (*N* = 21–30)	Boys (*N* = 24–29)	Girls (*N* = 31–37)
CBCL maternal report *M* (*SD*)				
Total	50.58 (9.82)	50.70 (9.75)	48.14 (8.48)	43.30 (7.86)[b]
% Borderline score	2.8	13.3	3.6	0
% Clinical score	5.6	0	0	0
Externalizing	53.86 (9.74)	52.60 (8.97)	50.46 (8.25)	45.43 (8.44)[b]
% Borderline score	13.9	13.3	3.6	0
% Clinical score	2.8	0	0	0
Internalizing	49.11 (9.56)	48.67 (10.24)	45.79 (9.26)	42.65 (7.44)
% Borderline score	0	0	3.6	0
% Clinical score	5.6	3.3	0	0
CBCL paternal report *M* (*SD*)				
Total	47.65 (7.81)	51.61 (9.26)	47.52 (8.15)	44.25 (8.93)
% Borderline score	3.2	7.1	3.7	0
% Clinical score	0	0	0	0
Externalizing	50.81 (6.86)	53.25 (8.41)	49.89 (9.40)	46.22 (8.76)
% Borderline score	0	7.1	7.4	0
% Clinical score	0	3.6	0	0
Internalizing	44.97 (9.37)	50.29 (10.62)[a]	45.48 (8.18)	43.33 (9.29)
% Borderline score	0	7.1	0	0
% Clinical score	3.2	0	3.7	0
EAS scales *M* (*SD*)				
Sensitivity	5.7 (1.7)	6.4 (1.4)	6.1 (1.4)	6.1 (1.4)
Range	2.0–9.0	3.0–8.5	2.5–9.0	3.0–8.0
Structuring	3.4 (0.8)	3.7 (0.8)	3.5 (0.7)	3.7 (0.8)
Range	1.5–5.0	2.0–5.0	3.0–5.0	2.5–5.0
Nonintrusiveness	4.4 (0.7)	4.4 (0.9)	4.4 (0.9)	4.7 (0.7)
Range	3.0–5.0	2.0–5.0	2.0–5.0	2.0–5.0
Nonhostility	4.7 (0.6)	4.8 (0.6)	4.5 (0.9)	4.8 (0.7)
Range	3.0–5.0	3.0–5.0	2.0–5.0	2.5–5.0
Child responsiveness	5.0 (1.4)	5.5 (1.1)	5.3 (0.9)	5.2 (0.9)
Range	2.0–7.0	3.0–7.0	3.0–7.0	3.0–7.0
Child involvement	5.0 (1.4)	5.4 (1.1)	5.1 (0.9)	5.1 (1.1)
Range	2.0–7.0	2.0–7.0	3.0–6.5	2.0–7.0

[a] sex difference within the prenatally exposed group. [b] sex difference within the prenatally non-exposed group. Borderline score = CBCL *T*-score between 65-70. Clinical score = CBCL *T*-score > 70. NB see text for exposed versus non-exposed group differences.

Maternal prenatal emotional complaints, quality of interaction and behavioural problems of the children

Hierarchical regression analyses were performed to analyze if the overall quality of the postnatal maternal interaction style moderated the association between prenatal maternal emotional complaints and father reported child behavioural problems. Current emotional complaints and educational level of the fathers were associated with both predictor and dependent variables; these were used as confounding variables in the regression analyses and entered in step 1. Prenatal group (exposed or non-exposed) and the total maternal interaction score were entered in step 2 as predictors. An interaction term between prenatal group * total maternal interaction score was entered in step 3, in order to assess the moderating role of maternal interaction quality. Father reported behavioural problems of the children were used as dependent variables. Regression analyses were done separately for boys and girls. As can be seen in Table 4.3, after controlling for the confounding variables and including the interaction term, a significant main effect of prenatal group was found for CBCL internalizing problems ($\beta = .37$, $p < .01$) in the analyses for girls. Moreover, a significant interaction effect between prenatal group * maternal interaction style was found for CBCL internalizing problems of girls ($\beta = -.48$, $p < .05$). For the non-exposed girls, CBCL internalizing behavioural problems were found to be low regardless of the quality of the maternal interaction style. However, for the prenatally exposed girls, CBCL internalizing problems were higher when their mothers scored lower on the EAS and thus showed a less than optimal interaction style, compared to prenatally exposed girls with mothers with higher scores on the EAS. No significant results were found in the analyses for boys. The overall quality of the maternal interaction style moderated the association between prenatal maternal emotional complaints and father reported internalizing behavioural problems for girls.

Girls' internalizing problems in relation to different aspects of interaction quality

Furthermore, to analyze what aspects of the maternal interaction style specifically are most important in moderating the association between prenatal maternal emotional complaints and the girls' internalizing problems, four separate hierarchical regression analyses were performed with father reported CBCL internalizing problems as dependent variable and standardized scores of each of the four maternal EAS subscales (sensitivity, structuring, non-intrusiveness, and non-hostility) as predictors. Again, possibly confounding variables (current emotional complaints and educational level of the fathers) were entered in step 1. In each analyses, one maternal subscale of the EAS and prenatal group status were entered in step 2, and finally step 3 included an interaction term between prenatal group * a subscale of the EAS. As can be seen in Table 4.3, in the regression analyses regarding structuring as predictor variable, the interaction between prenatal group status * structuring added a significant 10.8% to the amount of explained variance, yielding a total of 36% of the variance in CBCL internalizing problems scores being explained by the five variables in the regression. A significant main effect of prenatal group ($\beta = .30$, $p < .05$) and a significant interaction effect between

Table 4.3 Hierarchical regression analyses for girls with CBCL internalizing problems according to fathers as dependent variable ($N = 49$)

Variable	Regression steps		
	1	2	3
Total maternal EAS score as predictor			
Current paternal emotional complaints	.22	.05	.05
Paternal education	-.32*	-.25	-.21
Prenatal group		.32*	.37**
Total maternal EAS		-.22	.14
Prenatal group * total maternal EAS			-.48*
R^2	14.8%	28.8%	38.9%
R^2 change		13.9%	10.1%
F	(2,46) = 4.00*	(2,44) = 4.31*	(1,43) = 7.14*
Structuring as predictor			
Current paternal emotional complaints	.22	.05	.07
Paternal education	-.32*	-.26	-.25
Prenatal group		.35*	.30*
Structuring		-.10	.23
Prenatal group * structuring			-.47*
R^2	14.8%	25.2%	36.0%
R^2 change		10.4%	10.8%
F	(2,46) = 4.00*	(2,44) = 3.05	(1,43) = 7.29*
Non-hostility as predictor			
Current paternal emotional complaints	.22	.08	.11
Paternal education	-.32*	-.29*	-.25
Prenatal group		.32*	.35*
Non-hostility		-.18	.07
Prenatal group * non-hostility			-.37*
R^2	14.8%	27.3%	34.3%
R^2 change		12.5%	7.0%
F	(2,46) = 4.00*	(2,44) = 3.78*	(1,43) = 4.57*

The coefficients are standardized coefficients. * $p < .05$, ** $p < .01$.

prenatal group * structuring ($\beta = -.47$, $p < .05$) was found. For prenatally exposed girls, CBCL internalizing problems were significantly higher when their mothers provided less adequate structuring during interaction compared to prenatally exposed girls of mothers providing more optimal structuring.

Moreover, in the regression analyses with non-hostility as predictor variable, in the final model, a significant main effect of prenatal group ($\beta = .35$, $p < .05$) and a significant interaction effect between prenatal group * non-hostility ($\beta = -.37$, $p < .05$) was found

(Table 4.3). For the non-exposed girls, CBCL internalizing behavioural problems were low regardless of the amount of maternal hostility, whereas for the prenatally exposed girls, CBCL internalizing problems were higher if their mothers showed more hostility during interaction. In the analyses with sensitivity and non-intrusiveness as predictor variables, no significant effects were found.

Discussion

The first aim of this study was to examine if the quality of the mother-child interaction differed between a group of mothers that had reported emotional complaints during pregnancy and a group that repeatedly had not reported such emotional complaints. No significant differences were found in the quality of the interaction; thus, contrary to our hypothesis, prenatal emotional complaints were not related to the quality of the postnatal mother-child interaction processes.

Next the quality of the postnatal maternal interaction style was studied as a moderator of the association between prenatal maternal emotional complaints and behavioural problems of toddlers and preschool aged boys and girls. For girls, a significant interaction effect between prenatal maternal emotional complaints and maternal interaction style was found. The influence of prenatal maternal emotional complaints on internalizing behavioural problems was modified by the quality of the postnatal maternal interaction style. Prenatally exposed girls showed more internalizing behavioural problems if the quality of their mothers' interaction style was generally less optimal, compared to prenatally exposed girls whose mothers had a more optimal interaction style. No significant interaction effects were found in the analyses for boys. This same moderating role of the mother-child interaction style was also found in the study of Leckman-Westin et al. (2009) in the association between postnatal maternal depressive symptoms and behavioural problems in the children and in the study of Kaplan et al. (2008) in the association between prenatal maternal psychiatric status and baseline salivary cortisol in infants.

As in the study of Kaplan et al. (2008) we also observed the quality of the maternal interaction style during a play session. However, Kaplan et al. (2008) focused only on postnatal maternal *sensitivity*. But the quality of maternal interaction style is more than just sensitivity, other interaction qualities, for example maternal structuring or hostility should also be taken into account. Biringen, Matheny, Bretherton, Renouf, and Sherman (2000) concluded that studies, focusing on the maternal interaction style, need to include the structuring dimension of emotional availability instead of assuming maternal sensitivity covers all ground, because it is also an important facet of the mother-child relationship. In our study, we analyzed all aspects of emotional availability. It was found that especially the quality of structuring and non-hostility during interaction moderated the associations between prenatal maternal emotional complaints and internalizing behavioural problems of girls. Surprisingly, the sensitivity aspect of the maternal interaction style did not act as a moderator variable, as was found in the study of Kaplan et al. (2008). However, Kaplan et al. (2008) studied infants,

we examined toddlers and preschool children between the age of 23 and 60 months. Sensitivity might be especially important during the infancy period, for forming a secure attachment relationship, whereas structuring and non-hostility might become more important for toddlers and preschoolers who need to be coached and monitored in their explorations. Moreover, mothers that score lower on the structuring scale of the EAS can either show an over-structuring or under-structuring interaction style or even become a passive member of the interaction. Furthermore, mothers with low scores on the non-hostility scale show more covert or even overt hostility to their children and might become frightening for their children. This might make the child more withdrawn and avoidant of their mothers and subsequently result in more internalizing behavioural problems, especially in girls. Mäntymaa et al. (2009) also found that a less optimal structuring style (as measured with the EAS) by the mothers was related to higher child behavioural problems scores. However, they found more externalizing behavioural problems. Furthermore, Keren, Feldman, and Tyano (2001) also noticed the importance of the structuring and non-hostility aspect of the interaction. They found that children referred to a clinic because of socio-emotional problems, had mothers that provided less structure and that the interaction of these dyads were characterized by higher portions of joint negative states, including anger.

An explanation of the gender difference regarding the moderating effect of maternal interaction style can be that girls are better at interpreting non-verbal cues compared to boys (Lindahl & Heimann, 1997). Mothers with lower scores on the EAS are less positive and enthusiastic in interaction with their child. They can display a passive and affectively flat style (Biringen et al., 1998). The prenatally exposed girls might be more influenced by the passivity of their mothers and they could show more internalizing behavioural problems. Moreover, as Connell and Goodman (2002) point out in their review, parents may exert more influence on children of the same gender. From a social learning standpoint (Bandura, 1977) children are more strongly influenced by models of greater similarity to themselves. In addition, parents might also be more likely to identify with children of the same gender and invest more time and energy in them. Parental mental health problems and non-optimal interaction style may be more strongly related to behavioural problems in same-sex children. The same gender difference was found in a study of Garai et al. (2009). They studied maternal sensitivity as a moderator in the relation between *current* maternal depressive symptoms and child internalizing and externalizing behavioural problems. They also found a significant combined effect of maternal sensitivity and depressive symptoms only for girls: High levels of maternal depressive symptoms together with low levels of sensitivity were associated with elevated internalizing problems for girls. It was suggested that girls might be particularly vulnerable to interpersonal and family stressors, including negative parenting and parental psychopathology (Garai et al., 2009; Davies & Windle, 1997). Their sample of mothers with depressive complaints may have included a lot of children that were also already prenatally exposed to emotional complaints.

The finding that the quality of maternal interaction style moderates the associations between prenatal maternal emotional complaints and internalizing behavioural

problems of girls, is consistent with a developmental perspective on emotional health which states, that the influence of one stressor (e.g. prenatal stress or genetic factor) is dependent on other factors (e.g. contextual factors like maternal interaction style) (Sroufe, 1997). It is important to conclude that the association between prenatal maternal emotional complaints and child development is not completely explained by the fetal programming hypothesis. This hypothesis should be extended with a developmental perspective: the early caregiving environment modulates the effects of the prenatal maternal emotional complaints on child behaviour.

The results of our study have important implications for prevention strategies. These strategies should not only be focused on the period of pregnancy but also on the postnatal period. Midwives during pregnancy should be alert when a pregnant woman shows feelings of anxiety or depression. They should spend some time in screening these feelings and they should refer pregnant women with emotional complaints for psychological support. Moreover, after pregnancy, children of women with high prenatal emotional complaints should be monitored carefully and when needed, mothers should receive support with parenting. The quality of the interaction style with her child should then be the focus of the intervention and special attention is needed for her structuring capabilities and reducing hostile behaviour.

References

Achenbach, T. M., & Rescorla, L. A. (2000). *Manual for the ASEBA Preschool Forms & Profiles*. Burlington, VT: University of Vermont, Research Center for Children, Youth, & Families.

Arrindell, W. A. & Ettema, J. H. M. (2003). *SCL-90. Handleiding bij een multidimensionele psychopathologie-indicator*. Lisse: Swets and Zeitlinger

Bandura, A. (1977). *Social learning theory*. Englewood Cliffs, NJ: Prentice Hall.

Becht, M.C., van Erp, C.F., Teeuwisse, T. M., van Heck, G. L., van Son, M. J, & Pop, V.J. (2001). Measuring depression in women around menopausal age towards a validation on the Edinburgh Depression Scale. *Journal of Affective Disorders*, *63*, 209–213.

Biringen, Z. (2000). Emotional Availability: Conceptualization and research findings. *American Journal of Orthopsychiatry*, *70*, 104–114.

Biringen, Z., Matheny, A., Bretherton, I., Renouf, A., & Sherman, M. (2000). Maternal representation of the self as parent: Connections with maternal sensitivity and maternal structuring. *Attachment & Human Development*, *2*, 218–232.

Biringen, Z., Robinson, J. L., & Emde, R. N. (1998). *Emotional Availability Scales* (3rd ed.). Ft. Collins: Department of Human Development and Family Studies, Colorado State University.

Connell, A. M. & Goodman, S. H. (2002). The association between psychopathology in fathers versus mothers and children's internalizing and externalizing behavior problems: a meta-analysis. *Psychological Bulletin*, *5*, 746–773.

Cox, J. L., Holden, J. M., & Sagovsky, R. (1987). Detection of postnatal depression. *British Journal of Psychiatry*, *150*, 782–786.

Cummings, E. M., & Davies, P. T. (1999). Depressed parents and family functioning: Interpersonal effects and children's functioning and development. In T. Joiner & J. C. Coyne (Eds.), *The interactional nature of depression* (pp. 299–327). Washington, DC: American Psychological Association.

Davies, P. T. & Windle, M. (1997). Gender-specific pathways between maternal depressive symptoms, family discord, and adolescent adjustment. *Developmental Psychology*, *22*, 657–668.

Davis, E. P., Glynn, L. M., Schetter, C. D., Hobel, C., Chicz-Demet, A., & Sandman, C. A. (2007). Prenatal exposure to maternal depression and cortisol influences infant temperament. *Journal of the American Academy of Child and Adolescent Psychiatry*, *46*, 737–746.

De Bruijn, T. C. E., van Bakel, H. J. A., & van Baar, A. L. (2009a). Sex differences in the relation between prenatal maternal emotional complaints and child outcome. *Early Human Development*, *85*, 319–324.

De Bruijn, T. C. E., van Bakel, H. J. A., Wijnen, H., Pop, V. J. M., & van Baar, A. L. (2009b). Prenatal maternal emotional complaints are associated with cotisol responses in toddler and preschool aged girls. *Developmental Psychobiology*, *51*, 553–563.

Derogatis, L. R., Lipman, R. S., & Covi, L. (1973). SCL-90: an outpatient psychiatric rating scale – preliminary report. *Psychopharmacological Bulletin*, *9*, 13–28.

Elgar, F. J., McGrath, P. J., Waschbusch, D. A., Stewart, S. H., & Curtis, L. J. (2004). Mutual influences on maternal depression and child adjustment problems. *Clinical Psychology Review*, *24*, 441–459.

Garai, E. P., Forehand, R. L., Colletti, C. J. M., Reeslund, K., Potts, J., & Compas, B. (2009). The relation of maternal sensitivity to children's internalizing and externalizing problems within the context of maternal depressive symptoms. *Behavior Modification*, *33*, 559–582.

Goodman, S. H. & Gotlib, I. H. (2002). Introduction. In S. H. Goodman & I. H. Gotlib (Eds.), *Children of depressed parents: Mechanisms of risk and implications for treatment* (pp. 3–9). Washington, DC: American Psychological Association.

Gutteling, B. M., De Weerth, C., Willemsen-Swinkels, S. H. N., Huizink, A. C., Mulder, E. J. H., Visser, G. H. A., & Buitelaar, J. K. (2005). The effects of prenatal stress temperament and problem behaviours of 27-month-old toddlers. *European Child and Adolescent Psychiatry*, *14*, 41–51.

Heron, J., O'Connor, T. G., Evans, J., Golding, J., & Glover, V. (2004). The course of anxiety and depression through pregnancy and the postpartum in a community sample. Journal of Affective Disorders, 80, 65–73.

Kaplan, L. A., Evans, L., & Monk, C. (2008). Effects of mothers' prenatal psychiatric status and postnatal caregiving on infant biobehavioral regulation: can prenatal programming be modified? *Early Human Development*, *84*, 249–256.

Keren, M., Feldman, R., & Tyano, S. (2001). Diagnoses and interactive patterns of infants referred to a community-based infant mental health clinic. *Journal of the American Academy of Child and Adolescent Psychiatry*, *40*, 27–35.

Leckman-Westin, E., Cohen, P. R., & Stueve, A. (2009). Maternal depression and mother-child interaction patterns: association with toddler problems and continuity of effects to late childhood. *Journal of Child Psychology and Psychiatry*, *50*, 1176–1184.

Lindahl, L. B. & Heimann, M. (1997). Research report: social proximity in early mother-infant interactions: implications for gender differences? *Early Development and Parenting*, *6*, 83–88.

Lovejoy, M. C., Graczyk, P. A., O'Hare, E., & Neuman, G. (2000). Maternal depression and parenting behavior: A meta-analytic review. *Clinical Psychology Review*, *20*, 561–592.

Mäntymaa, M., Puura, K., Luoma, I., Vihtonen, V., Salmelin, R. K., & Tamminen, T. (2009). Child's behaviour in mother-child interaction predicts later emotional and behavioural problems. *Infant and Child Development*, *18*, 455–467.

O'Connor, T. G., Heron, J., Golding, J., Beveridge, M., & Glover, V. (2002). Maternal antenatal anxiety and children's behavioural / emotional problems at 4 years. *British Journal of Psychiatry*, *180*, 502–508.

O'Donnell, K., O'Connor, T. G., & Glover, V. (2009). Prenatal stress and neurodevelopment of the child: Focus on the HPA axis and role of the placenta. *Developmental Neuroscience*, *31*, 285–292.

Pop, V. J., Komproe, I.H., & van Son, M.J. (1992). Characteristics of the Edinburgh Post Natal Depression Scale in the Netherlands. *Journal of Affective Disorders*, *26*, 105–110.

Rodriguez, A. & Bohlin, G. (2005). Are maternal smoking and stress during pregnancy related to ADHD symptoms in children? *Journal of Child Psychology and Psychiatry*, *46*, 246–254.

Spielberger, C. D., Gorsuch, R. L., & Lushene, R. E. (1970). *STAI Manual for the State-trait Anxiety Inventory*. Consulting Psychologists Press, Palo Alto, California.

Sroufe, L. A. (1997). Psychopathology as an outcome of development. *Development and Psychopathology*, *9*, 251–268.

Van den Bergh, B. R. H. & Marcoen, A. (2004). High antenatal maternal anxiety is related to ADHD symptoms, externalising problems, and anxiety in 8- and 9-year olds. *Child Development*, *75*, 1085–1097.

Van den Bergh, B. R. H., van Calster, B., Smits, T., van Huffel, S., & Lagae, L. (2008). Antenatal maternal anxiety is related to HPA-Axis dysregulation and self-reported depressive symptoms in adolescence: A prospective study on the fetal origins of depressed mood. *Neuropsychopharmacology*, *33*, 536–545.

Van der Ploeg, H. M. (2000). *Handleiding bij de Zelf-BeoordelingsVragenlijst ZBV*. Lisse: Swets and Zeitlinger.

5

Are fathers a buffer against the negative influences of prenatal maternal emotional complaints?

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Abstract

Prenatal maternal emotional complaints are associated with increased difficulties in child development. Fathers showing high interaction quality with their children may buffer against the negative influences of prenatal maternal emotional complaints. However, as emotional complaints tend to co-occur in mothers and fathers, they also might become an additional risk factor for their child's development.

Interaction processes and child behavioural problems are compared in two groups that differ according to prenatal maternal emotional complaints (N = 66), or not (N = 66). Healthy Dutch Caucasian women (N = 132, M age = 30.9 years, SD = 3.8) completed questionnaires of anxiety and depression in week 12, 24, and 36 of gestation. When the children were between 23–60 months of age (M age = 38.6 months, SD = 9.4) both parents completed the Child Behaviour Check List (CBCL 1½–5). During a home visit, mother-child and father-child interaction was observed using the Emotional Availability Scales (EAS).

Fathers of girls in the prenatally exposed group reported more current complaints (p < .01) than fathers in the non-exposed group, which adds to their daughters' risk. No relationships were found however, between paternal current complaints and behavioural problems of girls in the exposed group. No differences were found in the interaction quality of the fathers in both groups, for both girls and boys. However, fathers had better scores than mothers for the EA scales *sensitivity* (t (29) = -2.17, p < .05), *structuring* (t (29) = -2.16, p < .05), and *involvement* (t (29) = -2.39, p < .05) for prenatally exposed boys. This may indicate a buffering effect for the sons in the prenatally exposed group.

Introduction

Prenatal maternal emotional complaints are associated with more difficulties in child motor, cognitive and especially socio-emotional development from infancy to adolescence (O'Donnell, O'Connor, & Glover, 2009). Fetal programming effects partially explain this relationship (van den Bergh, van Calster, Smits, van Huffel, & Lagae, 2008). However, postnatal mother-child interaction processes are also important. Recent studies have shown that the quality of the postnatal maternal interaction style moderates the association between prenatal maternal emotional complaints and child outcome (de Bruijn, van Bakel, Wijnen, Pop, & van Baar, *submitted*; Kaplan, Evans, & Monk, 2008).

The *fathers'* role in the relationship between prenatal maternal emotional complaints and child behavioural problems is as yet unclear. However, mental health problems tend to co-occur in mothers and fathers (Merikangas & Brunetto, 1996). When mothers are depressed or anxious, fathers may also experience emotional complaints, which can affect their interaction quality with their child and become an additional risk factor for the development of their children.

As yet no studies have reported on the role of the father-child interaction in the association between *prenatal* maternal emotional complaints and child behavioural problems. However since the last two decades, studies did pay attention to the fathers' importance for the child in the context of maternal *postnatal* depressive mood. Hossain et al. (1994) analyzed the parent-child interaction in a group with depressed mothers and non-depressed fathers, and compared it to the interaction quality in a group of non-

depressed mothers and fathers. The non-depressed fathers received better interaction ratings compared to their depressed partners. The infants also received better ratings when interacting with their non-depressed fathers than with their depressed mothers. No differences in parent-child interaction ratings were found in the non-depressed mothers and fathers group. The authors suggested that non-depressed fathers may buffer the effects of maternal depression on infant interaction behaviour. Edhborg, Lundh, Seimyr, and Widström (2003) also examined father-child interactions in families where the mother showed depressive symptoms. They found that fathers in families where the mothers reported high levels of depressive complaints at 2 months postpartum were more positively involved in the interaction with their child at 15 to 18 months of age compared to fathers whose partners did not have depressive complaints. These authors also concluded that the fathers' early positive influences on the child might act like a buffer against the depressive symptoms of mothers.

Contrary to the above described findings, Mezulius, Hyde, and Clark (2004) found that non-depressed fathers did not protect their children for the effects of maternal depression, even if fathers spent much time interacting with their infants. In addition Brennan, LeBrocque, and Hammen (2003) did not find that the absence of psychiatric problems in the father acted as a protective factor for adolescent children of depressed mothers. Moreover, Goodman (2008) reported that the father-infant interaction was *negatively* affected, when the mother was experiencing depression during the early postpartum period. Higher maternal depression scores were associated with significantly less optimal scores on father-infant interaction quality. Hence father-infant interaction suffered when mothers were depressed and the negative effects of maternal depression on the father-child interaction behaviours, was thought to form an additional risk factor for the development of the children. Expectations for the role of the father-child interaction quality when a mother experienced emotional complaints during pregnancy can be elaborated based on these findings, into the following questions: Does the father-child interaction form a protective buffer, or an additional risk factor, when mothers reported prenatal emotional complaints?

We studied the quality of the father-child interaction processes in a group of families where the mothers reported prenatal emotional complaints (prenatally exposed group) compared to a group that did not report emotional complaints during pregnancy (prenatally non-exposed group). First, we studied if the fathers in the prenatally exposed group report more current emotional complaints compared to the fathers in the non-exposed group and to what extent such complaints are related to the behavioural outcome in the children. Second, we examined differences in the father-child interaction styles between these groups and to what extent the interaction quality is related to the behavioural outcome in the children. Next, we studied if the quality of the father-child interaction differed from the mother-child interaction within the exposed and non-exposed group. Based on the findings of Hossain et al. (1994) we hypothesized to find better interaction scores for the fathers compared to the mothers in the prenatally exposed group. We expected no significant differences between mother-child and father-child interaction scores in the prenatally non-exposed group. Finally,

we studied if a protective, buffering, effect of the father-child interaction quality could be found in a moderation of the relationship between prenatal maternal emotional complaints and child behavioural outcome. Furthermore, in our previous study the pattern of associations between prenatal maternal emotional complaints and child behavioural problems was found to differ for boys and girls (de Bruijn, van Bakel, & van Baar, 2009a). Hence we hypothesized that the associations between paternal interaction styles, prenatal emotional complaints, and behavioural outcome of the children differs for boys and girls.

Methods

Participants

This study is part of a prospective ongoing research line, which investigates the influence of prenatal maternal emotional complaints on the socio-emotional adjustment of toddlers and preschoolers in relation to parental interaction styles (de Bruijn et al., 2009a). For this part of the study, 222 families were asked for participation and 132 women and 119 husbands/partners agreed to participate with their children (67 girls, 65 boys, *M* age = 38.61 months, *SD* = 9.4, range = 23–60 months). No differences were found between participants and non-participants in scores on prenatal anxiety and / or depression measures. Children whose mothers scored above a standardized cut off, or higher than one standard deviation above the mean on one of the three prenatal measurements of anxiety or depression at 12, 24 or 36 weeks in pregnancy were selected for the target group (prenatally exposed, *N* = 66). For the comparison group (prenatally non-exposed, *N* = 66), children were selected whose mothers had at least given information in two separate periods during pregnancy and did not report high scores for any of the prenatal depression or anxiety questionnaires. The comparison children were matched to the target cases regarding month of birth and sex (de Bruijn, van Bakel, Wijnen, Pop, & van Baar, 2009b). The Medical Ethical Committee of the St. Elisabeth Hospital in Tilburg approved this study.

Measures

Depression

Prenatal maternal depression was assessed using the Dutch version of the Edinburgh Depression Scale (EDS) (Cox, Holden, & Sagovsky, 1987; Pop, Komproe, & van Son, 1992) at 12, 24 and 36 weeks' gestation. The EDS is a 10-item self-report scale designed as a screening instrument for depression and has been shown valid in and outside the postnatal period. Items are scored on four-point rating scales. Total scores range between 0 and 30. A cut-off score of 12 and higher was used (Becht et al., 2001) to indicate major depressive complaints (normal population mean 5.89, *SD* = 4.03) (Pop et al., 1992).

Anxiety

Prenatal maternal anxiety was assessed with the State version of the State-Trait Anxiety Inventory (STAI) (Spielberger, Gorsuch, & Lushene, 1970) at 12, 24 and 36 weeks' gestation. The STAI consists of two subscales each containing 20 items. The state anxiety subscale measures transient anxiety or anxiety at the moment of scoring. Trait anxiety measures dispositional anxiety or anxiety in general. The State version was used to assess the feelings of anxiety of the women during a specific period in their pregnancy. Total scores on the State subscale range between 20 and 80. The Dutch version of the STAI has been validated previously (Cronbach's alpha = .95; normal population mean for non-pregnant women < 40 years = 38.0, *SD* = 12.8) (van der Ploeg, 2000). In our study a score above 39 (that is > 1 *SD* above the mean in our sample of pregnant women) was used as cut off, reflecting a high level of complaints.

Prenatal anxiety was also assessed with the anxiety subscale of the Dutch version of the Symptom Check List (SCL-90) (Derogatis, Lipman, & Covi, 1973; Arrindell & Ettema, 2003) a 90 item self-report scale that measures several dimensions in psychopathology. The SCL-90 has been validated before in the Netherlands and its use as well as the use of several subscales only, has revealed appropriate psychometric properties (Cronbach's alpha of anxiety subscale = .87) (Arrindell & Ettema, 2003). Total scores of the anxiety subscale range between 10 and 50 (normal population mean for women = 13.43, *SD* = 4.91; for men: 12.23, *SD* = 3.80) (Arrindell & Ettema, 2003). In our study, a score above 17 (that is > 1 *SD* above the mean in our sample of pregnant women) was used as cut off, reflecting a high level of complaints.

Current emotional complaints

Both parents answered the EDS, STAI, and SCL to measure their current emotional complaints. Because of high inter-correlations between these measures (de Bruijn et al., 2009a) these were also standardized and summed to create a total current emotional complaints score for mothers and for fathers separately.

Parent-child interaction

The mother-child and father-child interaction processes were videotaped in semi-structured situations at home on different days to avoid tiring the children. Three different games were observed, for five minutes each. The parent was instructed to play with his or her child. The first game was a semi-structured game; mothers were asked to play together with clay, and fathers with blocks. The second game was a more structured game in which both parents were asked to make a puzzle together with their child. The final game was a free play session during which the parent and child could choose toys of their own to play with. Assessment of interaction behaviour was based on the total of 15 minutes of play observation during these different tasks. This was coded using the Emotional Availability Scales (EAS), Infancy to Early Childhood Version, 3rd Edition (Biringen, Robinson, & Emde, 1998; Biringen, 2000). The EAS is a global rating scale that emphasizes behavioural style rather than discrete behaviours.

It consists of six subscales: parental sensitivity, structuring, non-intrusiveness, and non-hostility, and child responsiveness and child involvement. The sensitivity scale is a 9-point scale that refers to a variety of adult qualities, tapping the adult's ability to be warm and emotionally connected with the child. A high score is given to a parent that displays much genuine, authentic, and congruent interest and pleasure with her/his child and accurately reads the child's signals. The structuring scale is a 5-point scale and assesses the degree to which the adult appropriately structures the child's play by taking care to follow the child's lead, and setting limits for appropriate child behaviour and/or misbehaviour. A high score on this scale is given to an adult that provides adequate structuring. The parental non-intrusiveness scale is a 5-point scale that reflects the parent's ability to provide autonomy for the child and to be available without being interfering. High scores are given to parents that support the child without interrupting the child by being over directive or interfering. The 5-point non-hostility scale reflects the absence of overt (e.g. hitting or threatening the child) and covert (e.g. a slightly raised voice, irritability, boredom, impatience) hostility to the child. A high score is given to a parent that does not show any signs of hostility to the child. The child responsiveness scale is a 7-point scale and assesses the eagerness and willingness of a child to engage with the parent, following a suggestion as well as clear signs of pleasure in interaction. High scores are given to children that are optimally responsive to their parents. Finally, the 7-point child involvement scale assesses the degree to which the child attends to and engages the parent in play. High scores are given to children that show a balanced pattern between autonomous play and drawing the parent into interaction (Biringen et al., 1998). Two independent and blind raters, who had achieved reliability on the established coding construct with both the EAS developer Zeynep Biringen, and with each other, rated the videotaped interactions. Interrater reliability (Cronbach's alpha) was above 0.87 for all EAS dimensions.

The ratings on the four parent interaction scales were standardized and subjected to principal components analysis, separately for the maternal and paternal scales. This analysis revealed the presence of one underlying component with an eigenvalue exceeding 1, explaining 56.6% of the variance of the maternal scales and 55.5% of the variance of the paternal scales. Therefore, the standardized scores of the four maternal EAS subscales and four paternal EAS subscales were summed to obtain an additional overall score for the quality of maternal and paternal interaction style (Cronbach's alpha maternal overall scale = .74, paternal scale = .70), next to the scores on the separate subscales.

Child behavioural problems

Both parents completed the Child Behaviour Check List (CBCL 1½– 5) to evaluate the behaviour of their children (Achenbach & Rescorla, 2000). The CBCL 1½–5 is a parent-completed questionnaire that contains 100 behavioural and emotional problem items, for which is indicated if a problem is seen sometimes (1), frequently (2) or not (0). Next to a total scale score, the results are differentiated according to internalizing (anxiety, depression, withdrawn behaviour) or externalizing (attention difficulties, aggressive behaviour) problems. Raw scores are converted into standardized *T*-scores.

A norm referenced *T*-score of >70 is considered to be in the clinical range and *T*-scores of 65–70 in the borderline-clinical range (Achenbach & Rescorla, 2000). CBCL scores reported by mothers and fathers for the total, externalizing, and internalizing subscales were summed and mean scores for the three subscales were used, as the maternal and paternal scores were found to be strongly correlated; for boys *r* range between .55–.62 and for girls *r* range between .61–.66 (de Bruijn et al., 2009a).

Results

Participants

Descriptive characteristics of prenatally exposed and non-exposed boys and girls and postnatal data are shown in Tables 5.1, 5.2, and 5.3. At the time of assessment the age of boys in the prenatally exposed group was significantly higher compared to the age of boys in the non-exposed group (mean difference = 5.48 months, t (63) = 2.22, p < .05), consequently age was used as a covariate in the analyses. As expected, in view of the selection criteria, the groups differed significantly in *prenatal* maternal emotional complaints (p < .05) (Table 5.1).

Table 5.1 Descriptive characteristics

	Prenatally exposed *N* = 66		Prenatally non-exposed *N* = 66	
	Boys (*N* = 25–36)	Girls (*N* = 24–30)	Boys (*N* = 19–29)	Girls (*N* = 27–37)
Age child, months *M* (*SD*)	40.6 (4.0)*	37.6 (9.0)	35.1 (8.7)*	40.2 (8.2)[b]
Birth weight child in grams *M* (*SD*)	3658 (562)	3408 (415)[a]	3827 (434)	3457 (429)[b]
Gestational age *M* (*SD*)	40.0 (1.3)	40.0 (1.2)	40.3 (1.2)	40.0 (1.1)
Age mother at birth, years *M* (*SD*)	31.9 (4.0)	30.4 (3.5)	30.6 (3.9)	30.6 (3.7)
Age father at birth, years *M* (*SD*)	33.3 (4.2)	33.0 (3.7)	34.1 (4.1)	32.6 (3.1)
Education mother				
% low	8.3	13.3	3.4	2.7
% middle	61.1	43.3	58.6	40.5
% high	30.6	43.3	37.9	54.1
Education father				
% low	8.3	16.7	10.3	2.7
% middle	44.4	46.7	41.4	54.1
% high	38.9	36.7	44.8	43.2
Prenatal complaints				
EDS *M* (*SD*)	7.4 (3.0)*	8.2 (3.4)*	3.1 (2.3)*	2.6 (2.1)*
STAI *M* (*SD*)	38.0 (6.0)*	40.0 (5.8)*	26.5 (4.3)*	26.2 (4.3)*
SCL *M* (*SD*)	14.7 (2.8)*	15.8 (4.4)*	11.3 (1.1)*	11.1 (1.4)*

[a] sex difference within the prenatally exposed group. [b] sex difference within the prenatally non-exposed group.
* significant difference (p < .05) between exposed and non-exposed group.

Table 5.2 Current emotional complaints

	Prenatally exposed *N* = 66		Prenatally non-exposed *N* = 66	
	Boys (*N* = 31–36)	Girls (*N* = 21–30)	Boys (*N* = 24–29)	Girls (*N* = 31–37)
Paternal				
EDS	3.3 (3.6)	6.6 (5.0)*	2.6 (3.2)	2.4 (2.9)*
SCL	12.2 (5.4)	12.9 (4.3)	10.8 (2.2)	10.6 (2.3)
STAI	31.6 (9.9)	34.4 (6.8)*	29.6 (7.1)	31.7 (6.1)*
Total sum score	.09 (2.92)	1.22 (2.04)*	-.96 (1.56)	-.51 (1.59)*
Maternal				
EDS	6.0 (4.6)	9.6 (5.4)*	4.0 (4.3)	3.6 (4.1)*
SCL	13.5 (5.5)*	16.2 (8.6)*	10.8 (1.9)*	10.8 (2.4)*
STAI	38.2 (10.0)*	36.5 (10.7)*	27.5 (5.5)	28.7 (7.3)*
Total sum score	.77 (2.21)*	1.92 (3.24)*	-1.35 (1.26)*	-1.12 (1.56)*

* significant difference ($p < .01$) between exposed and non-exposed group. NB Total sum score: sum score of the standardized scores on the EDS, SCL, and STAI.

Girls in the prenatally exposed group showed significantly more CBCL behavioural problems on all three subscales ($p < .01$) compared to the non-exposed group. No significant differences on the CBCL were found for boys (Table 5.3).

Current emotional complaints

Differences in *current* emotional complaints of the parents between the subgroups of exposed and non-exposed *girls* were significant for all maternal measures ($p < .01$). The fathers in both groups differed on the EDS, STAI, and total emotional complaints score ($p < .01$), indicating that fathers of girls in the exposed group indeed had more current emotional complaints than fathers in the non-exposed group.

For *boys*, the current SCL, STAI, and total emotional complaints scores of mothers differed significantly between the exposed and non-exposed group ($p < .01$), but no group differences were found in the paternal results for all three questionnaires (Table 5.2).

Associations between current emotional complaints of fathers and behavioural outcome of the children

Pearson correlations were done between the current emotional complaints of the fathers and CBCL behavioural problems of the children. Analyses were done for the exposed and non-exposed group and for boys and girls separately. For the prenatally exposed boys, significant associations were found between paternal STAI scores and CBCL Total ($r = .42$, $p < .05$) and Internalizing ($r = .41$, $p < .05$) behavioural problems. Furthermore, significant associations between paternal SCL scores and CBCL Total (*r*

Table 5.3 Outcome data

	Prenatally exposed *N* = 66		Prenatally non-exposed *N* = 66	
	Boys (*N* = 31–36)	Girls (*N* = 21–30)	Boys (*N* = 24–29)	Girls (*N* = 31–37)
CBCL *M* (*SD*)				
Total	49.03 (7.81)	51.18 (8.84)*	47.93 (7.85)	43.65 (7.42)[a]*
Externalizing	52.03 (7.13)	53.07 (7.98)*	50.31 (8.40)	45.67 (7.61)[a]*
Internalizing	47.08 (8.38)	47.08 (8.38)*	45.69 (7.83)	42.85 (7.38)*
Maternal EAS Scales *M* (*SD*)				
Sensitivity	5.7 (1.7)	6.4 (1.4)	6.1 (1.4)	6.1 (1.4)
Range	2.0–9.0	3.0–8.5	2.5–9.0	3.0–8.0
Structuring	3.4 (0.8)	3.7 (0.8)	3.5 (0.7)	3.7 (0.8)
Range	1.5–5.0	2.0–5.0	3.0–5.0	2.5–5.0
Nonintrusiveness	4.4 (0.7)	4.4 (0.9)	4.4 (0.9)	4.7 (0.7)
Range	3.0–5.0	2.0–5.0	2.0–5.0	2.0–5.0
Nonhostility	4.7 (0.6)	4.8 (0.6)	4.5 (0.9)	4.8 (0.7)
Range	3.0–5.0	3.0–5.0	2.0–5.0	2.5–5.0
Child responsiveness	5.0 (1.4)	5.5 (1.1)	5.3 (0.9)	5.2 (0.9)
Range	2.0–7.0	3.0–7.0	3.0–7.0	3.0–7.0
Child involvement	5.0 (1.4)	5.4 (1.1)	5.1 (0.9)	5.1 (1.1)
Range	2.0–7.0	2.0–7.0	3.0–6.5	2.0–7.0
Paternal EAS Scales *M* (*SD*)				
Sensitivity	6.4 (1.4)	6.6 (1.1)	6.6 (0.9)	6.8 (1.1)
Range	3.0–8.0	4.0–8.5	5.0–8.0	5.0–9.0
Structuring	3.7 (0.9)	3.8 (0.7)	3.6 (0.7)	3.9 (0.8)
Range	2.0–5.0	2.0–5.0	2.5–5.0	1.5–5.0
Nonintrusiveness	4.2 (0.7)	4.0 (0.8)	4.1 (0.9)	4.3 (0.9)
Range	3.0–5.0	2.5–5.0	2.0–5.0	2.0–5.0
Nonhostility	4.9 (0.4)	4.9 (0.4)	4.9 (0.3)	4.8 (0.6)
Range	3.0–5.0	3.0–5.0	4.0–5.0	2.0–5.0
Child responsiveness	5.5 (1.2)	5.7 (0.9)	5.5 (0.8)	5.6 (0.9)
Range	3.0–7.0	4.0–7.0	3.0–7.0	4.0–7.0
Child involvement	5.7 (1.2)	5.6 (0.9)	5.6 (0.8)	5.7 (0.9)
Range	3.0–7.0	3.0–7.0	3.5 –7.0	4.0–7.0

[a] sex difference within the prenatally exposed group. * significant difference ($p < .01$) between exposed and non-exposed group.

= .47, $p < .01$) and Internalizing ($r = .51$, $p < .01$) behavioural problems were found. For prenatally exposed girls, no significant correlations were found. However, for prenatally non-exposed girls, significant associations were found between paternal EDS scores and CBCL Total ($r = .34$, $p < .05$) and Externalizing ($r = .44$, $p < .01$) behavioural problems. For prenatally non-exposed boys, no significant associations were found.

Father-child interaction quality in relation to prenatal maternal emotional complaints

Next, multivariate analyses of covariance (MANCOVA) were done to examine if the father-child interaction quality scores on the six subscales of the EAS differed between both groups (Table 5.3). No significant results are found for both sexes (for boys: Wilks' Lambda = .97, $F(6,49) = .27$, *ns*; for girls: Wilks' Lambda = .82, $F(6,54) = 2.03$, *ns*). Prenatal maternal emotional complaints were not associated with the quality of the father-child interaction style.

Furthermore, Pearson correlations were done to assess the strength of the associations between current paternal emotional complaints and father-child interaction quality. Analyses were done separately for boys and girls and for the prenatally exposed and non-exposed group. The correlations found varied between .01 and .39 and were not significant. So, current emotional complaints of fathers were not associated with the father-child interaction quality.

The quality of father-child interaction and child behavioural problems

Next, associations between the four paternal subscales of the EAS and CBCL behavioural problems of the children were analyzed with Pearson correlations. Analyses were done separately for boys and girls. The correlations varied between -.01 and -.25 and were not significant in both groups.

Emotional availability of fathers compared to mothers

Differences on the EAS subscales between mothers and fathers were analyzed with paired samples *t*-tests. Analyses were done separately for boys and girls, as well as separately for the exposed and non-exposed group. For boys in the prenatally exposed group, significant differences were found for *sensitivity* (t (29) = -2.17, $p < .05$), *structuring* (t (29) = -2.16, $p < .05$), and *involvement* (t (29) = -2.39, $p < .05$). Fathers score better on these subscales compared to mothers. For prenatally exposed girls, a significant difference was found for *non-intrusiveness* (t (27) = 2.07, $p < .05$): Mothers of girls in the prenatally exposed group are found to be less intrusive compared to the fathers.

In the prenatally non-exposed group, for boys, a significant difference was found for *involvement* (t (26) = -2.15, $p < .05$). Boys show more involving behaviours towards their fathers compared to their mothers. For prenatally non-exposed girls, significant differences were found for *sensitivity* (t (33) = -2.17, $p < .05$) and *non-intrusiveness* ($t(33) = 2.30$, $p < .05$); fathers interacting with daughters in the prenatally non-exposed group score better on sensitivity compared to mothers. However mothers score better on non-intrusiveness.

Maternal prenatal emotional complaints, father-child interaction quality, and child behavioural problems

Hierarchical regression analyses were performed to analyze if the overall quality of the father-child interaction style moderated the association between prenatal maternal emotional complaints and child behavioural problems. Current emotional complaints of both parents and children's age were used as potentially confounding variables and entered in step 1. Prenatal group (exposed or non-exposed) and the total paternal interaction score were entered in step 2 as predictors. An interaction term between prenatal group * total paternal interaction score was entered in step 3, in order to assess the moderating role of paternal interaction quality. CBCL scores were used as dependent variables. Analyses were done separately for boys and girls. In the analyses for girls, a significant main effect of prenatal group was found for CBCL total (β = .35, p <.05) and internalizing behavioural problems (β = .35, p < .05). Neither a significant main effect of father-child interaction quality nor a significant interaction effect between prenatal group and father-child interaction quality was found. In the analyses for boys, no significant results were found overall. Father-child interaction did not affect the relationship between prenatal maternal emotional complaints and the behavioural outcome of girls.

Discussion

This study examined the role of father-child interaction quality in the association between prenatal maternal emotional complaints and behavioural problems of girls and boys. More specifically, it was analyzed if the interaction quality of the fathers formed an additional risk factor or a protective buffer when mothers reported prenatal emotional complaints. First, for boys, no significant differences were found in the current emotional complaints of fathers between the prenatally exposed and non-exposed group. For girls, however fathers in the prenatally exposed group reported significantly more emotional complaints compared to fathers in the non-exposed group. So the fathers may pose an additional risk factor for girls. Could this extra risk factor explain why we find a stronger relationship between prenatal maternal emotional complaints and the behavioural problems for girls than for boys (de Bruijn et al., 2009a, 2009b)? Probably not as no significant associations were found between paternal current emotional complaints and behavioural problems for girls in the prenatally exposed group. So the behaviour of the exposed girls was not associated with the amount of current emotional complaints of their fathers. Moreover, no significant differences in the father-child interaction quality between the prenatally exposed and non-exposed group were found, for both boys and girls. So it seems that the fathers do not pose an additional risk factor for the children, even when they experienced more current emotional complaints, as was the case for the girls in the prenatally exposed group. This is in line with the assumption that maternal depression may be more closely associated with children's behavioural problems than paternal depression because of the greater parenting disturbances displayed by depressed women than depressed men (Connell &

Goodman, 2002). For example, depressed fathers displayed better interaction quality, more game playing and higher quality vocalizations with their 3–6-month-old infants than depressed mothers (Field, Hossain, & Malphurs, 1999). Field and colleagues (1999) proposed that the more active coping style of depressed men compared to depressed women or the more playful style of interaction displayed by men in general, might compensate for the presence of depression on their interaction style.

Some group differences were found in the quality of the father-child interaction compared to the mother-child interaction. For boys in the prenatally exposed group, fathers scored better on the subscales sensitivity, structuring and the child's involvement scale compared to mothers, consequently fathers of sons might act as a protective buffer. However, for the girls in the prenatally exposed group, the mothers scored better on the subscale non-intrusiveness compared to the fathers. The mothers of prenatally exposed girls were less intrusive than the fathers. Boys were showing more involvement with their fathers than with their mothers. Moreover, due to the better interaction quality of fathers for prenatally exposed boys, fathers' interaction quality might indeed have a buffering effect for boys, and not for girls. These findings can be explained by the social learning theory of Bandura (1977). This theory states that children are more strongly influenced by social models of greater similarity to themselves. In addition, parents might also be more likely to identify with children of the same gender and invest more time and energy in them. Hence, fathers may form a protective buffer especially for their sons. To examine if the father-child interaction moderated the association between prenatal maternal emotional complaints and behavioural problems of boys and girls, as was the case for the maternal interaction style in our previous study (de Bruijn et al., 2009, *submitted*) hierarchical regression analyses were performed. However no significant effects of the father-child interaction quality were found.

In sum, fathers and the quality of the father-child interaction played a modest role in the association between prenatal maternal emotional complaints and child outcome. Fathers did not form an important additional risk factor, but their interaction quality may have become a protective buffer, specifically for their sons.

Unfortunately, the amount of time a father was spending with his child was not measured in our study. Mezulius et al. (2004) reported that paternal depression exacerbated the negative effects of maternal depression on child behavioural problems only if the fathers spent large amounts of time with the infant. Fathers were not an additional risk factor if they spent only low or moderate amounts of time with their infants. Additionally, non-depressed fathers also did not buffer the effects of maternal depression, even if they spent large amounts of time interacting with their infants. The authors suggested that non-depressed fathers might not form a direct buffer but instead an *indirect* buffer against the negative influences of maternal depression. The non depressed fathers may reduce certain stressors in the women's lives, which may indirectly serve to reduce depressive symptoms in the mothers that can result in more optimal maternal interaction quality (Mezulius et al., 2004).

In our study the mothers in most families were the prime caregivers as they stayed at

home or worked part-time and most of the fathers worked full-time. It is possible that the fathers did not have the chance to interact with their children as much as the mothers. Hence the chance to buffer against the negative influences of the prenatal maternal emotional complaints, or to become an additional risk factor could be overruled by the lesser frequency of father-child contact compared to mother-child contact.

As only a few studies so far measured emotional availability of fathers with the EAS and compared it to the emotional availability of mothers, measurement issues may be important. Lovas (2005) found, except for non-hostility, higher scores on the EAS for (healthy) mothers compared to fathers. Volling, McElwain, Notaro, and Herrera (2002) also found that mothers were more emotionally available than fathers. However, de Falco, Venuti, Esposito, and Bornstein (2009) examined mother-child and father-child emotional availability in families with a child with Down's syndrome. They found no significant differences between mothers and fathers on the subscales of the EAS. To what extent the EAS is suitable and valid to measure the quality of the interaction style of fathers needs further study. Moreover, in our study we used the same type of games for mothers and fathers, in order to improve the conditions for comparisons. The games used however may need to be differentiated and may not be optimal for measuring father-child interaction. Fathers' play is often characterized by a physical active play style, or rough and tumble play. Maternal play style is characterized as more object focused, conventional, quiet, and verbal (Ross & Taylor, 1989). Hence, further study comparing fathers and mothers in their interaction quality, may need to use different games for both, that more closely characterize their usual play activities.

Unfortunately, emotional complaints of fathers were not measured during pregnancy. Van den Berg et al. (2009) recently studied the influences of paternal depression during pregnancy on excessive crying of infants. They found that paternal depressive symptoms during pregnancy formed a risk factor for excessive infant crying, independently of maternal depressive symptoms and other relevant confounders. Future studies should include not only postnatal father data but also examine emotional complaints of fathers during pregnancy. Moreover, our sample sizes of boys and girls were rather small. However, the effect sizes of the group differences in father-child interaction quality were also very small (varying from 0–0.3) and may not be clinically relevant. Future studies nevertheless should try to increase sample size.

This study was among the first that included fathers in the examination of the influences of prenatal maternal emotional complaints on child development. Overall, research has focused on the influence of maternal psychiatric disorders on child development and neglected the influence of the fathers. As Ramchandani and Psychogiou point out in their review (2009), there are several reasons for this dearth of research on the influences of fathers on child development. In many societies, women are the primary care givers for children, and thus have a greater role than men in their children's early development and socialization. Furthermore, several influential theories of child development, e.g. attachment theories, emphasize the key role of mothers. Finally, practical reasons also play a role, in that fathers might be less willing or have less time than mothers to participate in research (Ramchandani & Psychogiou, 2009).

We did not find a definite answer if the fathers form either a buffer or an additional risk factor for the behavioural development of their sons and daughters, when the mothers had reported emotional complaints during pregnancy. Some support was found for both points of view. Important is that fathers of girls in the prenatally exposed group also reported more current complaints than fathers in the non-exposed group, which adds to their daughters' risk, both on a behavioural level, as well as on a genetic level. No relationships were found however, between the current complaints of the fathers and the rating of behaviour problems of the exposed girls, and no differences were found in the interaction quality of the fathers in both groups. The differences found in interaction quality of fathers compared to mothers indicate sex-related patterns in interaction. Fathers especially got more involved behaviour of their sons and they showed more sensitivity and non-intrusiveness in interaction with their sons compared to the mothers. This may indicate a buffering effect for the sons in the prenatally exposed group, because a relationship between prenatal maternal emotional complaints and behavioural outcome is not found as strongly for boys, as for girls.

References

Achenbach, T. M. & Rescorla, L. A. (2000). *Manual for the ASEBA Preschool Forms & Profiles*. Burlington, VT: University of Vermont, Research Center for Children, Youth, & Families.

Arrindell, W. A. & Ettema, J. H. M. (2003). *SCL-90. Handleiding bij een multidimensionele psychopathologie-indicator*. Lisse: Swets and Zeitlinger.

Bandura, A. (1977). *Social learning theory*. Englewood Cliffs, NJ: Prentice Hall.

Becht, M. C., van Erp, C. F., Teeuwisse, T. M., van Heck, G. L., van Son, M. J., & Pop, V. J. (2001). Measuring depression in women around menopausal age towards a validation on the Edinburgh Depression Scale. *Journal of Affective Disorders*, *63*, 209–213.

Biringen, Z., Robinson, J. L., & Emde, R. N. (1998). *Emotional Availability Scales* (3rd ed.). Ft. Collins: Department of Human Development and Family Studies, Colorado State University.

Biringen, Z. (2000). Emotional Availability: Conceptualization and research findings. *American Journal of Orthopsychiatry*, *70*, 104–114.

Brennan, P.A., LeBrocque, R., & Hammen, C. (2003). Maternal depression, parent-child relationships, and resilient outcomes in adolescence. *Journal of the American Academy of Child and Adolescent Psychiatry*, *42*, 1469–1477.

Connell, A. M. & Goodman, S. H. (2002). The association between psychopathology in fathers versus mothers and children's internalizing and externalizing behavior problems: A meta-analysis. *Psychological Bulletin*, *128*, 746–773.

Cox, J. L., Holden, J. M., & Sagovsky, R. (1987). Detection of postnatal depression. *British Journal of Psychiatry*, *150*, 782–786.

De Bruijn, T. C. E., van Bakel, H. J. A., & van Baar, A. L. (2009a). Sex differences in the relation between prenatal maternal emotional complaints and child outcome. *Early Human Development*, *85*, 319–324.

De Bruijn, T. C. E., van Bakel, H. J. A., Wijnen, H., Pop, V. J. M., & van Baar, A. L. (2009b). Prenatal maternal emotional complaints are associated with cortisol responses in toddler and preschool aged girls. *Developmental Psychobiology*, *51*, 553–563.

De Falco, S., Venuti, P., Esposito, G., Bornstein, M. H. (2009). Mother-child and father-child emotional availability in families of children with Down's syndrome. *Parenting*, *9*, 198–215.

Derogatis, L. R., Lipman, R. S., & Covi, L. (1973). SCL-90: an outpatient psychiatric rating scale-preliminary report. *Psychopharmacological Bulletin*, *9*, 13–28.

Edhborg, M., Lundh, W., Seimyr, L., & Widström, A. M. (2003). The parent-child relationship in the context of maternal depressive mood. *Archives of Women's Mental Health*, *6*, 211–216.

Field, T., Hossain, Z., & Malphurs, J. (1999). Depressed fathers' interaction with their infants. *Infant Mental Health Journal*, *20*, 322–332.

Goodman, J. H. (2008). Influences of maternal postpartum depression on fathers and on father-infant interaction. *Infant Mental Health Journal*, *29*, 624–643.

Hossain, Z., Field, T., Gonzalez, J., Malphurs, J., Del Valle, C., & Pickens, J. (1994). Infants of "depressed" mothers interact better with their nondepressed fathers. *Infant Mental Health Journal*, *15*, 348–357.

Kaplan, L. A., Evans, L., & Monk, C. (2008). Effects of mothers' prenatal psychiatric status and postnatal caregiving on infant biobehavioral regulation: can prenatal programming be modified? *Early Human Development*, *84*, 249–256.

Lovas, G. S. (2005). Gender and patterns of emotional availability in mother-toddler and father-toddler dyads. *Infant Mental Health Journal*, *26*, 327–353.

Merikangas, K. & Brunetto, W. (1996). Assortative mating and psychiatric disorders. *Bailliere's Clinical Psychiatry*, *2*, 175–185.

Mezulius, A. H., Hyde, J.S., & Clark, R. (2004). Father involvement moderates the effect of maternal depression during a child's infancy on child behaviour problems in kindergarten. *Journal of Family Psychology*, *18*, 575–588.

O'Donnell, K., O'Connor, T. G., & Glover, V. (2009). Prenatal stress and neurodevelopment of the child: Focus on the HPA axis and role of the placenta. *Developmental Neuroscience*, *31*, 285–292.

Pop, V. J., Komproe, I. H., & van Son, M. J. (1992). Characteristics of the Edinburgh Post Natal Depression Scale in the Netherlands. *Journal of Affective Disorders*, *26*, 105–110.

Ramchandani, P. & Psychogiou, L. (2009). Paternal psychiatric disorders and children's psychosocial development. *Lancet*, *374*, 646–653.

Ross, H. & Taylor, H. (1989). Do boys prefer daddy or his physical style of play? *Sex Role*, *20*, 23–33.

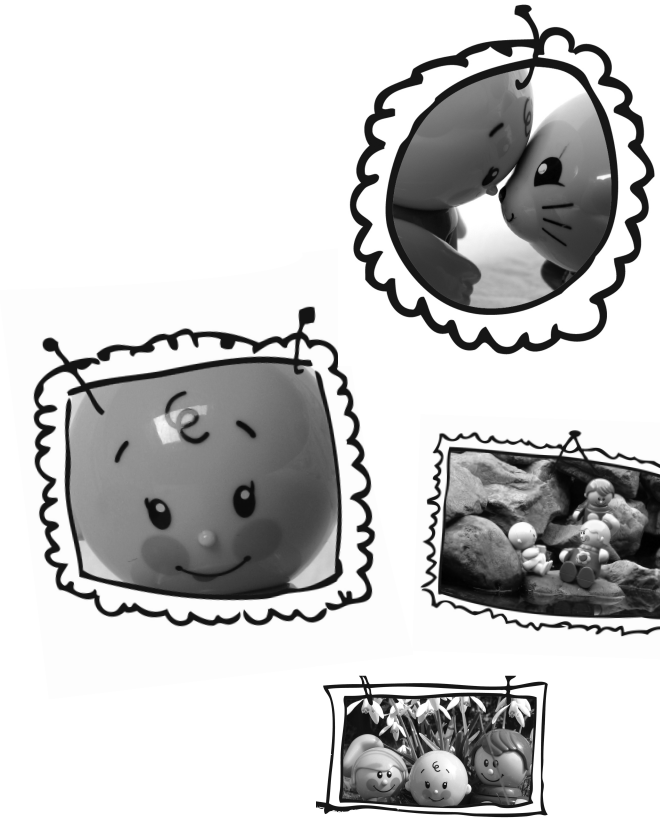
Spielberger, C. D., Gorsuch, R. L., & Lushene, R. E. (1970). *STAI Manual for the State-trait Anxiety Inventory*. Consulting Psychologists Press, Palo Alto, California.

Van den Berg, M. P., van der Ende, J., Crijnen, A. A. M., Jaddoe, V. W. V., Moll, H. A., Mackenbach, J. P., Hofman, A., Hengeveld, M. W., Tiemeier, H., & Verhulst, F. C. (2009). Paternal depressive symptoms during pregnancy are related to excessive infant crying. *Pediatrics*, *124*, e96–e103.

Van den Bergh, B. R. H., van Calster, B., Smits, T., van Huffel, S., & Lagae, L. (2008). Antenatal maternal anxiety is related to HPA-Axis dysregulation and self-reported depressive symptoms in adolescence: A prospective study on the fetal origins of depressed mood. *Neuropsychopharmacology*, *33*, 536–545.

Van der Ploeg, H. M. (2000). *Handleiding bij de Zelf-BeoordelingsVragenlijst ZBV*. Lisse: Swets and Zeitlinger.

Volling, B. L., McElwain, N. L., Notaro, P. C., & Herrera, C. (2002). Parents' emotional availability and infant emotional competence: predictors of parent-infant attachment and emerging self-regulation. *Journal of Family Psychology*, *16*, 447–465.



6

General discussion and conclusions

In the present thesis the influence of prenatal maternal emotional complaints on child development is studied in relation to sex differences, stress responses of the children at toddler and preschool age and parental interaction styles. From infancy to adolescence, children have been found to show more difficulties in motor, cognitive, and especially socio-emotional development, when their mothers had prenatal complaints reflecting distress, anxiety or depression (O'Donnell, O'Connor, & Glover, 2009). A potentially important underlying mechanism to explain these associations is fetal programming of the Hypothalamic-Pituitary-Adrenal (HPA) axis (van den Bergh, Mulder, Mennes, & Glover, 2005; van den Bergh, van Calster, Smits, van Huffel, & Lagae, 2008). Maternal prenatal stress may induce overactivity and/or dysregulation of the HPA-system of their children. Next to these neurobiological processes involved in child development, also contextual and psychological processes are important. Specifically, the quality of the mother-child and father-child interaction style might mediate or moderate the association between prenatal maternal emotional complaints and child outcome. However, up until now, no human study investigated the role of the quality of the maternal and paternal interaction style on the association between prenatal maternal emotional complaints and child outcomes.

The studies presented in this thesis show that the association between prenatal maternal emotional complaints and child development may be explained by the fetal programming hypothesis. In addition, the postnatal caregiving environment is important, as the quality of the maternal interaction style has been found to modulate the effects of the prenatal experiences (i.e. maternal emotional complaints) on child behaviour. In explaining the associations between prenatal maternal emotional complaints and child development we also learned that we need to consider sex differences, both at a neurobiological level, as well as at a psychological level.

The empirical studies presented, focus upon different facets of the relationship between prenatal maternal emotional complaints and child development. In the first study (*Chapter 2*) associations between prenatal maternal emotional complaints during the three trimesters of pregnancy and behavioural problems of toddlers and preschoolers were assessed. Whereas in animal studies, sex differences appeared in these associations, only a few human studies had addressed sex differences. Therefore, analyses were done separately for boys and girls. A clear difference in the association between prenatal maternal emotional complaints and behavioural problems of the children – as assessed through questionnaires filled in by mothers and fathers – was found for boys and girls. For boys, maternal emotional complaints during the *first* trimester of gestation showed a significant effect on total and specifically internalizing behavioural problems. For girls, maternal emotional complaints during the *third* trimester of gestation were associated with total, internalizing as well as externalizing behavioural problems.

An explanation for these differences between boys and girls can be found in the differences in the amount of sex hormones involved in the development of the fetus. When a woman is experiencing high levels of emotional complaints during pregnancy, her HPA-axis is stimulated and releases cortisol (O'Connor et al., 2005). Maternal cortisol is not fully metabolized by the placenta and crosses to the fetus (Gitau,

Cameron, Fisk, & Glover, 1998). Sarkar, Bergman, Fisk, O'Connor, and Glover (2007) have found a positive relation between cortisol and testosterone levels in amniotic fluid, in both male and female fetuses. Studies also have found that exposure to prenatal stress and to testosterone are associated with some similarities in neurodevelopmental outcome. For example, a significant association has been found between prenatal stress and a cluster of neurodevelopmental outcomes, including attention-deficit hyperactivity disorder (van den Bergh & Marcoen, 2004) and mixed-handedness, which have also been suggested to be associated with increased in utero testosterone exposure (Glover, O'Connor, Heron, & Golding, 2004). The positive correlation between amniotic fluid cortisol and testosterone suggests that fetal stress may be associated with increased testosterone exposure in utero, which could contribute to child behavioural problems (Sarkar, Bergman, O'Connor, & Glover, 2008). Testosterone may mediate the relationship between prenatal stress and behavioural outcome (Sarkar et al., 2007).

In genetically male fetuses, testosterone secretion is highest between week 10 and week 20 of gestation (Knickmeyer & Baron-Cohen, 2006), whereas testosterone levels in female fetuses increase significantly with gestational age (Gitau, Adams, Fisk, & Glover, 2005). Hence, time of prenatal maternal emotional complaints may have a different effect for boys and girls because of the differential rate in increase of testosterone during gestation.

Sarkar et al. (2007) argued that the positive relationship between fetal cortisol and testosterone may indicate a pathway whereby prenatal stress may be associated with elevated fetal testosterone and associated behavioural masculinization of the offspring. Several animal studies indeed indicated more externalizing problems in female offspring compared to male offspring after exposure to prenatal distress (Kaiser & Sachser, 2005). This masculinization effect due to elevated fetal testosterone might be an explanation of our finding that in girls maternal prenatal emotional complaints are especially related to externalizing behavioural problems.

In *Chapter 3* we studied if the prenatal maternal emotional complaints were associated with neurobiological functioning of the toddlers and preschoolers in our sample. More specifically, the role of the HPA-axis functioning and stress responses in the association between prenatal maternal emotional complaints and child outcome was examined. As we found clear sex differences in the previous study (*Chapter 2*), we did the analyses separately for boys and girls. The data were gathered during a home visit with the mother. To analyze cortisol levels, child saliva was collected at three times during the home visit. First at the start of the home visit, second collection was approximately 22 minutes after a mother-child interaction episode and final collection was 22 minutes after a potential frustrating task for the children.

Cortisol response patterns of the group of children that were prenatally exposed to high levels of maternal emotional complaints were compared to the cortisol response patterns of the non-exposed group. Repeated measures analyses showed that prenatally exposed girls showed overall higher cortisol levels across the three episodes of the home-

visit compared to the non-exposed girls. No differences in cortisol levels were found for boys. Prenatally exposed girls show higher basal cortisol compared to prenatally exposed boys. No significant differences were found for prenatally non-exposed boys and girls. The girls seemed to be affected more clearly by prenatal maternal emotional complaints than the boys. This is in accordance with the sex differences reported by van den Bergh et al. (2008). Consequently, prenatal maternal emotional complaints are related differently to functioning and maybe programming of the HPA-axis for boys and girls. Gender seems to affect the processes involved in neurobiological functioning, indicating that sex hormones, or sex related genetic factors play an important role in the association between prenatal emotional complaints and child development.

But what about the postnatal experiences of the boys and girls in our study? The quality of the interactive behaviour of mother and child after birth might also be important in explaining the above described results. The mothers, especially those of the prenatally exposed girls, also were found to be bothered more by emotional complaints after birth compared to the mothers without prenatal emotional complaints. If the mothers are postnatally suffering from emotional complaints, they might interact more negatively and less sensitively with their child, which subsequently might lead to more behavioural problems in their children and higher cortisol levels (Elgar, McGrath, Waschbusch, Stewart, & Curtis, 2004; Blair, Douglas, Willoughby, & Kivlighan, 2006).

This potential mediating or moderating role of the quality of the maternal postnatal interaction style was studied in the third study that is reported in Chapter 4. Mother-child interaction processes and child behavioural problems of the prenatally exposed and non-exposed group were compared. Data were gathered during the home visit with the mother. The quality of the mother-child interaction style was coded according to the Emotional Availability Scales (EAS; Biringen, Robinson, & Emde, 1998) that consisted of six subscales: parental sensitivity, structuring, non-intrusiveness, and non-hostility, child responsiveness, and child involvement. Analyses were done separately for boys and girls in line with our first results. Multivariate analyses revealed no significant differences on the six subscales of the EAS between the prenatally exposed and non-exposed boys and girls. Thus prenatal emotional complaints were not related to the quality of the postnatal maternal interaction style and no mediation effect was found.

Multiple hierarchical regression analyses did show a significant moderator effect of maternal interaction style on the relation between prenatal emotional complaints and internalizing behavioural problems of girls, while controlling for postnatal maternal emotional complaints. For the non-exposed girls, CBCL internalizing behavioural problems were found to be low regardless of the quality of the maternal interaction style. Contrary, for the prenatally exposed girls, CBCL internalizing problems were higher when their mothers scored lower on the EAS showing a less than optimal interaction style. For prenatally exposed girls, CBCL internalizing problems were found to be higher especially when their mothers provided less structure and showed more hostile behaviour during interaction. No moderation effects were found for boys. A possible explanation for these findings may be found in the social learning theory of Bandura (1977). Children are more strongly influenced by role models of greater

similarity to themselves, which may include gender. In addition, parents might also be more likely to identify with children of the same gender and invest more time and energy in them (Connell & Goodman, 2002). Consistent with this idea is the finding that harsh parenting has more influence on child externalizing behavioural problems when the parent is of the same gender as the child (Deater-Deackard & Dodge, 1997). Moreover, depressive symptoms in mothers are related to similar symptoms only in their daughters (Hops, 1992). As such, parental mental health problems and a non-optimal interaction style may be more strongly related to behavioural problems in same-sex children (Connell & Goodman, 2002). Hence, (prenatal) maternal emotional complaints and the quality of the interaction style of mothers might have more effect on the development of girls than on boys. This is in accordance with the findings of Hops, Sherman, and Biglan (1990). They found that 11- to 16-year old daughters of depressed mothers exhibited more dysphoric affect and less happy affect than boys. This finding was replicated by Inoff-Germain, Nottelman, and Radke-Yarrow (1992) who also found that daughters of depressed mothers were more likely than their sons to match their mother's negative and depressed mood.

The finding that the quality of maternal interaction style moderates the associations between prenatal maternal emotional complaints and internalizing behavioural problems of girls, is consistent with a developmental and ecological perspective on emotional health. The influence of one stressor (e.g. prenatal stress or genetic factor) is dependent on other factors (e.g. contextual factors like maternal interaction style) (Sroufe, 1997). Therefore the association between prenatal maternal emotional complaints and child behavioural problems cannot solely be explained by fetal programming processes. The postnatal caregiving environment is important in modulating the effects of the prenatal experiences (i.e. maternal emotional complaints) on child behaviour.

Many studies focus exclusively on maternal behaviour and its mediating and moderating role. However, not only the mother is important in the early caregiving environment. Fathers may play an important role too. Until recently, fathers were more or less neglected in research and most studies only focused on the influences of mothers on child development (Ramchandani & Psychogiou, 2009). In the final study of this thesis (*Chapter 5*) the possible mediating or moderating role of the quality of the paternal interaction style in the association between prenatal maternal emotional complaints and behavioural problems of the children was examined. We studied two questions; do fathers form a protective buffer, or an additional risk factor for the development of their children? Fathers showing high interaction quality with their children might provide a buffer against the negative influences of prenatal maternal emotional complaints. However, as emotional complaints tend to co-occur in mothers and fathers, fathers also might become an additional risk factor for their child's development because of their own emotional complaints. Paternal interaction style was videotaped during a play situation in a second home visit and coded, like the maternal interaction style, with the Emotional Availability Scales (EAS). The quality of the father-child interaction and behavioural problems of boys and girls were analyzed separately again, and compared

in the prenatally exposed and non-exposed groups.

Fathers of girls in the prenatally exposed group reported more current emotional complaints compared to fathers of girls in the non-exposed group. Therefore these fathers could present an additional risk factor for prenatally exposed girls. However, no significant associations were found between current emotional complaints of fathers and behavioural problems of the children. Moreover, no significant differences in paternal interaction style were found between the prenatally exposed and non-exposed group. Furthermore, fathers had better scores on the EAS subscales *sensitivity*, *structuring*, and *non-intrusiveness* compared to mothers for the prenatally exposed boys. This indicates support for a buffering effect for the sons in the prenatally exposed group. To examine if the father-child interaction moderated the association between prenatal maternal emotional complaints and behavioural problems of boys and girls, hierarchical regression analyses were performed, as was done for the maternal interaction style (*Chapter 4*). No moderation effects of the father-child interaction quality were found.

It was concluded that we did not find a definite answer if the fathers formed either a buffer or an additional risk factor for the behavioural development of their sons and daughters, when the mothers had reported emotional complaints during pregnancy. Some support was found for both points of view. Further research including fathers is needed. Another point of view is that fathers may not provide a direct buffering effect against the negative influences of maternal emotional complaints, but an indirect effect might exist (Mezulius, Hyde, & Clark, 2004). A supporting partner might have a positive influence on the well-being of a woman experiencing (prenatal) emotional complaints. Non-depressed husbands could reduce certain stressors in the women's lives, which might indirectly serve to reduce depressive symptoms in the mothers that could result in more optimal maternal interaction quality. Furthermore, fathers also play an indirect role through their marital relationship with the mother. An affectionate marital relationship is associated with better maternal sensitivity (Lamb, 1980). Bergman, Sarkar, O'Connor, Modi, and Glover (2007) found that prenatal relationship strain is particularly harmful for the child, as this accounted for 73.5% and 75% of the total variance of prenatal stressful life events on infant mental developmental scores and fearfulness scores.

Strength and limitations of the study

Several strengths of this study should be noted. First, the study used a prospective population-based design and important confounders (including current maternal emotional complaints) were taken into account. Second, the present study is one of the first studies that included and assessed both the quality of the mother-child and the father-child interaction quality. Most studies concerning the association between prenatal maternal stress and child outcome, discussed the possible moderating role of the mother-child interaction quality, but only a few studies actually have examined this topic. Moreover, none of the studies in this field have included relevant father data and investigated their role.

However, some limitations of the studies must also be discussed. 70% of the women and their partners who were studied during pregnancy, agreed to participate in the first wave of our study and 444 of them (63%) actually answered the questionnaires. The participating mothers did not differ from the non-participants in prenatal emotional complaints, maternal age at birth and marital status. However, the mothers who participated did have a higher educational level than non-participants and they smoked less during pregnancy (although smoking during pregnancy was rare for both participants and non-participants). As such, the studied group was probably more affluent. Overall, our study group was higher educated compared to the general Dutch population (42.4% of the participants in our sample was highly educated compared to 25% in the normal Dutch population) (CBS, 2009). Therefore, our sample, living in The Kempen in Brabant, is not representative for the general Dutch population. In our study group, lower educational level is associated with more child behavioural problems. This is in accordance with Jansen et al. (2009) who found in a sample of 6 month old infants that lower SES was associated with more difficult infant temperament.

As other researchers in this field, we also had to deal with the more general difficulties that arise when pre- and postnatal influences need to be disentangled. The possible effect of the prenatal complaints on behavioural problems of the children, as assessed by mothers, can be statistically diminished as confounding factors such as current emotional complaints, smoking and low education are all already associated with prenatal feelings of depression or anxiety of the mothers. Perceived stress increases the likelihood of continued smoking during pregnancy (Rodriguez, Bohlin, & Lindmark, 2000). Furthermore, depressed pregnant women tend to have lower educational levels (Field, Hernandez-Reif, & Diego, 2006). Smoking, low education and current feelings of depression and anxiety can be considered as a behavioural cluster or a lifestyle that forms an inherent part of (prenatal) emotional complaints. If this cluster is controlled in the regression analyses, a form of over-control results, which also extracts a part of the effect of prenatal depressive or anxious functioning from the analyses.

Finally, our design is not genetically sensitive. When a genetic predisposition for emotional complaints exists, children may inherit this genetic risk for emotional problems, and the behavioural problems then may be affected more through genetic factors than through fetal programming processes combined with a specific maternal interaction style. Van der Valk, Verhulst, Stroet, and Boomsma (1998) studied the genetic influences on externalizing and internalizing behavioural problems (as measured with the Child Behavior Checklist) in preschool aged boys and girls. They found that genetic factors accounted for 68% of the variance for internalizing behavioural problems. For externalizing problems a sex difference was found: Genetic factors accounted for 74–75% of the variance in females, versus 49–51% for males.

However, even in this well-designed genetic study genetic and fetal neurobiological processes could not be disentangled in detail and effects could not be ascribed to genetic effects solely.

Nevertheless, genetic factors may be important too and need to be studied in relation

to fetal programming, maternal interaction style and child behavioural problems, although the factors involved may always be difficult to disentangle.

Clinical implications

The results of our study have important implications for prevention and treatment strategies. First, high levels of emotional complaints of women should be prevented, especially during pregnancy. But also the postnatal period should be considered for preventive strategies when emotional complaints did occur, as our results have shown an important moderating role of the mother-child interaction style. Midwives should be alert when a pregnant woman shows feelings of anxiety or depression. They should use screening measures for these feelings and they should refer pregnant women with emotional complaints for psychological support. Moreover, after pregnancy, children of women with high prenatal emotional complaints should be monitored carefully. Especially when mothers suffer from emotional complaints after birth and their children show behavioural problems, the mothers should receive support with parenting. The quality of the interaction style of a mother might be a port of entry and could be the focus of an intervention program. Based on the results of this thesis, special attention should be given to improve the structuring capabilities of the parents and to reduce their hostile behaviour.

Suggestions for future research

In the present study we focused on the quality of the parent-child interaction style. However, the quality of mother-child *attachment* might also be an important moderator in the association between prenatal maternal emotional complaints and child outcome. Postpartum depression is found to interfere with the mother's emotional availability and sensitivity to the child's needs and as such, it might disrupt the development of a secure attachment bond (Cicchetti, Rogosch, & Toth, 1998). The long-term consequences of an insecure attachment between child and parent entail chronic difficulties in emotional regulation, sensitivity to stress, and social functioning. Prenatally exposed children might be less securely attached to their mothers, due to a less than optimal postnatal maternal interaction style and as a consequence, might show more behavioural problems. One study found that depression during pregnancy and at 4 months postpartum predicted attachment insecurity when the child was 14 months old and problem behaviours and intellectual competencies when the child was 30 months old (Carter, Garrity-Rokous, Chazan-Cohen, Little, & Brigss-Gowan, 2001). Moreover, Bergman, Sarkar, Glover, and O'Connor (2008) found that attachment classification moderated the link between prenatal stress and observed fearfulness in 17 month-old children. An early Insecure-Ambivalent attachment accentuated the positive association between exposure to antenatal stress and infant fearfulness. In future follow-up studies, the role of the quality of mother-child attachment should be examined in more detail.

Furthermore, the child's *self-regulation capacities* should be taken into account. Emotional and behavioural regulation represent an important child characteristic that could promote resiliency or exacerbate risk in the context of maternal emotional complaints in the prenatal period and in the first years of a child's life (Silk, Shaw, Skuban, Oland, & Kovacs, 2004). Silk, Shaw, Forbes, Lane, and Kovacs (2006) studied emotion regulation strategies in children whose mothers had a history of childhood-onset depression. They found that children who generated positive affect in the face of a potential frustration (delay task; waiting for a cookie or toy), formed a protective emotion regulation strategy especially for children at risk for depression. These children show less internalizing behavioural problems. No studies to date have examined the role of emotion regulation strategies in the association between *prenatal* maternal emotional complaints and child outcome. A prenatally exposed child may also show less behavioural problems if he or she is capable to regulate negative emotions adaptively.

In the present thesis, we focused on the influences of prenatal maternal emotional complaints on the child behavioural development. However, emotional complaints of women during pregnancy might also be associated with child *cognitive development* (Bergman et al., 2007; Brouwers, Van Baar, & Pop, 2001; Huizink, Robles de Medina, Mulder, Visser, & Buitelaar, 2003). Most studies focusing on cognitive development have not focused on sex differences. Future studies should examine the cognitive development of the children after exposure to prenatal maternal stress separately for boys and girls.

In addition, the role of the fathers should be studied in more detail. Quantity of the paternal involvement should be taken into account, next to further details regarding important qualitative aspects of their role. Moreover, in line with the study of van den Berg et al. (2009), fathers should be already included in research during the prenatal period. They found that paternal depressive symptoms during pregnancy might be a risk factor for excessive infant crying. More research on the influence of paternal emotional complaints during pregnancy is important. Moreover, information on the marital relationship during pregnancy should be collected, as Bergman et al. (2007) found that prenatal relationship strain is particularly harmful for the child, as this accounted for 73.5% and 75% of the total variance of prenatal stressful life events on infant mental developmental scores and fearfulness scores.

Finally, as mentioned above, genetic factors may be important too and need to be studied in relation to fetal programming effects and maternal interaction style.

General conclusion

The association between prenatal maternal emotional complaints and child development cannot solely be explained by the fetal programming hypothesis. The postnatal caregiving environment is also important, as it was found to modulate the effect of prenatal maternal emotional complaints on child behavioural problems, specifically for girls.

References

Bandura, A. (1977). *Social learning theory*. Englewood Cliffs, NJ: Prentice Hall.

Bergman, K., Sarkar, P., O'Connor, T. G., Modi, N., & Glover, V. (2007). Maternal stress during pregnancy predicts cognitive ability and fearfulness in infancy. *Journal of Academic Child and Adolescent Psychiatry*, *46*, 1454–1463.

Bergman, K., Sarkar, P., Glover, V., & O'Connor, T. G. (2008). Quality of child-parent attachment moderates the impact of antenatal stress on child fearfulness. *Journal of Child Psychology and Psychiatry*, *49*, 1089–1098.

Biringen, Z., Robinson, J. L., & Emde, R. N. (1998). *Emotional Availability Scales* (3rd ed.). Ft. Collins: Department of Human Development and Family Studies, Colorado State University.

Blair, C., Douglas, G., Willoughby, M., & Kivlighan, K. (2006). Maternal sensitivity is related to hypothalamic-pituitary-adrenal axis stress reactivity and regulation in response to emotion challenge in 6-month-old infants. *Annals of the New York Academy of Sciences*, *1094*, 263–267.

Brouwers, E. P. M., Van Baar, A. L., & Pop, V. J. M. (2001). Maternal anxiety during pregnancy and subsequent infant development. *Infant Behaviour and Development*, *24*, 95–106.

Carter, A. S., Garrity-Rokous, F. E., Chazan-Cohen, R., Little, C., & Briggs-Gowan, M. J. (2001). Maternal depression and comorbidity: Predicting early parenting, attachment security, and toddler social-emotional problems and competencies. *Journal of the American Academy of Child and Adolescent Psychiatry*, *40*, 18–26.

Central Institution of Statistics/Centraal Bureau voor de Statistiek (CBS). Retrieved december 17, 2009, from http://statline.cbs.nl/StatWeb.

Cicchetti, D., Rogosch, F. A., & Toth, S. L. (1998). Maternal depressive disorder and contextual risk: Contributions to the development of attachment insecurity and behavior problems in toddlerhood. *Developmental Psychopathology*, *10*, 283–300.

Connell, A. M. & Goodman, S. H. (2002). The association between psychopathology in fathers versus mothers and children's internalizing and externalizing behavior problems: a meta-analysis. *Psychological Bulletin*, *5*, 746–773.

Deater-Deckard, K. & Dodge, K. A. (1997). Externalizing behavior problems and discipline revisited: Nonlinear effects and variation by culture, context, and gender. *Psychological Inquiry*, *8*, 161–175.

Elgar, F. J., McGrath, P. J., Waschbusch, D. A., Stewart, S. H., & Curtis, L. J. (2004). Mutual influences on maternal depression and child adjustment problems. *Clinical Psychology Review*, *24*, 441–459.

Field, T., Hernandez-Reif, M., & Diego, M. (2006). Risk factors and stress variables that differentiate depressed from nondepressed pregnant women. *Infant Behavior and Development*, *29*, 169–174.

Gitau, R., Adams, D., Fisk, N. M., & Glover, V. (2005). Fetal plasma testosterone correlates positively with cortisol. *Archives of Disease in Childhood. Fetal and Neonatal Edition*, *90*, F166–F169.

Gitau, R., Cameron, A., Fisk, N. M., & Glover, V. (1998). Fetal exposure to maternal cortisol. *Lancet*, *352*, 707–708.

Glover, V., O'Connor, T. G., Heron, J., & Golding, J. (2004). Antenatal maternal anxiety is linked with atypical handedness in the child. *Early Human Development*, *79*, 107–118.

Hops, H. (1992). Parental depression and child behavior problems. Implications for behavioural family intervention. *Behaviour Change*, *9*, 126–138.

Hops, H., Sherman, L., & Biglan, A. (1990). Maternal depression, marital discord, and children's behaviour: A developmental perspective. In G. R. Patterson (Ed.), *Depression and aggression in family interactions*. (pp. 185–208). Hillsdale, NJ: Erlbaum.

Huizink, A. C., Robles de Medina, P. G., Mulder, E. J. H., Visser, G. H. A., & Buitelaar, J. K. (2003). Stress during pregnancy is associated with developmental outcome in infancy. *Journal of Child Psychology and Psychiatry*, *44*, 810–818.

Inoff-Germain, G., Nottelmann, E. D., & Radke-Yarrow, M. (1992). Evaluative communications between affectively ill and well mothers and their children. *Journal of Abnormal Child Psychology*, *20*, 189–212.

Jansen, P. W., Raat, H., Mackenbach, J. P., Jaddoe, V. W. V., Hofman, A., Verhulst, F. C., & Tiemeier, H. (2009). Socioeconomic inequalities in infant temperament. *Social Psychiatry and Psychiatric Epidemiology*, *44*, 87–95.

Kaiser, S. & Sachser, N. (2005). The effects of prenatal social stress on behaviour: mechanisms and function. *Neuroscience and Biobehavioral Reviews*, *29*, 283–294.

Knickmeyer, R. C. & Baron-Cohen, S. (2006). Fetal testosterone and sex differences. *Early Human Development*, *82*, 755–760.

Lamb, M. E. (1980). The father's role in the facilitation of infant mental health. *Infant Mental Health Journal*, *1*, 140–149.

Merikangas, K. & Brunetto, W. (1996). Assortative mating and psychiatric disorders. *Bailliere's Clinical Psychiatry*, *2*, 175–185.

Mezulius, A. H., Hyde, J. S., & Clark, R. (2004). Father involvement moderates the effect of maternal depression during a child's infancy on child behaviour problems in kindergarten. *Journal of Family Psychology*, *18*, 575–588.

O'Connor, T. G., Ben-Shlomo, Y., Heron, J., Golding, J., Adams, D., & Glover, V. (2005). Prenatal anxiety predicts individual differences in cortisol in pre-adolescent children. *Biological Psychiatry*, *58*, 211–217.

O'Donnell, K., O'Connor, T. G., & Glover, V. (2009). Prenatal stress and neurodevelopment of the child: Focus on the HPA axis and role of the placenta. *Developmental Neuroscience*, *31*, 285–292.

Ramchandani, P. & Psychogiou, L. (2009). Paternal psychiatric disorders and children's psychosocial development. *Lancet*, *374*, 646–653.

Rodriguez, A., Bohlin, G., & Lindmark, G. (2000). Psychosocial predictors of smoking and exercise during pregnancy. *Journal of Reproductive and Infant Psychology*, *18*, 203–223.

Sarkar, P., Bergman, K., Fisk, N. M., O'Connor, T. G., & Glover, V.(2007). Amniotic fluid testosterone: relationship with cortisol and gestational age. *Clinical Endcrinology*, *67*, 743–747.

Sarkar, P., Bergman, K., O'Connor, T. G., & Glover, V. (2008). Maternal antenatal anxiety and amniotic fluid cortisol and testosterone; possible implications for foetal programming. *Journal of Neuroendocrinology*, *20*, 489–496.

Silk, J. S., Shaw, D. S., Forbes, E. E., Lane, T. L., & Kovacs, M. (2006). Maternal depression and child internalizing: the moderating role of child emotion regulation. *Journal of Clinical Child and Adolescent Psychology*, *35*, 116–126.

Silk, J.S., Shaw, D.S., Skuban, E.M., Oland, A.A., Kovacs, M. (2004). Emotion regulation strategies in off-spring of childhood-onset depressed mothers. *Journal of Child Psychology and Psychiatry*, *44*, 1025–1036.

Sroufe, L. A. (1997). Psychopathology as an outcome of development. *Development and Psychopathology*, *9*, 251–268.

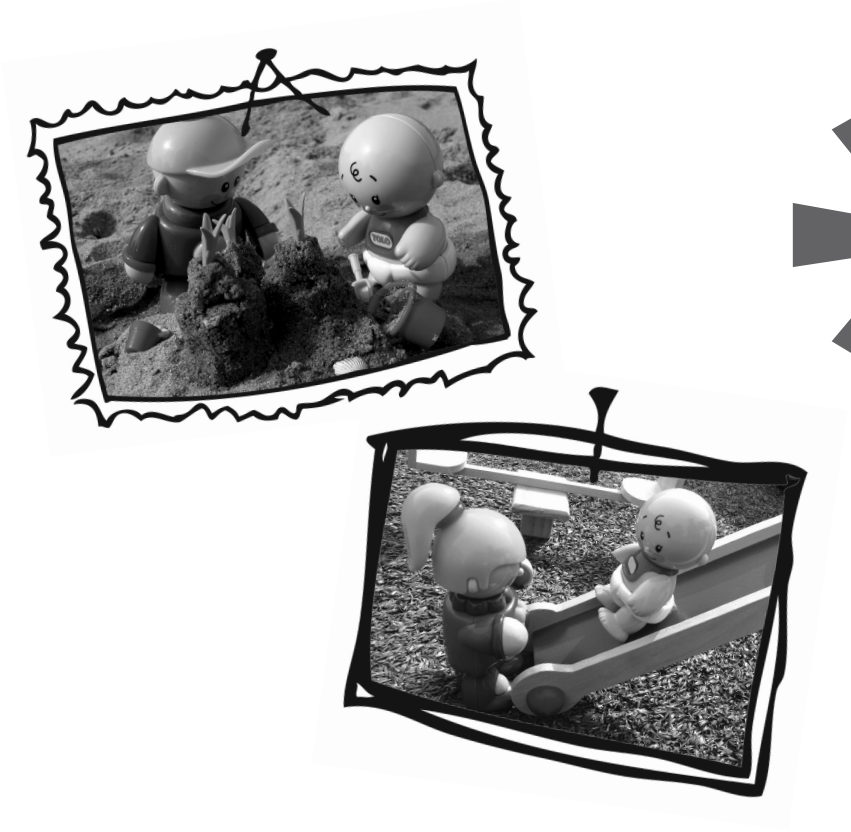
Van den Berg, M. P., van der Ende, J., Crijnen, A. A. M., Jaddoe, V. W. V., Moll, H. A., Mackenbach, J. P., Hofman, A., Hengeveld, M. W., Tiemeier, H., & Verhulst, F. C. (2009). Paternal depressive symptoms during pregnancy are related to excessive infant crying. *Pediatrics*, *124*, e96–e103.

Van den Bergh, B. R. H. & Marcoen, A. (2004). High antenatal maternal anxiety is related to ADHD symptoms, externalising problems, and anxiety in 8- and 9-year olds. *Child Development*, *75*, 1085–1097.

Van den Bergh, B. R. H., Mulder, E. J. H., Mennes, M., & Glover, V. (2005). Antenatal maternal anxiety and stress and the neurobehavioural development of the fetus and child: links and possible mechanisms. A review. *Neuroscience and Biobehavioral Reviews*, *29*, 237–258.

Van den Bergh, B. R. H., van Calster, B., Smits, T., van Huffel, S., & Lagae, L. (2008). Antenatal maternal anxiety is related to HPA-Axis dysregulation and self-reported depressive symptoms in adolescence: A prospective study on the fetal origins of depressed mood. *Neuropsychopharmacology*, *33*, 536–545.

Van der Valk, J. C., Verhulst, F. C., Stroet, T. M., & Boomsma, D. I. (1998). Quantitative genetic analysis of internalising and externalising problems in a large sample of 3-year-old twins. *Twin Research*, *1*, 25–33.



Samenvatting

De lichamelijke conditie van een vrouw tijdens haar zwangerschap is van invloed op de ontwikkeling van haar ongeboren kind. Ziektes van de moeder, zoals een te hoge bloeddruk of diabetes, of een bepaalde levensstijl zoals roken en alcoholgebruik tijdens de zwangerschap, kunnen een negatieve invloed hebben op de ontwikkeling van de foetus. Maar niet alleen de lichamelijke conditie van de moeder is belangrijk, ook haar psychisch welbevinden na de zwangerschap speelt een belangrijke rol voor de ontwikkeling van het kind. De laatste decennia laten veel studies een negatieve invloed zien van depressie of angstklachten van moeder. Baby's van moeders met een postpartum depressie blijken een moeilijker temperament te hebben, behalen lagere scores op mentale en motorische ontwikkelingstesten en zijn minder veilig gehecht aan hun moeder (Field, 1998). Peuters van depressieve moeders reageren negatiever op stress en de ontwikkeling van effectieve zelf-regulatie strategieën is vertraagd. Op schoolleeftijd laten deze kinderen meer schoolproblemen zien, zijn ze minder sociaal vaardig en hebben ze een lager zelfvertrouwen en meer gedragsproblemen (Goodman & Gotlib, 1999).

Niet alleen *na* de zwangerschap, maar ook al *tijdens* de zwangerschap blijkt het psychisch welbevinden van de moeder van belang te zijn voor de ontwikkeling van het dan nog ongeboren kind. Emotionele klachten van moeders, zoals gevoelens van depressie of angst, zwangerschapsgerelateerde angst, dagelijkse stressoren en positieve en negatieve levensgebeurtenissen (bijvoorbeeld een huwelijk of het overlijden van een familielid) zijn gerelateerd aan negatieve zwangerschapsuitkomsten, zoals een spontante abortus of zwangerschapsvergiftiging van de moeder, een vroeggeboorte of een laag geboortegewicht van het kind (voor een overzicht zie Mulder et al., 2002). De laatste jaren is er ook onderzoek verricht naar de invloed van emotionele klachten van moeders tijdens de zwangerschap op de ontwikkeling van kinderen op de langere termijn. Kinderen blijken meer problemen te hebben met hun motorische, cognitieve en vooral sociaal-emotionele ontwikkeling als hun moeders emotionele problemen hebben gehad tijdens de zwangerschap (O'Donnell, O'Connor, & Glover, 1999).

Een mogelijk biologisch mechanisme dat hieraan ten grondslag lijkt te liggen is 'foetale programmering' van de Hypothalamus-Hypofyse-Bijnier-as (Hypothalamic-Pituitary-Adrenal; HPA) (van den Bergh, Mulder, Mennes, & Glover, 2005; van den Bergh, van Calster, Smits, van Huffel, & Lagae, 2008). De HPA-as produceert het hormoon cortisol in reactie op stress. Als aanpassing aan nieuwe en stressvolle gebeurtenissen treden normaliter matige cortisol reacties op. Effectieve reactiviteit van de HPA-as is adaptief, waardoor de mens zich kan voorbereiden op een adequate gedragsmatige reactie op een stressor. Hyperactiviteit van het systeem kan echter negatieve effecten hebben op het immuunsysteem (Coe, Rosenberg, & Levine, 1988), de gezondheid (Flinn & England, 1995), het cognitieve functioneren en geheugen (de Kloet, Oitzl, & Joëls, 1999; Heffelfinger & Newcomer, 2001) van kinderen. Prenatale stress van de moeder kan leiden tot overactivatie en/of dysregulatie van de HPA-as van de kinderen door foetale programmering.

Het concept foetale programmering komt oorspronkelijk van Barker's (1995) "fetal origins of adult disease hypothesis". Deze theorie stelt dat de foetus zich fysiologisch

aanpast aan de kenmerken van de intra-uteriene omgeving waarin het zich ontwikkelt. Uit dieronderzoek blijkt dat de HPA-as van de foetus gevoelig is voor input vanuit de omgeving, zoals prenatale stress van de moeder (Weinstock, Matlina, Maor, Rosen, & McEwen, 1992). Prenatale angst en stress van de moeder stimuleert activatie van de HPA-as van de moeder waardoor zij meer cortisol produceert (O'Connor et al., 2005). Door de hoge productie kan een deel van deze cortisol via de placenta de foetus bereiken (Gitau, Cameron, Fisk, & Glover, 1998) en zo de HPA-as van de foetus beïnvloeden. Dit heeft als gevolg dat de HPA-as van de foetus wordt geprogrammeerd doordat de omgeving van de foetus waarin het zich ontwikkelt verandert. De foetus wordt zo beïnvloed door de cortisol productie van moeder en er kan een overactivatie of dysregulatie van het stresssysteem van de foetus ontstaan.

Naast dit neurobiologische mechanisme tijdens de zwangerschap, spelen omgevings- en psychologische processen na de zwangerschap ook een belangrijke rol voor de ontwikkeling van het kind. Vooral de kwaliteit van de (postnatale) moeder-kind en vader-kind interactie zou een belangrijke mediator of moderator kunnen zijn in de relatie tussen prenatale stress van de moeder en uitkomsten bij het kind. Tot nu toe zijn er weinig studies die de rol hebben onderzocht van de moeder-kind en vader-kind interactie in de relatie tussen emotionele problemen van de moeder tijdens de zwangerschap en gedragsproblemen bij het kind.

In dit proefschrift is de relatie onderzocht tussen emotionele problemen van moeders, meer in het bijzonder angst en depressieve klachten tijdens de zwangerschap, en de ontwikkelingsuitkomsten bij de peuters en kleuters vanuit een gedrags- en neurobiologisch perspectief. Dit proefschrift is onderdeel van een groot, prospectief follow-up onderzoek dat gestart is in 2002, waarin vrouwen tijdens hun zwangerschap (in week 12, 24 en 36) allerlei vragenlijsten hebben ingevuld, onder andere over hun emotionele klachten (Wijnen, 2005). De belangrijkste vragen die in dit proefschrift zijn bestudeerd zijn als volgt: Wat is de relatie tussen prenatale emotionele klachten van moeders en gedragsproblemen van peuters en kleuters? Wat is de relatie tussen prenatale emotionele klachten van moeders en stress reacties en het neurobiologisch functioneren van de kinderen? Welke rol speelt de kwaliteit van de moeder-kind en vader-kind interactie in de relatie tussen prenatale emotionele klachten van moeders en gedragsproblemen van kinderen? Bij al deze vragen zijn sexe verschillen tussen jongens en meisjes steeds bestudeerd.

In de eerste studie in *hoofdstuk 2* is de relatie tussen prenatale emotionele klachten van moeders tijdens de drie trimesters van de zwangerschap en gedragsproblemen van peuters en kleuters onderzocht. De data zijn verzameld tijdens de eerste fase van het onderzoek, waarin 444 moeders en vaders vragenlijsten hebben ingevuld over de gedragsproblemen van hun kinderen (CBCL). In dierstudies waren verschillen gevonden tussen mannelijke en vrouwelijke nakomelingen, maar in studies bij mensen waren de verschillen in uitkomsten bij jongens en meisjes nog nauwelijks onderzocht. Daarom zijn de analyses apart uitgevoerd voor jongens en meisjes. Een duidelijk verschil werd gevonden tussen jongens en meisjes in de relatie tussen prenatale stress van moeders en gedragsproblemen van de kinderen. Voor jongens bleek dat

emotionele problemen in het *eerste* trimester van de zwangerschap gerelateerd waren aan totale en internaliserende gedragsproblemen. Voor meisjes werd duidelijk dat emotionele problemen van moeders in het *derde* trimester waren gerelateerd aan totale, internaliserende en externaliserende gedragsproblemen.

In *hoofdstuk 3* is onderzocht of prenatale emotionele klachten van moeders ook gerelateerd zijn aan het neurobiologisch functioneren van peuters en kleuters. In het bijzonder werden de cortisol reacties bij de kinderen onderzocht voor en na een mogelijk frustrerend spelletje. Aangezien in hoofdstuk 2 verschillen werden gevonden tussen jongens en meisjes, zijn de analyses in dit hoofdstuk ook apart uitgevoerd voor jongens en meisjes. De data zijn verzameld in de tweede fase van het onderzoek waarvoor twee groepen werden geselecteerd, die meer in detail werden onderzocht tijdens een huisbezoek; een groep waarin de moeders veel emotionele klachten tijdens de zwangerschap hebben ervaren (exposed groep; $N = 66$) en een vergelijkingsgroep met vrouwen die weinig emotionele klachten tijdens de zwangerschap hebben ervaren (non-exposed groep; $N = 66$). De vrouwen in de groep met veel emotionele klachten hadden een score boven een gestandaardiseerde cut-off of een score hoger dan één standaarddeviatie boven het groepsgemiddelde op één van de drie angst- en depressie vragenlijsten in week 12, 24, of 36 van de zwangerschap. De vrouwen in de vergelijkingsgroep hadden op zijn minst in twee van de drie trimesters van de zwangerschap de vragenlijsten ingevuld en hadden op geen enkele vragenlijst een hoge score behaald.

Tijdens het huisbezoek werd het speeksel van de kinderen verzameld om de cortisol niveaus gedurende het huisbezoek te analyseren. De eerste speekselafname vond plaats aan het begin van het huisbezoek, de tweede afname vond ongeveer 22 minuten na een moeder-kind interactietaak plaats en de laatste speeksel afname vond plaats ongeveer 22 minuten na een taak die mogelijk frustratie opwekte bij de kinderen.

De cortisol niveaus tijdens het huisbezoek van de exposed kinderen werden vergeleken met de cortisol niveaus van de non-exposed kinderen, waarbij opnieuw apart naar jongens en meisjes werd gekeken. Analyses voor herhaalde metingen lieten zien dat *meisjes* van moeders die *veel* emotionele klachten hadden gehad tijdens de zwangerschap hogere cortisol niveaus tijdens de drie meetmomenten hadden dan de meisjes van moeders die *weinig* prenatale emotionele klachten hadden. Tussen de exposed en non-exposed *jongens* zijn geen verschillen gevonden in cortisol niveaus. Emotionele klachten van vrouwen tijdens de zwangerschap zijn kennelijk op een verschillende manier voor jongens en meisjes gerelateerd aan het functioneren van de HPA-as.

In *hoofdstuk 4* werd de rol van de kwaliteit van de moeder-kind interactie in de relatie tussen emotionele klachten van moeders tijdens de zwangerschap en gedragsproblemen van kinderen onderzocht. Het is goed mogelijk dat de vrouwen die tijdens de zwangerschap veel emotionele klachten hebben gehad, na de zwangerschap nog steeds of opnieuw emotionele problemen hebben. Als de moeders na de zwangerschap veel emotionele klachten ondervinden, gaan ze misschien ook op een andere, wellicht meer

negatieve en minder sensitieve manier met hun kinderen om. Deze minder optimale moeder-kind interactie zou vervolgens kunnen leiden tot meer gedragsproblemen bij de kinderen. Tijdens een huisbezoek met de moeders, is de moeder-kind interactie onderzocht aan de hand van de Emotional Availability Scales (EAS). De EAS bestaat uit zes subschalen; de moederschalen sensitiviteit, structuur, niet-intrusiviteit en niet-vijandigheid en de kindschalen responsiviteit en betrokkenheid. Multivariate analyses lieten geen verschillen zien op de zes subschalen van de EAS tussen de groep kinderen van moeders met veel emotionele klachten tijdens de zwangerschap en kinderen van moeders met weinig emotionele klachten tijdens de zwangerschap. Prenatale emotionele klachten tijdens de zwangerschap blijken dus niet gerelateerd te zijn aan de kwaliteit van de moeder-kind interactie na de zwangerschap en de moeder-kind interactie is geen *mediator* in de relatie tussen prenatale emotionele klachten van de moeder en gedragsproblemen van het kind.

Multivariate hiërarchische regressie analyses lieten wel een *moderator* effect zien van de moeder-kind interactie voor de *meisjes*. Meisjes van moeders die *weinig* emotionele klachten hadden gehad tijdens de zwangerschap (non-exposed), lieten weinig internaliserende gedragsproblemen zien, ongeacht de kwaliteit van de moeder-kind interactie. Meisjes van moeders die *veel* emotionele klachten hadden gehad tijdens de zwangerschap (exposed), lieten meer internaliserende gedragsproblemen zien als hun moeders een minder optimale interactiestijl hadden. Vooral wanneer hun moeders minder structuur boden en meer vijandig gedrag lieten zien, had deze groep (exposed) meisjes meer internaliserende gedragsproblemen. Voor *jongens* werden deze effecten niet gevonden. De relatie tussen emotionele problemen van moeders tijdens de zwangerschap en gedragsproblemen van kinderen kan dus niet alleen neurobiologisch verklaard worden, via het programmeren van de foetale HPA-as. De postnatale moeder-kind interactie speelt ook een belangrijke rol in de relatie met gedragsproblemen van meisjes.

In *hoofdstuk 5* is de rol van de kwaliteit van de vader-kind interactie onderzocht in de relatie tussen prenatale emotionele klachten van moeders en gedragsproblemen van kinderen. De vaders krijgen in onderzoek vaak weinig tot geen aandacht , terwijl zij ook een belangrijke bijdrage kunnen leveren aan de opvoeding en ontwikkeling van hun kinderen. Vaders die een optimale interactie laten zien met hun kind, kunnen misschien een beschermende buffer vormen tegen de negatieve invloed van emotionele klachten van moeders tijdens de zwangerschap. Maar wanneer vrouwen last hebben van emotionele klachten, komen deze klachten mogelijk ook vaker voor bij hun partners. Vaders zouden dan juist een extra risicofactor kunnen zijn voor de ontwikkeling van hun kinderen door hun eigen emotionele problemen. De vraag of vaders een buffer of een extra risicofactor vormen in de relatie tussen emotionele klachten van moeders tijdens de zwangerschap en gedragsproblemen van kinderen is onderzocht in hoofdstuk 5.

De kwaliteit van de vader-kind interactie is gemeten tijdens een huisbezoek met de EAS en is vergeleken tussen de exposed en non-exposed groep, afzonderlijk voor jongens en meisjes. Vaders van de exposed meisjes lieten meer emotionele klachten

zien dan vaders van de non-exposed meisjes, zoals postnataal gemeten is. Door dit hogere niveau van emotionele klachten, zouden de vaders een extra risicofactor kunnen vormen voor de exposed meisjes. Er kwam echter geen relatie naar voren tussen de huidige emotionele klachten van vaders en de gedragsproblemen van de meisjes in de exposed groep. In de kwaliteit van de vader-kind interactie met de exposed of de non-exposed jongens en meisjes is ook geen verschil duidelijk geworden.

Vaders bleken sensitiever te zijn en meer structuur te bieden en minder intrusief gedrag te laten zien dan moeders tijdens de interactie met de *jongens* in de exposed groep. Dit geeft aan dat vaders voor hun zoons een beschermende buffer zouden kunnen vormen door hun meer optimale interactiestijl met hun zoons, wanneer de moeders veel emotionele klachten hebben ervaren in de zwangerschap. Multipele hiërarchische regressie analyses hebben geen modererend effect duidelijk gemaakt van de vader-kind interactie, zoals wel gevonden is in hoofdstuk 4 voor de moeder-kind interactie.

Kortom, er werd geen duidelijk antwoord gevonden op de vraag of de vaders een beschermende buffer of extra risicofactor zijn voor de ontwikkeling van hun kinderen, wanneer de moeders veel emotionele problemen hebben gehad tijdens de zwangerschap. Voor beide alternatieven is enig bewijs gevonden. Meer onderzoek naar de rol van vaders is belangrijk om hier meer duidelijkheid over te krijgen.

In *hoofdstuk 6* werden de resultaten besproken, gevolgd door een overzicht van de sterke en zwakke punten van de studie, de klinische implicaties en overwegingen voor toekomstig onderzoek. De huidige studies tonen aan dat emotionele problemen van moeders tijdens de zwangerschap verschillend gerelateerd zijn aan de gedragsproblemen en neurobiologisch functioneren van jongens en meisjes. Naast het neurobiologisch stressreactie systeem spelen ook de geslachtshormonen in deze relatie een rol. Maar ook de psychologische en contextuele factoren zijn van belang in de relatie tussen maternale prenatale emotionele klachten en gedragsproblemen van de kinderen. De kwaliteit van de moeder-kind interactie speelt voor meisjes een belangrijke rol; wanneer de moeders veel emotionele klachten hebben gehad tijdens de zwangerschap en na de zwangerschap op een minder optimale manier met hun kind omgaan (weinig structuur, meer vijandig gedrag) worden meer gedragsproblemen gezien. Vaders kunnen naast een mogelijke extra risicofactor als gevolg van een verhoogde mate van eigen emotionele klachten, ook een beschermende rol vormen. Kortom, de relatie tussen emotionele klachten van moeders tijdens de zwangerschap en ontwikkelingsuitkomsten van kinderen kan niet alleen verklaard worden door foetale programmering van de HPA-as. De postnatale omgeving, met name de moeder-kind interactie, speelt hierin ook een belangrijke rol.

Deze conclusie heeft een belangrijke waarde voor de praktijk met betrekking tot preventie en behandeling. Tijdens de zwangerschap zouden verloskundigen alert moeten zijn op emotionele klachten bij de vrouwen. Zij zouden een screeningsvragenlijst kunnen afnemen en vrouwen met verhoogde emotionele klachten door kunnen verwijzen voor psychologische hulp. Daarnaast zouden deze vrouwen met verhoogde prenatale emotionele klachten ook na de zwangerschap extra begeleiding en ondersteuning

moeten krijgen. Interventies zouden zich dan specifiek kunnen richten op de kwaliteit van de moeder-kind interactie.

Referenties

Barker, D. J. P. (1995). The fetal origins of adult disease. Proceedings of the Royal Society of London. Series B. *Biological Sciences*, *262*, 37–43.

Coe, C. L., Rosenberg, L. T., & Levine, S. (1988). Immunological consequences of psychological disturbance and maternal loss in infancy. In C. Rovee-Collier & L. P. Lipsitt (Eds.), *Advances in Infancy Research: Vol. 5* (pp. 97-134). Norwood, NJ: Ablex.

De Kloet, E. R., Oitzl, M. S., & Joëls, M. (1999). Stress and cognition: Are corticosteroids good or bad guys? *Trends in Neurosciences*, *22*, 422–426.

Elgar, F. J., McGrath, P. J., Waschbusch, D. A., Stewart, S. H., & Curtis, L. J. (2004). Mutual influences on maternal depression and child adjustment problems. *Clinical Psychology Review*, *24*, 441–459.

Field, T. (1995). Infants of depressed mothers. *Infant Behavior and Development*, *18*, 1–13.

Field, T. (1998). Maternal depression effects on infants and early interventions. *Preventive Medicine*, *27*, 200–203.

Flinn, M. V. & England, B. G. (1995). Childhood stress and family environment. *Current Anthropology*, *36*, 854–866.

Gitau, R., Cameron, A., Fisk, N. M., & Glover, V. (1998). Fetal exposure to maternal cortisol. *Lancet*, *352*, 707–708.

Goodman, S. H. & Gotlib, I. H. (1999). Risk for psychopathology in the children of depressed mothers: A developmental model for understanding mechanisms of transmission. *Psychological Review*, *106*, 458–490.

Heffelfinger, A. K. & Newcomer, J. W. (2001). Glucocorticoid effects on memory function over the human life span. *Development and Psychopathology*, *13*, 491–513.

Leckman-Westin, E., Cohen, P. R., & Stueve, A. (2009). Maternal depression and mother-child interaction patterns: association with toddler problems and continuity of effects to late childhood. *Journal of Child Psychology and Psychiatry*, *50*, 1176–1184.

Lovejoy, M. C., Graczyk, P. A., O'Hare, E., & Neuman, G. (2000). Maternal depression and parenting behavior: A meta-analytic review. *Clinical Psychology Review*, *20*, 561–592.

Mulder, E. J. H., Robles de Medina, P. G., Huizink, A. C., Van den Bergh, B. R. H., Buitelaar, J. K., & Visser, G. H. A. (2002). Prenatal maternal stress: effects on pregnancy and the (unborn) child. *Early Human Development*, *70*, 3–14.

O'Connor, T. G., Ben-Shlomo, Y., Heron, J., Golding, J., Adams, D., & Glover, V. (2005). Prenatal anxiety predicts individual differences in cortisol in pre-adolescent children. *Biological Psychiatry*, *58*, 211-217.

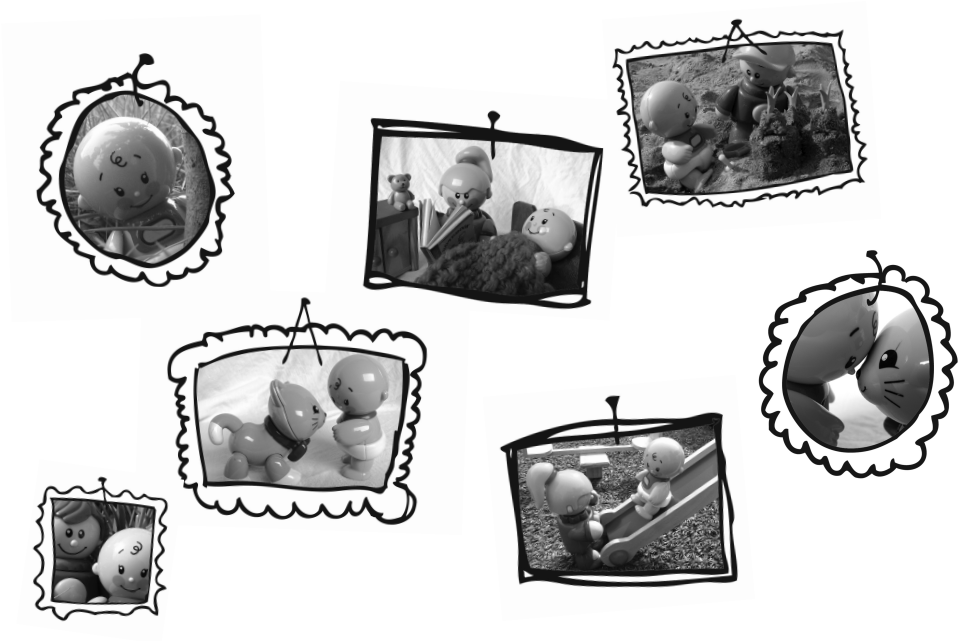
O'Donnell, K., O'Connor, T. G., & Glover, V. (2009). Prenatal stress and neurodevelopment of the child: Focus on the HPA axis and role of the placenta. *Developmental Neuroscience*, *31*, 285–292.

Van den Bergh, B. R. H., Mulder, E. J. H., Mennes, M., & Glover, V. (2005). Antenatal maternal anxiety and stress and the neurobehavioural development of the fetus and child: links and possible mechanisms. A review. *Neuroscience and Biobehavioral Reviews*, *29*, 237–258.

Weinstock, M., Matlina, E., Maor, G. I., Rosen, H., & McEwen, B. S. (1992). Prenatal stress selectivley alters the reactivity of the hypothalamic-pituitary-adrenal system in the female rat. *Brain Research*, *595*, 195–200.

Wijnen, H. (2005). *The Kempen study: Aspects of maternal well-being and obstetrical outcome in relation to gestational thyroid function*. PhD Thesis, Tilburg University, The Netherlands.

Dankwoord



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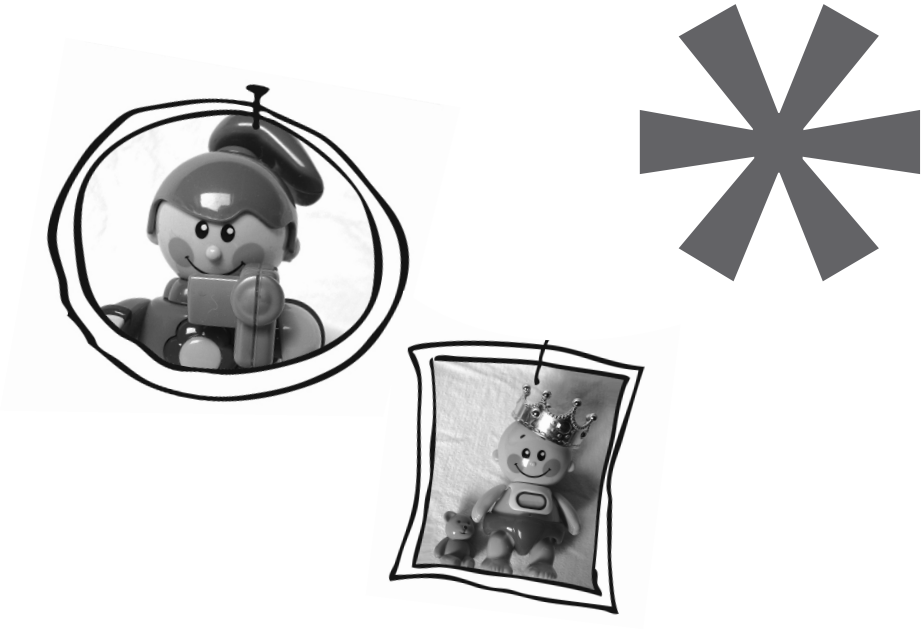

Curriculum vitae

Anouk de Bruijn werd op 1 augustus 1982 geboren in Roosendaal. Na het behalen van haar VWO diploma in 2000 heeft zij een jaar gestudeerd aan de Hogere Hotelschool in Maastricht. Omdat het hotelleven toch niet was wat zij zocht, is ze in 2001 begonnen met de studie psychologie aan de Universiteit van Tilburg. Zij studeerde in 2005 cum laude af in de afstudeerrichting Kinder- en Jeugdpsychologie, met als minor klinische neuropsychologie. Zij schreef haar scriptie over de cognitieve ontwikkeling van matig te vroeg geboren kinderen. Na haar afstuderen werkte zij als psycholoog in het Tilburgs Ambulatorium Neuropsychologie, waar ze ook haar stage had gelopen. In 2006 begon zij met haar promotieonderzoek aan de Universiteit van Tilburg. Tegelijkertijd is zij aan de slag gegaan als redacteur bij Stichting Babywerk. Voor deze stichting is zij nog steeds werkzaam als webredacteur waar zij o.a. de website up to date houdt op het gebied van onderzoek bij baby's en jonge kinderen. In 2008 is zij naast haar promotieonderzoek begonnen aan de tweejarige Infant Mental Health opleiding, 'van nul tot drie', bij de RINO in Amsterdam. Deze opleiding heeft zij in april 2010 succesvol afgerond. Sinds januari 2010 is Anouk werkzaam als psycholoog bij de combipoli psychiatrie/ kinder- en jeugdpsychiatrie van het Erasmus Medisch Centrum in Rotterdam. Zij is hier betrokken bij de moeder-kind dagbehandeling, voor moeders met psychiatrische stoornissen en hun baby's.