# Parents and Infants:

## Determinants of Attachment in a Longitudinal Population-Based Study

Anne Tharner

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**Ouders en hun Jonge Kinderen:**
Voorspellers van Gehechtheid in een
Longitudinaal Onderzoek

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**There are two lasting bequests we can give our children. One is roots. The other is wings.**

Hodding Carter, Jr.

# 1

# Introduction

# The importance of infant attachment for child development

Attachment theory is one of the most widely used and most extensively studied conceptual frameworks in the field of social and emotional development. John Bowlby, 'founding father' of attachment theory, defined attachment as follows "To say of a child that he […] has an attachment to someone means that he is strongly disposed to seek proximity to and contact with a specific figure and to do so in certain situations, notably when he is frightened, tired or ill." (Bowlby, 1969/1982). Bowlby argued that the formation of an attachment relationship is evolutionary rooted and that every child will form an attachment relationship with a person he regularly interacts with. The quality of the attachment relationship, however, is traditionally thought to be a result of interactions between the infant and the attachment figure (Ainsworth, Blehar, Waters, & Wall, 1978; Bowlby, 1969/1982).

The gold standard procedure to assess attachment quality in infancy is the Strange Situation Procedure (SSP, Ainsworth et al., 1978). This standardized laboratory procedure consists of eight 3-minute episodes that are designed to evoke mild stress in the infant to trigger attachment behavior. The infant is exposed to the unfamiliar lab environment, a female stranger trying to engage with him and finally, the caregiver leaving the room twice. Based on the child's behavior on return of the caregiver, the infant can be classified as securely attached, insecure-avoidant, insecure-resistant (Ainsworth et al., 1978) or disorganized (Main & Solomon, 1990). Securely attached children readily approach the caregiver to be comforted and then return to exploration and play. Insecure-avoidant children minimize attachment behavior and avoid contact with the caregiver. Insecure-resistant children maximize their attachment behavior, anxiously clinging to the caregiver while at the same time angrily resisting contact. The breakdown of an organized attachment strategy that characterizes disorganized attachment relationships is reflected in contradictory and inexplicable behavior, such as stereotypical rocking, laying down on the floor without moving or approaching the caregiver while showing signs of avoidance or fear.

The importance of early attachment relationships for the socio-emotional development of children is one of the central tenets of attachment theory and has been demonstrated in numerous studies over the past thirty years. Young infants are not yet able to deal with stressful situations on their own and therefore rely on a caregiver to help them modulate their stress. It has been argued that children develop adaptive or maladaptive emotion-regulation strategies within their early attachment relationships and that these strategies affect the way they will respond to future stressful situations (Carlson, 1998; Sroufe, 1996; for a review see Weinfield, Sroufe, Egeland, & Carlson, 2008). Based on previous experiences, securely attached infants are confident that their caregiver will be available in stressful situations. This confidence provides these children with an effective mechanism to cope with stress: they can approach the attachment figure for help and comfort in stressful situations. Insecure and disorganized children on the other hand lack such an effective coping strategy, which decreases the children's ability to regulate their emotions and reactions to stress (Cassidy, 1994; Greenberg, Speltz, DeKlyen, & Jones, 2001; Guttman-Steinmetz & Crowell, 2006). Different attachment classifications reflect different strategies of dealing with stressful situations: Insecure-avoidant children have a hypoactivating regulation strategy to avoid further rejection from an already unresponsive caregiver. Insecure-resistant children have a hyperactivating strategy, to assure the attention of an inconsistently available caregiver. Disorganized children, whose regulation strategies are thought to collapse in stressful situations, are left without a reliable mechanism to regulate their emotions.

It has repeatedly been shown that individual differences in attachment quality have important implications for later adjustment (see DeKlyen & Greenberg, 2008 for a review). Whereas secure attachment is related to social competence and resilience (e.g. Belsky & Fearon, 2002; Edwards, Das Eiden, & Leonard, 2006; NICHD ECCRN, 2006), insecure and especially disorganized attachment are associated with the development of emotional and behavioral problems in later life (McCartney, Tresch Owen, Booth, Clarke-Stewart, & Lowe Vandell, 2004; for a review see Guttmann-Steinmetz & Crowell, 2006). A recent meta-analysis including data of 5947 participants from 69 samples confirmed that early insecure and disorganized attachment are related to externalizing problems in middle and later childhood and even adolescence (Fearon, Bakermans-Kranenburg, Van IJzendoorn, Lapsley, & Roisman, 2010). This meta-analysis showed that insecure-avoidant but not insecure-resistant attachment in infancy was associated with externalizing problems. The strongest effect was found for attachment disorganization. Also, stronger effects were found in clinical samples than in nonclinical samples. Insecure-resistant and disorganized attachment, but not insecure-avoidant attachment, are also related to internalizing problems as a narrative review concluded (Brumariu & Kerns, 2010). In childhood, these attachment patterns were related to anxiety, and in preadolescents and adolescents also with depression. These results indicate that early regulation strategies that develop in the context of infant attachment relationships might be considered the blueprint for strategies that are handled throughout the further life, which makes it important to study factors that determine individual differences in these early attachment relationships.

## Determinants of infant attachment

Considering the importance of early attachment quality for socio-emotional development, many past studies have addressed the question which factors are involved in the etiology of individual differences in attachment quality. Sensitive responsiveness, the ability to respond appropriately to the child's attachment needs (Ainsworth, Bell, & Stayton 1974), is the most reliable predictor of attachment security (Bakermans-Kranenburg, Van IJzendoorn, & Juffer, 2003; De Wolff & Van IJzendoorn, 1997; McElwain & Booth-Laforce, 2006). A caregiver, who is routinely responsive to the child's attachment signals and needs, elicits confidence in the child about the availability of the caregiver if needed. Conversely, if the caregiver is unresponsive or inconsistently responsive, the development of secure attachment is undermined. In these instances, children are likely to form an insecure attachment relationship (Ainsworth et al., 1978). Attachment disorganization is thought to be the result of inexplicable and therefore potentially frightening caregiver behavior, including for example extreme insensitivity, parental dissociation or child maltreatment (for a meta-analysis see Madigan, Bakermans-

Kranenburg, Van IJzendoorn, Moran, Pederson, & Benoit, 2006). In stressful situations, disorganized children experience "fright without solution": they need the caregiver to help them deal with the stress, but they cannot approach the caregiver who is also a source of fear. In this paradoxical situation, the attachment strategy is thought to collapse (Hesse & Main, 2006; Main & Hesse, 1990).

**Environmental factors**

Previous studies have identified several environmental factors that are related to a higher risk of attachment insecurity and disorganization (for a meta-analysis see Van IJzendoorn, Schuengel, & Bakermans-Kranenburg, 1999). Most of these factors, such as circumstances that put caregivers under stress, for example a low socio-economic status or single parenthood, are thought to affect attachment quality because they decrease sensitive responsiveness and increase frightening behavior of the caregiver. There is some consensus that severe and chronic clinical parental psychopathology also affects attachment related caregiver behavior, for example caregivers may be less responsive to their children's needs due to depressive symptoms such as concentration problems, fatigue, loss of interest, negative cognitions and negative affect (Campbell, Brownell, Hungerford, Spieker, Mohan, & Blessing, 2004; Gelfand & Teti, 1990; Mills-Koonce, Gariepy, Sutton & Cox, 2008). Other common symptoms of depression such as dissociative periods, irritability, and flattened affect, may be related to attachment disorganization because they can be inexplicable for a child and therefore potentially frightening.

Research in this area has been mainly conducted with mother-infant dyads. Studies concerning sensitive responsiveness and attachment relationships of fathers are scarce and findings to date are equivocal. Some studies failed to find a significant relation between paternal sensitivity and attachment security (Braungart-Rieker, Garwood, Powers, & Wang, 2001; Volling et al., 2002). Others, however, found that fathers who spent more time with their infants had more positive interactions with them and that paternal sensitive behavior was related to attachment security (Cox, Owen, Henderson, & Margand, 1992; Das Eiden, Edwards, & Leonard, 2002). These studies provide some empirical evidence suggesting that similar factors are involved in infant-father and infant-mother attachment, but infant-father attachment remains understudied.

Another factor often considered to be important for the infant-mother relationship is breastfeeding. The close bodily contact promotes attunement of emotional and attentive states between infant and mother (for a review see Jansen, de Weerth, & Riksen-Walraven, 2008). Also, hormones such as oxytocin and prolactin that are released during breast-feeding mainly to support milk production and secretion facilitate maternal caregiving behavior (Neville, McFadden, & Forsyth, 2002; Uvnas-Moberg, 1999). Oxytocin is also related to parenting style and sensitive responsiveness in human parents (Feldman, Gordon, Schneiderman, Weisman, & Zagoory-Sharon, 2010; Naber, Van IJzendoorn, Deschamps, Van Engeland, & Bakermans-Kranenburg, 2010). However, there is surprisingly little direct empirical support for an effect of breastfeeding on attachment security and disorganization (Jansen et al., 2008).

**Biological factors**

More recently, research has also focused on biological factors related to infant attachment, such as genetics, that may alone or in interaction with environmental factors affect attachment quality (for a review see Bakermans-Kranenburg & Van IJzendoorn, 2007). Also, indices of physiological stress-regulation systems, mainly the Hypothalamic-Pituitary-Adrenal (HPA-) axis and the autonomic nervous system (ANS), have been studied in relation to attachment, because of the importance of attachment strategies for (dyadic) stress-regulation. The most consistent finding with regard to the association of attachment quality and HPA-axis functioning is that securely attached infants show no or only little adrenocortical activation measured by cortisol levels after the Strange Situation Procedure (Gunnar, Brodersen, Nachmias, Buss, & Rigatuso, 1996; Spangler & Grossman, 1993). Increases in cortisol have been found in disorganized infants (Hertsgaard, Gunnar, Erickson, & Nachmias, 1995; Spangler & Grossman, 1993; Spangler & Schieche, 1998), in insecure-avoidant and also in insecure-resistant children (Spangler & Grossman, 1993, Spangler & Schieche, 1998). Mixed results are also reported for associations of attachment quality and infant autonomic functioning measured by proxies such as heart rate (HR) or vagal tone (VT). A small study (Zelenko, Kraemer, Huffman, Gschwendt, Pageler, & Steiner, 2005) and a study that did not take attachment disorganization into account (Stevenson-Hinde & Marshall, 1999) found no association between attachment classification and infant autonomic functioning. Others reported less optimal autonomic functioning in disorganized children (Oosterman, De Schipper, Fisher, Dozier, & Schuengel, 2010; Spangler & Grossmann, 1993).

Individual differences in attachment quality are traditionally thought to be the result of differences in the quality of early interactions between the child and the caregiver. However, disrupted parenting only partly explains attachment disorganization. In order to fill this so called "transmission gap", recent studies have addressed the role of biological factors such as genetics in explaining disorganized attachment (for a review, see Bakermans-Kranenburg & Van IJzendoorn, 2007). Little is known about the neurobiology of infant attachment. The largest study to date investigating possible (neuro-) biological antecedents such as maternal medical history, infant anomalies at birth or neonatal behavioral orientation response, found no relation of these proxies of the child's neuro-biological status and later attachment disorganization (Carlson, 1998; Sroufe, Egeland, Carlson, & Collins, 2005). However, other studies found that the behavioral orientation response of newborns predicted later attachment disorganization (Spangler, Fremmer-Bombik, & Grossmann, 1996). Also the risk of attachment disorganization was higher in infants with neuro-developmental problems, such as autism, Down's syndrome, and neurological abnormalities due to maternal alcohol abuse during pregnancy, or premature birth (for a meta-analysis see Van IJzendoorn et al., 1999). These findings suggest that neurobiological factors may be involved in the etiology of attachment disorganization, but studies addressing the role of neurobiological differences for attachment quality in human infants are scarce.

## The current study

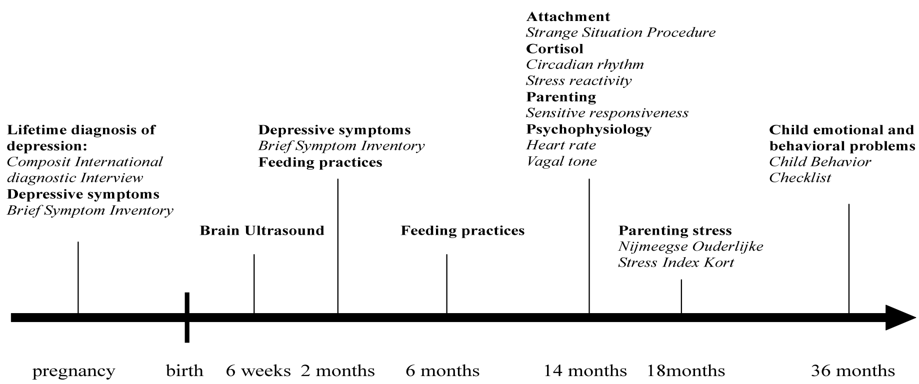
**Attachment in Generation R**

Attachment insecurity and disorganization are risk factors for later socio-emotional problems. Yet, they are frequent even in general population samples as shown by findings from the National Institute of Child Health and Human Development (NICHD) Early Child Care Research Network (ECCRN). The normative distribution derived by a meta-analysis including 920 non-US Western infant-parent dyads from the general population is: 51% secure (B), 20.2% insecure-avoidant (A), 10.3% insecure-resistant and 18.5% disorganized (D) (Van IJzendoorn et al., 1999). However, most studies have been conducted with either high risk samples with multiple problems or relatively small convenience samples. Findings from these studies may not be easily applicable to the general population and the large group of families who are not at high risk nor struggling with clinical problems.

In the current series of studies, we therefore examined environmental and biological factors that may help explain individual differences in infant attachment quality in the general population (for an overview see Figure 1). We conducted the Strange Situation Procedure with 881 infant-parent dyads participating in the Generation R Study when the child was 14 months old.

The Generation R study was designed to identify determinants of growth, development and health from fetal life onwards (Jaddoe, Van Duijn, Van der Heijden, Mackenbach, Moll, Steegers, et al., 2010). Detailed measurements of physical and psychological child development were obtained in a subgroup that included only children of Dutch national origin, meaning that the children, their parents and their grandparents were all born in the Netherlands. The participating children were born between February 2003 and August 2005. This study-population is the largest to date with data on attachment, observed parenting and biological markers. Due to the eligibility criteria, this is a rather homogeneous subgroup of participants, with a majority of two-parent families from the middleclass with a rather high education. This study-population reflecting low risk families with the same ethnic background from the general population is especially suited to study non-clinical and biological determinants of infant attachment quality.

**Figure 1.** Measurements in the Generation R study used in the current thesis



# Aim of this thesis

The general aim of this thesis is to provide more insight in the role of environmental and biological factors in the development of the infant attachment relationship in the general population. In Chapter 2 the question is addressed whether maternal lifetime history of depression and peri- and postnatal maternal depressive symptoms are related to infant-mother attachment insecurity and disorganization. Chapter 3 extends this question to infant-father dyads. Here we address the role of paternal psychopathology and sensitive responsiveness for infant-father attachment in an empirical study and in a meta-analysis. In Chapter 4, we take underlying physiological systems into account. Here we study the association between maternal depression, infant-mother attachment quality and child autonomic functioning, reflecting the functioning of the child's stress regulation system. Chapter 5 examines the same association using cortisol as a biological marker of stress-regulation capabilities. Chapter 6 addresses the question whether early structural neurobiological differences may predict attachment disorganization. In Chapter 7, we report findings concerning the role of breastfeeding for maternal sensitive responsiveness and infant-mother attachment quality. Finally, we conducted a first study examining the consequences of infant attachment quality and parenting stress for emotional and behavioral problems at 3 years of age. The findings are described in Chapter 8. Against the background of our results, the determinants of infant attachment quality in the general population will be discussed (Chapter 9).

# 5

# Attachment, depression, and cortisol: Deviant patterns in insecure-resistant and disorganized infants

Maartje P. C. M. Luijk, Nathalie Saridjan, Anne Tharner, Marinus H. van IJzendoorn, Marian J. Bakermans-Kranenburg, Vincent W.V. Jaddoe, Albert Hofman, Frank C. Verhulst, and Henning Tiemeier (2010). *Developmental Psychobiology, 52,* 441-452.

# ABSTRACT

Both attachment insecurity and maternal depression are thought to affect infants' emotional and physiological regulation. In the current study, Strange Situation Procedure (SSP) attachment classifications, and cortisol stress reactivity and diurnal rhythm were assessed at 14 months in a prospective cohort study of 369 mother-infant dyads. Maternal lifetime depression was diagnosed prenatally using the Composite International Diagnostic Interview (CIDI). Insecure-resistant infants showed the largest increase in cortisol levels from pre to post SSP; the effect was even stronger when they had depressive mothers. Disorganized children showed a more flattened diurnal cortisol pattern compared to non-disorganized children. Findings are discussed from the perspective of a cumulative risk model.

# Introduction

The infant-parent attachment relationship can be considered the infant's most important emotion regulation system (Bowlby, 1969/1982, Cassidy, 1994), since regulation is primarily externally organized in the first year of life. Early experiences are thought to shape the attachment relationship and thereby influence the regulation of behavioral and physiological responses. Most studies of the physiology of attachment relationships focused on measures of heart rate and cortisol during the Strange Situation Procedure (SSP, Ainsworth, Blehar, Waters, & Wall, 1978; e.g. Gunnar, Mangelsdorf, Larson & Hertsgaard, 1989; Oosterman & Schuengel, 2007; Sroufe & Waters, 1977). The current study includes the largest sample to date, which makes it possible to address issues of stress reactivity on the level of the various insecure attachment classifications. Furthermore, we examine the moderating role of maternal depression.

Early experiences have been shown to influence the behavioral and physiological organization of infants. Studies in humans and other animals document that deprivation of care has a major impact on the infant's developing system of stress regulation (Boyce, Champoux, Suomi, & Gunnar, 1995; Caldji, Tannenbaum, Sharma, Francis, Plotsky, & Meaney, 1998; Carlson & Earls, 1997; Levine & Wiener, 1988; Liu, Diorio, Tannenbaum, Caldij, Francis, Freedman, et al., 1997; Meaney, 2001; Plotsky & Meaney, 1993). In relatively low risk populations, differences in quality of care can predict differences in infant stress regulation. In the first year of life, regulation and coping are primarily externally organized. This makes the caregiver's responses to the infant's distress an important source of coping (Van Bakel & Riksen-Walraven, 2004). The availability of responsive, sensitive care is thought to promote infant attachment security and to mediate the infant's response to stressors (Gunnar & Donzella, 2002). Through their history of care, infants learn to what extent the caregiver is emotionally available in times of stress. Variation in parental availability, i.e. consistent sensitivity, inconsistent sensitivity, and consistent insensitivity, may lead to different secure and insecure attachment strategies in the infant (Sroufe, 1997).

Infants of consistently sensitive parents learn to expect their parents to be available in times of stress and have increased chances for developing a secure attachment relationship with their parent, which provides them with a powerful coping mechanism to regulate stressful stimuli. In contrast, infants of inconsistently sensitive or consistently insensitive parents do not come to expect their parents to be available in stressful situations. As a consequence, these children develop insecure attachment relationships with their parents. Insecure-resistant infants maximize their distress signals in order to get their parent's attention, whereas insecure-avoidant infants minimize signs of distress as they have learnt that they might be rejected (Main, 1990). In both cases the insecure children manage to create the best possible proximity to an attachment figure who is not optimally available. When the parent is extremely insensitive or even frightening, parental behaviors may cause a temporary breakdown in the child's strategy to keep close to the attachment figure which leads to dysregulation of negative emotions, as apparent in a disorganized attachment relationship (Main & Solomon, 1990).

Hertsgaard, Gunnar, Erickson, and Nachmias (1995) suggested that assessment of cortisol levels may be particularly useful in attachment research because the neuroendocrine system is believed to be stimulated when coping behaviors are inadequate or coping sources are unavailable. Studies on attachment quality and cortisol have focused mainly on stress reactivity, with assessment of cortisol levels before and after a potentially stressful event. The Strange Situation Procedure has often been used as the stressful event, as it is based on a series of brief infant-caregiver separations and reunions. The SSP is the gold standard procedure to assess the quality of the attachment relationship. Other methods of observing attachment quality, such as the Attachment Q-set (AQS; Waters, 1995) have not been widely used in cortisol research (but see Oosterman & Schuengel, 2007; Van Bakel & Riksen-Walraven, 2004).

Observations of infant behavior in the SSP allow for classification of infant behavior patterns into secure, insecure-avoidant, and insecure-resistant strategies. A secure (B) child seeks contact with the parent upon reunion, either physically or by distance interaction, to be comforted or reassured after the separation and resume exploration of the environment when he/she is settled. Insecure-avoidant (A) children, on the other hand, focus on the environment at the moment of reunion, ignoring the parent or even turning away from the parent. The reunion behavior of an insecure-resistant (C) child is characterized by anxious contact seeking and clinging and at the same time resisting contact with the parent. Resistant children are usually clearly distressed and their interaction with the parent may have an angry quality. On top of these classifications, the level of disorganization can be determined. Disorganized (D) children show a temporary breakdown of their secure, avoidant or resistant strategy of dealing with the return of the parent after separation, for example by simultaneous display of contradictory behaviors such as distress and avoidance (Main & Solomon, 1990).

Cortisol is released as a result of many aspects of an organism's interaction with the environment, including response to novelty and psychological stressors (Gunnar, 1994; Kirschbaum & Hellhammer, 1989, 1994). In normal situations, production of cortisol follows a diurnal rhythm with high levels at awakening, an increase in secretion shortly after awakening, followed by a decline throughout the day (Kirschbaum & Hellhammer, 1989; Watamura, Donzella, Kertes, & Gunnar, 2004). This diurnal rhythm in basal cortisol levels is relatively stable in adults, but early in life the Hypothalamic-Pituitary-Adrenal (HPA) system shows instability, and it continues to mature throughout infancy and childhood (De Weerth & Van Geert, 2002; De Weerth, Zijl, & Buitelaar, 2003; Watamura et al., 2004).

In stressful conditions, cortisol levels may rise. The cortisol response to stress serves an important function in adaptation to novel or stressful circumstances (Gunnar & Donzella, 2002; Van Bakel & Riksen-Walraven, 2004). Various studies have tested the effect of stressful events on HPA-axis functioning in infants, most of them focusing on cortisol levels around the SSP as related to infant attachment classification. Several non-clinical studies on physiological reactions to the SSP documented children's tendency to show elevated cortisol levels after the procedure. The most consistent finding is that no or only little adrenocortical activation is observed in securely attached infants (Gunnar, Brodersen, Nachmias, Buss, & Rigatuso, 1996; Spangler & Grossmann, 1993). Several studies reported increases in cortisol levels for the disorganized infants (Hertsgaard et al., 1995; Spangler & Grossmann, 1993; Spangler & Schieche, 1998).

Results for both insecure-avoidant and insecure-resistant groups are equivocal. In some studies, both insecure groups were found to have raised cortisol levels after the SSP (Spangler & Grossmann, 1993), others found increased cortisol levels only for insecure-resistant children (Spangler & Schieche, 1998). Spangler and Schieche (1998) interpreted their findings for the insecure-resistant group as supporting an arousal model, assuming associations between behavioral and physiological activation during stress. This model implies that temperamental factors are possibly involved in the physiology of attachment. For example, as found by Gunnar and Donzella (2002), more reactive and irritable children display higher levels of cortisol when faced with a stressor, especially when they have an insecure attachment relationship. However, the aforementioned studies involved relatively small samples, and larger samples with substantial numbers of children in each of the attachment classification groups are needed to draw firmer conclusions on the association between attachment and cortisol reactivity and diurnal rhythm.

Until now, studies have only investigated attachment in relation to stress reactivity, neglecting the relation between attachment and infant diurnal rhythm of cortisol excretion (but see Adam & Gunnar, 2001, for diurnal rhythm and attachment status in adults). However, differences in cortisol reactivity for the different attachment categories may be related to systematic differences in slope of their diurnal rhythms. Although considerable intra- and inter-individual variation is found in cortisol diurnal rhythm in young infants (De Weerth & Van Geert, 2002) some stability after the first birthday has been suggested (Larson, White, Cochran, Donzella, & Gunnar, 1998) and is in fact presumed in studies on cortisol reactivity in the SSP. In the current study diurnal cortisol rhythm is assessed and related to infant attachment classification.

Parental depression may negatively influence infants' physiological regulation. More specifically, in several studies maternal depression was related to higher cortisol levels in infants, which could indicate both environmental and biological mechanisms of transmission (Ashman, Dawson, Panagiotides, Yamada, & Wilkinson, 2002; Essex, Klein, Cho, & Kalin, 2002; Halligan, Herbert, Goodyer, & Murray, 2004; Lupien, King, Meaney, & McEwen, 2000; Young, Vazquez, Jiang, & Pfeffer, 2006). Maternal depression has also been associated with attachment quality. Depression is thought to compromise sensitive parenting behavior, which in turn can undermine the development of a secure attachment relationship. However, the empirical evidence for this association is not unequivocal (see Cummings & Davies, 1994). Research on severe and chronic depression, as well as studies with clinical samples showed a significant association between maternal depression and attachment insecurity (e.g. Teti, Gelfand, Messinger, & Isabella, 1995). In community-based samples, however, the effect of maternal depressive symptoms on attachment quality is less clear; meta-analyses reported small or even insignificant effect sizes (Atkinson et al., 2000; Van IJzendoorn, Schuengel & Bakermans-Kranenburg, 1999). Other studies suggested that pre- and postnatal depression might influence mother-child interaction (Lundy et al., 1999; Righetti-Veltema, Bousquet & Manzano, 2003).

In the current study we examine both cortisol reactivity to a stressor and the diurnal rhythm of cortisol in relation to infants' attachment status. We expect higher stress reactivity in insecurely attached children than in securely attached children. Furthermore, we expect that infants in the disorganized group differ in their cortisol reactivity from non-disorganized infants. With respect to diurnal rhythm, we expect to find a general pattern with higher morning than evening cortisol values. Since this study is the first to explore cortisol diurnal rhythm in relation to infant attachment status, we have no directed hypothesis on differences among attachment groups. Furthermore, we examine the moderating role of maternal depression on the association between attachment quality and cortisol levels. As maternal depression is related to insecure infant attachment and sub-optimal cortisol outcomes, maternal depression is hypothesized to act as an additional risk factor in the relation between insecure attachment and cortisol.

# Method

### Setting

The current investigation is embedded within the Generation R Study, a prospective cohort study investigating growth, development and health from fetal life into young adulthood in Rotterdam, the Netherlands, which has been described in detail elsewhere (Jaddoe et al., 2007; 2008). In the Generation R Study, we obtained detailed measurements of the child's development in a rather homogeneous subgroup: The Generation R Focus Study. Only children of Dutch national origin were included in this group, meaning that the children, their parents and their grandparents were all born in the Netherlands. The participating children were born between February 2003 and August 2005. The children visited the research center regularly for various somatic and behavioral assessments. Written informed consent was obtained from all participants. The study has been approved by the Medical Ethical Committee of the Erasmus Medical Center, Rotterdam.

**Study Population**

In the current investigation, data are presented of the 14 months visit of the Generation R Focus Study. A total of 882 infants and their parents participated between June 2004 and November 2006. In the first part of the visit, that lasted about 30 minutes, anthropometric and physiological measurements were conducted. Then, the Strange Situation Procedure (SSP) was administered, followed by assessments of the infants' motor functioning. In the SSP, 24 parents participated with two children (on different days). One child of each sibling pair was randomly excluded to avoid bias due to paired data. Another 29 children were excluded because of technical or procedural problems during the SSP. Of the remaining children, another 108 were not eligible for analysis because they completed the SSP with their fathers. After exclusion of these children, the study population consisted of 721 mother-infant dyads. Of this group, we had complete data on cortisol reactivity for 369 children, and 363 children were included in one or more measures of cortisol diurnal rhythm. Reasons for non-response were lack of time and failure to obtain saliva samples. A high rate of refusal to chew on cotton swabs is not uncommon in this age group and has been reported before (Goldberg et al., 2003). This is typically found in infants that are not familiar with pacifiers. A non-response analysis was conducted to check for differences between children with and without cortisol data. For cortisol diurnal rhythm, differences between the groups were found for age at assessment, ($p < .05$) gender ($p < .01$), and breastfeeding at the age of six months ($p < .05$). The group with diurnal cortisol data consisted of younger children, more boys, and the children were breastfed more often at six months of age. For cortisol stress reactivity, the groups differed on age at assessment ($p < .05$) and gender ($p < .01$); again, these children were younger and there were more boys in the group for which the data was available. For both cortisol reactivity and diurnal rhythm, non-response analyses did not show differences on maternal depression. Information about lifetime depression was available for 627 mothers.

**Procedures and Measures**

*Strange Situation Procedure.* Parent-infant dyads were observed in the Strange Situation Procedure (SSP) when the infant was about 14 months of age ($M = 14.7$, $SD = 0.9$). The SSP is a widely used and well-validated procedure to measure the quality of the attachment relationship. The procedure consists of eight episodes of 3 minutes each and is designed to evoke mild stress in the infant to trigger attachment behavior evoked by the unfamiliar lab environment, a female stranger entering the room and engaging with the infant, and the parent leaving the room twice (see Ainsworth et al., 1978, for the protocol). The SSP used in the current study included all these stimuli but to make it fit into a tight time schedule, we shortened the (pre-)separation episodes with one minute keeping the critical reunion episodes intact. Attachment behavior was coded from DVD-recordings according to the Ainsworth et al. (1978) and Main and Solomon (1990) coding systems by two reliable coders, trained at the University of Minnesota. Inter-coder agreement was calculated on 70 SSPs that were coded by both coders. For ABCD classification, inter-coder agreement was 77% ($\kappa = .63$); agreement on disorganization was 87% ($\kappa = .64$). Of all cases, 8% were discussed with one of two expert coders and classification was assigned after consensus was reached.

*Salivary cortisol: diurnal rhythm and stress reactivity.* Prior to the 14 months visit of the Generation R Focus Study parents were asked to collect saliva samples from their child at home using Salivette sampling devices (Sarstedt, Rommelsdorf, Germany). Parents received detailed written instructions with pictures concerning the saliva sampling. They were asked to collect five saliva samples during one single weekday at home: immediately after awakening, 30 minutes later, between 11 am and 12 pm, between 3 and 4 pm, and at bedtime; and to note down the sampling times. The child was supposed not to eat or drink 30 minutes before each sampling. The children were otherwise free to follow their normal daily routines on the sampling day. Parents were asked to keep the samples stored in a freezer until they visited the research centre. If parents forgot to bring the samples, they were asked to send the Salivettes by postal mail. For 397 children (55%) one or more home saliva samples were returned. One child was excluded because he/she was older than 20 months. To compute a cortisol composite measure, at least the first sample and, depending on the measure, one or two subsequent samples had to be obtained, which left 363 children for the diurnal assessments. None of the children used systemic corticosteroid medication, but 12 children used other corticosteroid-containing medication. Excluding these children did not change the results, so they were included in further analyses. During the visit at the research centre at 14 months of age, three saliva samples were taken; the first prior to the SSP, the second directly after the SSP (which was on average 10 minutes after the first separation of the SSP) and the third about 15 minutes later ($M = 16.3$, $SD = 8.3$). For 369 children (51%) three samples were obtained.

Samples were centrifuged and frozen at -80°C. After completion of the data collection, all samples were sent in one batch (frozen, by courier) to the Kirschbaum laboratory (Technical University of Dresden, Biological

Psychology, Professor Dr. Kirschbaum) for analysis. Salivary cortisol concentrations were measured using a commercial immunoassay with chemiluminescence detection (CLIA; IBL Hamburg, Germany). Intra- and interassay coefficients of variation were below 7% and 9%, respectively. For each time point, cortisol values that were above the 99th percentile (>200 nmol/L) were excluded from the analysis to reduce the impact of outliers ($n = 12$).

*Cortisol analyses.* The daytime profile of cortisol secretion was characterized by calculating composite variables of the separate cortisol measurements. In this way we took into account the relation between the separate cortisol values within each child. We determined the area under the curve with respect to ground ($AUC_G$), which is a measure of total cortisol secretion during the day (Pruessner, Kirschbaum, Meinlschmid, & Hellhammer, 2003). The $AUC_G$ was established by calculating the total area under the curve from the cortisol measurements in nmol/L on the y-axis and the time between the cortisol measurements on the x-axis. This takes into account the difference between the single measurements from each other and the distance of these measures from the ground, or zero (Pruessner et al., 2003, p. 918). To correct for differences in length of day, the $AUC_G$ was divided by number of hours between the first cortisol measurement (at awakening) and the last cortisol measurement (before going to bed) (see Watamura et al., 2004). Sleeping hours during the day were not associated with this composite measure. The $AUC_G$ was computed only for children having at least three saliva samples ($N = 228$). The cortisol awakening response (CAR) was used as an index of HPA axis activity. It was calculated as the difference between cortisol value at awakening and the value 30 minutes after awakening (Kunz-Ebrecht, Kirschbaum, Marmot, & Steptoe, 2004). For CAR, data was available for $n = 258$ children. As a measure of the diurnal cortisol decline we calculated the slope by fitting a linear regression line for each child, which predicted the cortisol values from time since awakening. The slope was computed by using the first and last saliva samples and at least one other cortisol measurement. To avoid any effect of the CAR on the slope (Adam, Hawkley, Kudielka, & Cacioppo, 2006; Cohen, Schwartz, Epel, Kirschbaum, Sidney, & Seeman, 2006), the second cortisol sample (30 minutes after awakening) was not included in this measure of the slope. Data were available for $N = 248$ children. These composite measures of cortisol were moderately intercorrelated ($AUC_G$-CAR: $r = .22$, $p < .01$; $AUC_G$-slope: $r = -.23$, $p < .01$; CAR-slope: $r = .51$, $p < .01$).

For stress reactivity a delta was calculated between the last sample ($cortisol_{postSSP}$) and the first sample ($cortisol_{preSSP}$). The second assessment, just after the SSP, was not used, as it was too close to the onset of stress to show an increase. To control for the Law of Initial Values (LIV; Wilder, 1968), which states that the direction of response of a body function depends to a large degree on the initial level of that function, in subsequent analyses this delta was adjusted for the first sample.

*Maternal lifetime depression*. The Composite International Diagnostic Interview (WHO, 1990) version 2.1 was conducted during a home-visit at 30 weeks of pregnancy to assess lifetime prevalence of psychiatric disorders in the pregnant women. The CIDI is based on the definitions and criteria of the DSM IV; good to excellent psychometric properties have been reported (Andrews & Peters, 1998; Wittchen, 1994). Interviewers had been trained at a WHO training center. The mother's partner was not present during the interview. In the current study we used lifetime diagnoses of unipolar depressive disorder. Unipolar depressive disorder was defined as diagnoses of dysthymia, a single episode of major depression (mild, moderate or severe) and recurrent major depression (mild, moderate or severe).

# Results

### Attachment

The distribution of the attachment classifications was as follows: 57.8% secure ($n = 413$), 19.0% avoidant ($n = 136$), 23.2% resistant ($n = 166$). Of all children, 22.5% were classified as disorganized ($n = 162$), 77.5% were non-disorganized ($n = 559$). No differences were found between the distribution of the complete group ($N = 721$), and the group for which data on cortisol reactivity or cortisol diurnal rhythm was available (respectively $\chi^2$ (3, $N = 721$) = 4.11, $p = .25$; $\chi^2$ (3, $N = 721$) = 4.15, $p = .25$).

**Table 1.** Child and parent characteristics of the secure, insecure-avoidant, and insecure-resistant attachment groups

| **Child characteristics** | **Secure ($n = 413$)** | **Insecure-avoidant ($n = 136$)** | **Insecure-resistant ($n = 166$)** |
|---|---|---|---|
| Gender, % female | 49.6 | 42.6 | 52.1 |
| Parity, % firstborn | 59.2 | 75.7 | 59.0** |
| Age at 14 months visit | 14.62 (0.88) | 14.77 (1.09) | 14.67 (0.87) |
| Time of assessment $cortisol_{preSSP}$ | 11:28 (1:58) | 11:31 (1:57) | 11:28 (2:07) |
| **Parent characteristics** | | | |
| Age at intake mother | 31.61 (3.94) | 31.74 (3.64) | 32.36 (3.69) |
| Maternal educational level, % low/ medium | 35.9 | 35.3 | 37.0 |
| Marital status, % single | 5.7 | 5.3 | 1.3 |
| Smoking during pregnancy, % | 12.4 | 14.2 | 8.0 |
| Alcohol during pregnancy, % | 56.4 | 48.9 | 61.3 |
| Alcohol during breastfeeding, % | 64.2 | 70.7 | 58.6 |

*Note.* Unless otherwise indicated, values are *M* and (*SD*). $^{**}p < .01$

Table 1 shows the demographic variables for attachment security. No overall differences were found, except for parity. Avoidant children were more often the first child, $\chi^2$ (2, $N = 714$) = 12.87, $p < .01$. In Table 2, demographics are shown according to disorganization status. Mothers of non-disorganized children consumed more alcohol during the period they breastfed, $\chi^2$ (1, $N = 490$) = 5.32, $p < .05$. Some demographic variables were related to the cortisol measures; age at 14-months visit was related to slope ($r = .16$, $p < .05$), and smoking during pregnancy was related to CAR ($F$ [2, 229] = 3.03, $p = .05$). Time of cortisol assessment was not related to cortisol measures or attachment classification, in fact, none of the demographic variables were related to both cortisol and attachment measures. Maternal lifetime depression was not related to attachment security ($F$ [2, 618] = 0.96, $p = .39$) nor to disorganization status ($F$ [1, 625] = 0.14, $p = .71$).

**Table 2.** Child and parent characteristics of the disorganized and non-disorganized attachment groups

| **Child characteristics** | **Not Disorganized ($n = 559$)** | **Disorganized ($n = 162$)** |
|---|---|---|
| Gender, % female | 48.1 | 51.2 |
| Parity, % firstborn | 63.3 | 58.6 |
| Age at 14 months visit | 14.67 (0.93) | 14.63 (0.89) |
| Time of assessment cortisol$_{preSSP}$ | 11:34 (1:59) | 11:06 (1:59) |
| **Parent characteristics** | | |
| Age at intake mother | 31.78 (3.83) | 31.96 (3.82) |
| Maternal educational level, % low/ medium | 36.8 | 33.1 |
| Marital status, % single | 4.7 | 3.8 |
| Smoking during pregnancy, % yes | 12.7 | 9.3 |
| Alcohol during pregnancy, % yes | 57.5 | 51.9 |
| Alcohol during breastfeeding, % yes | 66.4* | 54.5 |

*Note.* Unless otherwise indicated, values are *M* and (*SD*). *$p < .05$

## Attachment and Cortisol Stress Reactivity

To test whether cortisol stress reactivity differed across attachment classifications, an ANCOVA was performed. Because attachment security and attachment disorganization are considered orthogonal dimensions (Van IJzendoorn et al., 1999), they were entered as two separate factors. Maternal lifetime depression was entered as a covariate, as was the first cortisol assessment to control for initial cortisol values. We found a main effect for attachment security ($F$ [2, 308] = 9.03, $p < .01$, $\eta^2 = .06$. Resistant children differed from all other groups, displaying larger deltas, meaning larger differences between pre- and post-stressor assessment (post hoc analysis using Bonferroni criterion; $p < .01$), see Figure 1. In analyses, difference scores for cortisol (deltas) were used. In order to enhance interpretation, in Figure 1 cortisol values are shown. We did not find significant differences in stress reactivity between the disorganized group and the non-disorganized group. No main effect was found for maternal lifetime depression. A significant interaction effect was found for attachment security and maternal depression ($F$ [2, 308] = 4.22, $p < .05$, $\eta^2 = .03$).

**Figure 1.** Insecure-resistant children show high cortisol reactivity compared to the other groups; no differences in cortisol reactivity between disorganized and non-disorganized children

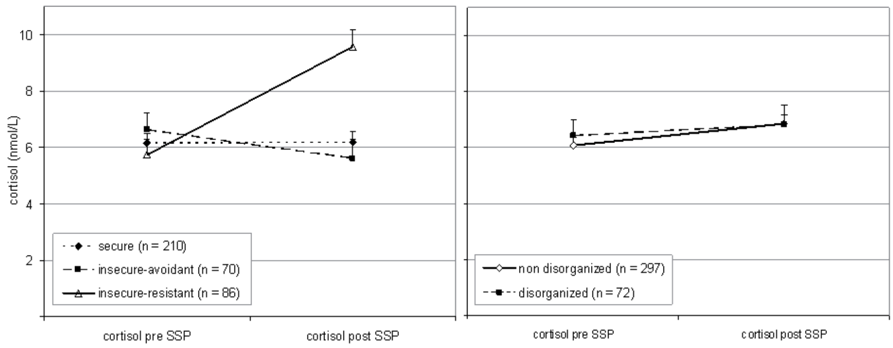
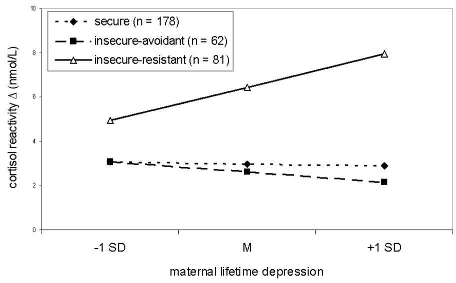



**Figure 2.** Stronger effect of maternal lifetime depression on cortisol reactivity of insecure-resistant children compared to insecure-avoidant and secure children



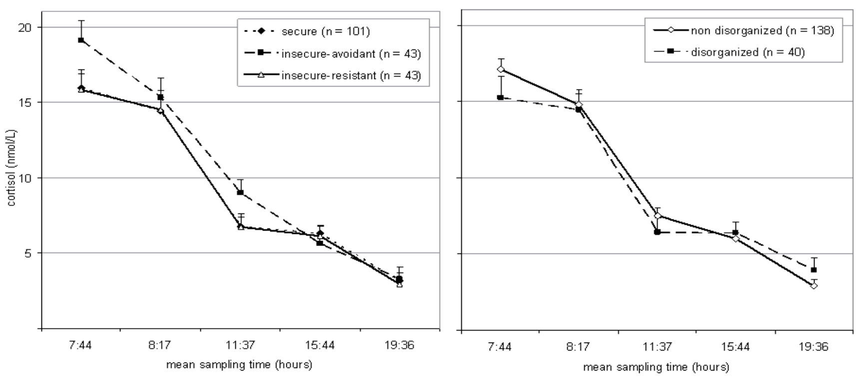

Locating the interaction effect, we found that resistantly attached infants showed highest cortisol reactivity, in particular when their mothers scored high on depression ($r$ [79] = .21, $p$ [one-tailed] < .05, see Figure 2). In a separate ANOVA, we found no differences in cortisol levels between the groups prior to the SSP (attachment security: $p = .53$; attachment disorganization: $p = .61$). When the middle cortisol assessment was aggregated with the first cortisol assessment as a baseline level, similar outcomes were obtained (data not shown).

### Attachment and Cortisol Diurnal Rhythm

The excretion of cortisol did show the expected diurnal pattern, with high levels at awaking and a decline throughout the day. In the cortisol diurnal curves of the infants, most children showed no morning rise. We performed an ANCOVA to test the effect of attachment quality on the cortisol measures $AUC_G$, slope, and CAR. Again, attachment security and attachment disorganization were entered as factors, and maternal depression was included as a covariate. A main effect of disorganization was found for slope ($F$ [1, 213] = 3.99, $p < .01$, $\eta^2 = .03$), indicating a more flattened slope for children with a disorganized attachment classification (slope disorganized group = -0.84, $SE$ = 0.11; slope non-disorganized group = -1.16, $SE$ = 0.06; Figure 3). Also, for $AUC_G$, an interaction effect was found for attachment security and disorganization, ($F$ [2, 195] = 3.34, $p = .04$, $\eta^2 = .03$).

Disorganized-secure infants showed higher cortisol excretion ($AUC_G$ = 10.49, $SE$ = 1.27) than disorganized-insecure infants ($AUC_G$ = 7.48, $SE$ = 1.27 for children with a secondary avoidant classification, and $AUC_G$ = 7.66, $SE$ = 1.05 for children with a secondary resistant classification). Compared to the non-disorganized group, cortisol excretion in the disorganized group was more divergent, dependent on the second classification. No effects were found for CAR or maternal lifetime depression.

**Figure 3.** No differences in cortisol diurnal rhythm for secure, insecure-avoidant, and insecure-resistant children; flattened slope for disorganized children compared to non-disorganized children



# Discussion

In a large cohort study with pertinent data on 369 mother-infant dyads, we found that infant attachment quality was related to cortisol stress reactivity, as assessed before and after the SSP. Resistant infants differed from all other groups, showing the largest increase in cortisol excretion after the SSP. Cortisol diurnal rhythm showed the expected diurnal pattern, with disorganized infants displaying a more flattened slope than non-disorganized infants. Maternal lifetime depression appeared to be a risk factor further elevating cortisol reactivity in infants with a resistant attachment relationship.

**Cortisol reactivity and insecure-resistant attachment**

Infants with a resistant attachment relationship showed the largest difference between pre and post SSP cortisol assessments compared to all other groups. This result converges partly with the outcomes of previous studies. Resistant infants were found to show higher cortisol levels after a stressful stimulus in some previous studies (e.g. Spangler & Schieche, 1998), but not in others (Gunnar et al., 1989; Nachmias, Gunnar, Mangelsdorf, Parritz, & Buss, 1996). In our study, infants classified as disorganized did not show increased reactivity, contrary to some of the previously reported results (Hertsgaard et al., 1995; Spangler & Grossmann, 1993). It may be the case that in previous studies reporting high reactivity in disorganized infants (Hertsgaard et al., 1995; Spangler & Grossmann, 1993) the majority of the infants had a secondary *resistant* classification; meta-analytic evidence confirms the suggestion that resistant infants have a strongly elevated chance of becoming classified as disorganized (Van IJzendoorn et al., 1999).

According to Weinfield, Sroufe, Egeland and Carlson (2008), resistant infants' history of erratic responsiveness renders them less able to direct attachment behaviors at caregivers when appropriate. Their 'maximizing' strategy might result in more physiological arousal than the 'minimizing' strategy of avoidant infants. Spangler and Schieche (1998) also proposed that resistant infants' high activation of the attachment system could not be terminated because they were not able to use the attachment figure effectively. Resistant infants 'maximize' their attachment behavior while they are at the same time unable to find a state of homeostasis in interaction with their caregiver (Cassidy & Berlin, 1994).

In contrast to the resistant infants, infants with secure or avoidant attachment classifications did not show significant increases in cortisol levels. This is partly convergent with previous literature. Both Hertsgaard et al.

(1995) and Spangler and Schieche (1998) did not find increases in cortisol in avoidant infants. Minimizing the display of negative emotions might protect avoidant infants against elevated physiological reactivity in mildly stressful settings. Securely attached infants showed hardly any heightened cortisol responses in previous studies. They exhibit appropriate behavioral strategies in coping with the separation (Spangler & Schieche, 1998). According to Bowlby (1973, p. 150), these behavioral strategies can be regarded as an 'outer ring' of life-maintaining systems. When this 'outer ring' is in homeostasis, an adaptation of the 'inner ring', or physiological system, is not necessary.

Another, complementary, explanation can be found in temperamental characteristics of the infant. The concept of regulation plays a central role in both attachment and temperament theory (Vaughn, Bost, & Van IJzendoorn, 2008). Temperamental characteristics of the infants have been found to play a role in stress physiology (e.g., Dettling, Parker, Lane, Sebanc, & Gunnar, 2000). In addition, previous studies documented the association between lowered temperamental reactivity in avoidant children, and heightened temperamental reactivity in resistant children (Vaughn et al., 2008). Interpreting our finding of elevated cortisol reactivity in resistant but not in avoidant children, we speculate that the dual risk of temperamental reactivity and an insecure-resistant attachment relationship may be responsible for the increased cortisol secretion after stress in resistant children. Avoidant infants are supposed to be buffered against elevated cortisol reactivity to mild stress because of their less reactive and somewhat more aloof temperament.

**Diurnal rhythm and disorganization**

Daytime cortisol showed the expected diurnal pattern, with higher levels at awakening and lower levels at the end of the day (e.g. Mantagos, Moustogiannis, & Vagenakis, 1998; Price, Close, & Fielding, 1983; Spangler, 1991). However, De Weerth and Van Geert (2002) state that while at group level there is evidence for the presence of a diurnal rhythm of cortisol from the early age of 2 months, individuals can vary greatly in the age at which they acquire the rhythm, which according to Gunnar and Donzella (2002) can be up to 4 years of age. To our knowledge, no previous studies related attachment quality to cortisol diurnal rhythm. In the current study, disorganized infants showed a more flattened slope of the diurnal rhythm than non-disorganized children. A flattened daytime pattern of cortisol – in its extreme form hypocortisolism – has often been found among children growing up in orphanages with structural neglect of basic emotional needs (see Gunnar & Vazquez, 2001, for a review). As a disorganized attachment relationship is thought to originate from extremely insensitive or even frightening parenting, this may cause similar physiological dysregulation in the disorganized group. Furthermore, higher diurnal cortisol excretion was found for disorganized-secure infants, whilst disorganized-insecure groups showed lower cortisol excretion. The interaction effect might indicate the intricate nature of these sub-groups. Cortisol excretion in children with a secondary insecure classification might be decreased in order to prevent enduring activation of the HPA-axis, whereas a secondary secure classification may indicate differential activation of the infants' endocrinological system, causing higher levels of excretion. Replications are essential to confirm these outcomes as our study is the first to be able to differentiate between these sub-groups.

**Cortisol reactivity and maternal depression**

Although several studies report maternal depression to affect both diurnal and reactivity cortisol levels in offspring (Azar, Paquette, Zoccolillo, Baltzer, & Tremblay, 2007; Brennan et al., 2008; Lupien et al., 2000; Young et al., 2006), in our study involving a non-clinical population such main effects were not found. Nevertheless, a clear interaction effect was found: infants with a resistant attachment relationship and a depressed mother displayed the strongest cortisol reactivity. The interaction between depression and attachment insecurity suggests a double risk model. In the case of resistant infants, the uncertainty about the mothers' availability is suggested to be associated with heightened attachment behavior, increasing the infant's monitoring of the caregiver and decreasing the exploratory competence (Cassidy & Berlin, 1994). In addition, infants of depressed mothers were found to experience reduced sensitivity and increased intrusiveness in interaction with their mothers (Goodman & Gotlib, 1999). Resistant attachment and maternal depression appear to compromise physiological regulation in an additive fashion.

**Limitations**

Some limitations of the current study need to be discussed. First, the Generation R Focus Study is a relatively homogeneous sample. However, the use of a homogeneous sample may have only led to an underestimation, and not an overestimation of the effects. Second, cortisol was sampled at 14 months of age. Cortisol levels at this age do show some intra- individual instability (De Weerth & Van Geert, 2002). However, data on the development of cortisol secretion throughout infancy and childhood are scarce, and we did find evidence for an established pattern. Again, instability may have led to an underestimation of the differences among attachment groups.

Third, a relatively large part of the participants could not be included in cortisol analyses, due to various reasons. Clearly informing parents about sampling could help to gain more and better saliva samples, however, sampling might remain difficult in 14-month-olds. Lastly, a slightly shortened version of the SSP was used, in order to make it fit into the schedule of the visit. This minimal procedural change did not appear to modify the stress of the SSP, since the number of infants for whom the situation appears to be most stressful (resistant and disorganized classifications) was not lower in the current study compared to the standard distribution.

## Conclusion

We documented the vulnerability of resistant infants in physiological stress regulation, especially in combination with care from a mother with a lifetime diagnosis of depression. Because of their small numbers in most attachment studies, resistant infants have been understudied as a separate insecure group. Our finding of elevated physiological stress reactivity in resistant children makes clear that this group can and should be differentiated from the other insecure attachment groups. We also showed that disorganized infants differed from non-disorganized infants in their diurnal cortisol rhythm, as they displayed a more flattened daily curve. This finding stresses the disturbed nature of disorganized attachments as one of the most important risks for developmental psychopathology. Our large-sample study suggests the differential physiological concomitants of avoidant, resistant, and disorganized attachments. Because infant attachment patterns have been shown to be relatively stable in stable environments (Fraley, 2002) insecure attachments may have long-term consequences for mental health, in particular in combination with other risk factors such as parental depression. Here we found that insecure-resistant and disorganized attachments can go 'under the skin' and may lead to deviating cortisol reactivity and daily patterns. From a biological perspective (Sapolsky, 2004) adverse early experiences can make humans and other animals more prone to stress and stress-related diseases, and attachment relationships may mediate the intergenerational transmission (Meaney, 2001) of this elevated vulnerability to emotional dysregulation.

# 6

## Subcortical structures and the neurobiology of infant attachment disorganization: A longitudinal ultrasound imaging study

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# ABSTRACT

Attachment disorganization in infancy is a risk factor for behavior problems and other psychopathology. Traditionally the role of parental behavior for qualitative differences in early attachment relationships has been emphasized. However, disrupted infant-parent interactions only partly explain attachment disorganization. A complementary focus on child factors such as early differences in the underlying neurobiological systems is needed. We examined whether early structural differences in the gangliothalamic ovoid, comprising of the basal ganglia and the thalamus, are involved in the etiology of infant attachment disorganization. Gangliothalamic ovoid diameter was measured by ultrasound in 6-week-old participants of a prospective population-based cohort study. Attachment classification of 629 of these infants was assessed with the Strange Situation at 14 months of age. Neurobiological differences within the normal range were prospectively associated with attachment disorganization. Infants with a larger gangliothalamic ovoid at 6 weeks had a lower risk of attachment disorganization at 14 months (*OR* 0.73 per *SD* increase in diameter, 95% *CI* 0.57 to 0.93, $p < .05$). Volume of the lateral ventricles as an index of general brain development was not associated with attachment disorganization. These findings provide new insight in the etiology of infant attachment disorganization that may in part be neurodevelopmentally determined.

## Introduction

During the first year of life, infants develop a stable emotional bond with a potentially protective attachment figure (Bowlby, 1969/1982). In the last 30 years, it has repeatedly been shown that early attachment relationships may have long-lasting consequences for the child's development (DeKlyen & Greenberg, 2008; Sroufe, Egeland, Carlson, & Collins, 2005). Secure early attachment relationships are related to social competence and resilience later in life (e.g. Belsky & Fearon, 2002; NICHD ECCRN, 2006). Disorganized attachment is considered the most insecure form of attachment and has consistently been associated with increased risk for later maladaptation and psychopathology (McCartney, Tresch Owen, Booth, Clarke-Stewart, & Lowe Vandell, 2004; for a review see Guttmann-Steinmetz & Crowell, 2006; for a meta-analysis see Fearon, Bakermans-Kranenburg, Van IJzendoorn, & Roisman, 2010).

The quality of the attachment relationship is traditionally thought to be a result of the quality of interactions between the infant and the attachment figure. Based on these interactions, the infant develops early internal working models of the self and other people in relation to the self (Bowlby, 1969/1982) that are used to manage emotional, behavioral and physiological systems. Disorganized attachment is thought to reflect the child's response to frightened, frightening or dissociative parental behavior (Hesse & Main, 2006; Lyons-Ruth, Bronfman, & Parson, 1999; Main & Hesse, 1990). The child is confronted with the irresolvable dilemma that the parent is at the same time the only potential source of comfort as well as a source of fear. The inclination to seek proximity as well as keep away from the parent may lead to the breakdown of a coherent attachment strategy to regulate responses to stressful situations (Hesse & Main, 2006). This breakdown of strategy is expressed in incoherent behavior in the presence of the parent, such as sequential or simultaneous display of contradictory behaviors (e.g. distress and avoidance); stereotypical or anomalous movements; freezing or stilling behaviors; expressions of fear or apprehension regarding the parent, and clear indices of confusion in the presence of the parent (Main & Solomon, 1990).

Disrupted parental behavior and attachment disorganization occur more frequently in high risk environments with for example low socio-economical status and parental psychopathology (Cyr, Euser, Bakermans-Kranenburg, & Van IJzendoorn, 2010; for a review see Lyons-Ruth & Jacobvitz, 1999). Disrupted infant-parent interactions, however, only partly explain attachment disorganization (Madigan, Bakermans-Kranenburg, Van IJzendoorn, Moran, Pederson, & Benoit, 2006; Van IJzendoorn, Schuengel, Bakermans-Kranenburg, 1999). Further research is needed to bridge this so called "transmission gap" (Madigan et al., 2006) and recent studies have begun to focus on the role of child factors such as genetics in explaining disorganized attachment (for a review see Bakermans-Kranenburg and Van IJzendoorn, 2007). Not much, however, is known about the role of structural neurobiological differences in the development of attachment relationships. Studies in human infants are scarce and often use indirect proxies of neuro-development. The largest study to date investigating possible biological antecedents of attachment disorganization (Carlson, 1998; Sroufe, Egeneland, Carlson, & Collins, 2005) found no relation between proxies of the child's neurobiological status such as maternal medical history, infant anomalies at birth, neonatal behavioral orientation response, or temperament, and later attachment disorganization. However, other studies found some support for the involvement of neurobiological factors in attachment disorganization. For example, the behavioral orientation response of newborns predicted later attachment disorganization (Spangler, Fremmer-Bombik, & Grossmann, 1996). Still other studies have shown that the risk of attachment disorganization is higher in infants with neuro-developmental problems, such as autism, Down's syndrome, and neurological abnormalities due to maternal alcohol abuse during pregnancy, or premature birth (Van IJzendoorn et al., 1999). Previous studies concerning the neural substrates of attachment in animal models and adult samples indicated the importance of prefrontal and limbic structures for attachment relationships in general (for a review see Coan, 2008). In addition, early parenting and attachment experiences have been shown to affect neuro-development (Suomi, 2008; Vaughn, Bost, & Van IJzendoorn, 2008). No study has examined yet whether neurobiological differences may at least partly determine disorganization of early attachment relationships in human infants.

In the current study, we examined whether early differences in subcortical structures predicted attachment disorganization at 14 months. We focused on the gangliothalamic ovoid, comprising of the basal ganglia (caudate head, putamen, and globus pallidus) and the thalamus. First of all, striatal regions (caudate and putamen) are known to play a crucial role in goal-directed learning (for reviews see Horvitz, 2008; Maia, 2009) in which prediction errors between expected and actual outcome are used to guide future behavior. This kind of learning is essential for the development of attachment-relationships. Furthermore, the basal ganglia are involved in voluntary motor action and have been conceptualized as a selection center that decides which behaviors to apply to achieve a certain set-goal (Redgrave, Prescott, & Gurney, 1999). Early structural differences in the basal ganglia may relate to the ability to select and execute goal-directed attachment behavior. The breakdown of this ability is the most salient characteristic of attachment disorganization (Hesse & Main, 2006; Lyons-Ruth et al., 1999; Main & Hesse, 1990). The thalamus, one of the output structures of the basal ganglia, may be involved in the development of attachment disorganization via connections with the emotion centers of the limbic system (Coan 2008; Kober, Barrett, Joseph, Bliss-Moreau, Lindquist, & Wager, 2008).

Attachment disorganization is a complex phenomenon, and it is likely to be the result of multiple mechanisms including contextual, genetic and possibly neurological factors. For example, evidence from genetic studies suggests that disorganization is not likely the direct product of additive genetic influences but rather affected by gene x environment interactions (for a review see Bakermans-Kranenburg & Van IJzendoorn, 2007). The same might be speculated for neuro-developmental factors. Barnett, Butler and Vondra (1999) suggested that neurobiological differences may predispose certain children to be more susceptible for contextual risk factors and proposed a conceptual framework that differentiates between three different kinds of atypical attachment relationships depending on the involvement of child factors and experience factors: 1) Children may develop atypical attachment relationships based on experience factors only, 2) Children may be falsely classified as atypically attached based on child factors such as neurological disorders, and 3) Children may develop atypical attachment relationships due to both experience and child factors. These children may be more susceptible for the influence of contextual factors due to neurodevelopmental predispositions.

The present study investigated whether disorganized attachment has a neurobiological component. We hypothesized that early structural differences in the gangliothalamic ovoid are related to later attachment disorganization. In contrast, we expected that early differences in general indicators of brain development, such as the volume of the lateral ventricles (Roza, Govaert, Vrooman, Lequin, Hofman, Steegers et al., 2008b) do not predict disorganized attachment. In addition, we examined the role of contextual risk factors for disorganized attachment to test whether the gangliothalamic ovoid diameter predicts attachment disorganization independent of a set of contextual risk factors.

# Method

### Study population

This research was conducted within Generation R, a population-based cohort from fetal life onwards in the Netherlands (Jaddoe, Van Duijn, Van der Heijden, Mackenbach, Moll, et al., 2008). The study was conducted in accordance with the guidelines of the World Medical Association Declaration of Helsinki and was approved by the Medical Ethics Committee of Erasmus Medical Center. Written informed consent was obtained from all adult participants. The study population consisted of 900 infants and their parents who participated in the visit at the research center scheduled six weeks postpartum. This cohort was ethnically homogeneous (indigenous Dutch) to reduce confounding and effect modification. All children were born between February 2003 and August 2005. During the 6-week visit, diameter of the gangliothalamic ovoid was successfully measured in 793 children. Nineteen children were excluded because they were twins and another 31 children because of lacking measures of head circumference. Attachment classification at 14 months was available for 629 of the remaining children (88% with the mother, 12% with the father). This group included no children with known neurological illnesses. Data on the volume of the lateral ventricles was available 596 of these children.

The group of included children ($n = 629$) differed from the children who could not be included due to missing data ($n = 271$) on the following measures: Mothers of included children were somewhat older ($M = 32.0$, *SD* = 3.70) than mothers of not included children (*M* = 31.25, *SD* = 4.68, $p < .01$), they were higher educated (Chi-Square [3] = 13.25, $p < .01$), were less often single parents (3.9% compared to 8.9%, $p < .01$), and breastfed for a longer period of time (Chi-Square [2] = 15.89, $p < .01$). Included children had a somewhat higher gestational age and weight at birth (40.10 weeks, 3521.03 grams) than not included children (39.71 weeks, 3433.78 grams, $p <$ .01 for both comparisons).

**Sample Characteristics**

Fifty percent of the children in our study were girls. Most of the children were firstborn (63%). Children were born between 31 and 43 weeks of gestation (*M* = 40.10, *SD* = 1.59) with a birth weight between 1435 and 4950 grams (*M* = 3521, *SD* = 508). Five minute APGAR scores were between 5 and 10 (*median* = 10.00). This indicates that this study was conducted in a normal, healthy sample. Furthermore, SES of the participants was high, as indicated by the educational level of the mother (67% had completed college or university). Only very few mothers did not have a partner (3.9%). Gangliothalamic ovoid diameter ranged from 3.75 mm to 4.84 mm (*SD* = 0.16). Twenty-one percent of the children were classified as disorganized, which is slightly more than expected (170 out of 920 participants [18.5%] of 12 normal Western non-US studies were classified as disorganized, see Van IJzendoorn et al., 1999). As shown in Table 1 there were no differences between disorganized and not disorganized infants concerning background variables such as gender, birth parameters or SES.

**Table 1.** Sample characteristics

| **Child characteristics** | | **Not disorganized ($n = 750$)** | **Disorganized ($n = 170$)** |
|---|---|---|---|
| Gender | % girl | 49.3 | 49.2 |
| Birthweight in grams, mean (*SD*) | | 3527 (503) | 3500 (526) |
| Gestational age at birth in weeks, mean (*SD*) | | 40.11 (1.54) | 40.05 (1.79) |
| 5 minute APGAR-score, mean (*SD*) | | 9.57 (0.78) | 9.66 (0.58) |
| Age at 6 weeks visit in months, mean (*SD*) | | 6.75 (1.77) | 6.64 (1.51) |
| Head circumference at 6 weeks in mm, mean (*SD*) | | 38.65 (1.46) | 38.48 (1.32) |
| Diameter gangliothalamic ovoid in mm, mean (*SD*) | | 4.33 (0.16) | 4.28 (0.18)** |
| Volume of lateral ventricles in $mm^3$, mean (*SD*) | | 0.99 (0.76) | 0.90 (0.62) |
| **Maternal characteristics** | | | |
| Maternal age at intake in years, mean (*SD*) | | 31.97 (3.67) | 32.06 (3.86) |
| Parity | % 0 | 64.3 | 57.6 |
| | % 1 | 27.2 | 33.3 |
| | % > 1 | 8.5 | 9.5 |
| Duration of breastfeeding | < 2 months | 28.7 | 35.8 |
| | 2 to 6 months | 37.4 | 39.0 |
| | > 6 months | 33.9 | 25.2 |
| **Contextual risk factors** | | | |
| Ethnicity | % not indigenous Dutch | 0 | 0 |
| Monthly family income | % low | 11.4 | 12.3 |
| Maternal educational level | % < 12 years | 8.7 | 13.7 |
| Marital status | % No partner | 3.7 | 4.7 |
| Family functioning, mean (*SD*) | | 1.40 (0.38) | 1.46 (0.41) |
| | % Low | 19.0 | 24.8 |
| Maternal psychopathology, mean (*SD*) | | 0.15 (0.20) | 0.15 (0.17) |
| | % High | 20.5 | 25.0 |
| Parenting stress, mean (*SD*) | | 0.47 (0.24) | 0.47 (0.26) |
| | % High | 19.1 | 15.9 |
| Cumulative contextual risk | % Few | 20.7 | 26.5 |
| | % Moderate | 9.5 | 7.6 |
| | % High | 18.5 | 23.5 |

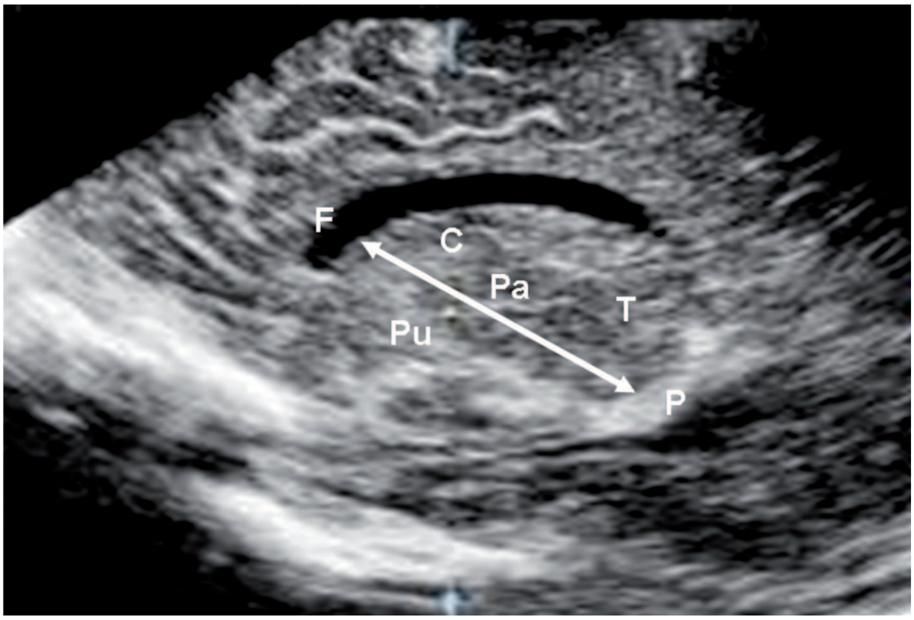
*Note:* Differences between disorganized and not disorganized infants were tested with Chi-Square tests and independent sample *t*-tests where appropriate. The two groups did not differ on any of the reported background variables at alpha ≥ .95. ** indicates a significant difference at $p < .001$.

**Measures**

*Ultrasound measurements.* The gangliothalamic ovoid was measured using cranial ultrasound through the baby's fontanelle, a non-invasive and cost-effective method to image the fetal and neonatal brain (Behnke, Eyler, Garvan, et al., 1999; Hintz & O'Shea, 2008; O'Shea, Kuban, Allred, Paneth, Pagano, Dammann et al., 2008). This technique is mainly used in clinical settings to examine the extent of brain damage and to estimate prognosis in very premature or high risk infants (O'Shea et al., 2008; Whitaker, Feldman, Van Rossem, Schonfeld, Pinto-Martin, Torre, et al., 1996). Within out research group, cranial ultrasounds have also been used to measure the brains of normally developing infants (Herba, Roza, Goveart, Van Rossum, Hofman, Jaddoe, et al., 2010; Roza Goveart, Lequin, Jaddoe, Moll, Steegers, et al., 2008a; Roza et al., 2008b). Ultrasound measurements were performed with a multi-frequency electronic transducer (3.7-9.3 MHz) with a scan angle of 146° (Voluson 730 Expert, GE Healthcare, Waukesha WI, USA). The probe was positioned on the anterior fontanelle and a volume box was placed at the level of the foramen of Monro in a symmetrical coronal section. We scanned a pyramid shaped volume of the brain tissue from which coronal, sagittal and axial sections were calculated (Roza et al., 2008a; Roza et al., 2008b). The diameter of the gangliothalamic ovoid, encompassing the basal ganglia, i.e. striatum: caudate head, putamen, globus pallidus, and thalamus, was measured offline as described by Naidich and colleagues (1986). In each infant the left and right gangliothalamic ovoid diameter in millimeters was measured by two raters (Cronbach's $\alpha = .84$). We used the average score of the two raters in the analyses.

Volume of the ventricular frontal horns, ventricular body and trigone on both sides were measured offline and quantified in milliliters (see Figure 1). Left and right ventricles were traced manually by four intensively trained raters. Intraobserver and interobserver reliability was calculated based on 20 images that were coded twice by each rater. Reliability was very good (ICC's ranged from 0.950 and 0.992).

**Figure 1.** Measurement of gangliothalamic ovoid diameter




*Note:* Cranial ultrasound was performed with a multifrequency electronic transducer (3.7-9.3 MHz) with a scan angle of 146° (Voluson 730 Expert, GE Healthcare, Waukesha WI, USA). The largest diameter was measured from the frontal horn (F) to approximately the middle of the choroid plexus (P). The following structures are identified: frontal horn (F), caudate head (C), putamen (Pu), pallidum (Pa), thalamus (T), and plexus (P).

*Attachment classification*. Parent-infant dyads were observed in the Strange Situation Procedure (SSP) when the infant was about 14 months of age ($M = 14.7$, $SD = 0.9$). The SSP is a widely used and well-validated procedure to measure the quality of the attachment relationship and is considered the gold-standard procedure to assess attachment in infants between 12-18 months of age. The procedure consists of eight episodes of 3 minutes each and is designed to evoke mild stress in the infant to trigger attachment behavior evoked by the unfamiliar lab environment, a female stranger entering the room and engaging with the infant, and the parent leaving the room twice (see Ainsworth et al., 1978, for the protocol). The SSP used in the current study included all these stimuli but to make it fit into a tight time schedule, we shortened the (pre-) separation episodes with one minute keeping the critical reunion episodes intact (Luijk, Saridjan, Tharner, Van IJzendoorn, Bakermans-Kranenburg, et al., in press). Attachment behavior during reunion episodes was coded from DVD-recordings according to the Ainsworth et al. (1978) and Main and Solomon (1990) coding systems by two reliable coders, trained at the University of Minnesota. Infants were classified as secure (B: $n = 321$), insecure-avoidant (A: $n = 78$), insecure-resistant (C: $n = 98$) (4) or disorganized (D: $n = 132$) (Ainsworth et al., 1978, Main and Solomon, 1990). Secure (B) infants seek proximity to and contact with the attachment-figure to be comforted or reassured after the separation and resume exploration of the environment when he/she is settled. Insecure-avoidant (A) infants evade direct contact with the attachment-figure and focus on the environment. Insecure- resistant (C) infants react ambivalently to the reunion: they anxiously seek contact while at the same time resisting contact with the attachment-figure (Ainsworth et al., 1978).

Disorganized classification was based on a score of > 5 on the attachment disorganization scale ranging from 1 (no signs of attachment disorganization) to 9 (strong signs of attachment disorganization) (Main & Solomon, 1990). The following behaviors were coded: sequential or simultaneous display of contradictory behaviors (e.g. distress and avoidance); undirected or misdirected movements and expressions; stereotypical or anomalous movements; freezing or stilling behaviors; expressions of fear or apprehension regarding the parent, and clear indices of confusion in the presence of the parent. Inter-coder agreement was calculated on 70 SSPs that were coded by both coders. For ABCD classification, inter-coder agreement was 77% ($\kappa = .63$); agreement on disorganization was 87% ($\kappa = .64$). Eight percent of the cases were discussed with one of two expert coders (MvIJ, MBK) and classification was assigned after consensus was reached.

It has been suggested that some of the behaviors that are coded as indices of a disorganized attachment relationship may in fact be medical symptoms of neurological impairments such as autism, cerebral palsy, Down syndrome or epilepsy (Pipp-Siegel, Siegel, & Dean, 1999). The following behaviors might fall into this category: dazed or impassive expressions, incomplete, slowed or limp movements, asymmetrical movements or facial expression, stereotypical repetitive movements, anomalous postures, jerky, unmonitored movements, freezing or stilling, disoriented movements or facial expressions. This is taken into account by the D-coding system that states that all behaviors have to occur in relation to the attachment-figure in order to be coded as indices for attachment disorganization. However, to exclude the possibility that D-classification merely reflected the level of neurological functioning, we distinguished two groups of disorganized infants: Those who were classified as disorganized due to the above mentioned behaviors that may be neurobiologically determined ($n = 28$), and those who were classified as disorganized due to behaviors that are relationship characteristic ($n = 95$).

*Cumulative contextual risk*. We constructed a contextual risk composite variable that has earlier been applied to predict child behavior problems in a large community based study (Belsky & Fearon, 2002). In the current study, this variable included 7 contextual risk factors out of 9 that were used in the Belsky and Fearon (2002) study: ethnic minority status, low family income (defined as below modal monthly family income in the Netherlands i.e. 2000 € after taxes), low maternal educational level (less than 12 years of education), single parenthood, low family functioning, high maternal psychopathological symptoms, high parenting stress. Family functioning was assessed with the Family Assessment Device (Epstein, Baldwin & Bishop, 1983; Miller, Epstein, Bishop & Keitner, 1985) in the last trimester of pregnancy. We measured maternal psychopathology at two months postpartum with the Brief Symptom Inventory, a validated self-report measure consisting of 53 items, which is widely used to assess psychological distress (De Beurs, 2004; Derogatis, 1993). Parenting stress was measured at 18 months postpartum with the Nederlandse Ouderlijke Stress Index – Kort (NOSIK, De Brock, Vermulst, Gerris, & Abidin, 1992), the Dutch version of the Parenting Stress Index – Short Form (Abidin, 1983). Analogous with the Belsky & Fearon (2002) approach, we defined risk status on the last three variables as the least favorable 20% of scores within our sample.

Cumulative risk was defined as the number of risk factors that applied to every participant divided by the number of risk factors endorsed by the participant to achieve a weighted index of cumulative risk with values between 0 (*none of the available factors have risk status*) and 1 (*all available factors have risk status*). For 96% of the participants information on all seven factors or six out of seven risk factors was available. To compare the distribution of cumulative risk with the distribution found by Belsky and Fearon (2002) in the NICHD sample, we created four risk groups in the same way as they did (see Table 1): No contextual risk (49.4%), low contextual risk (0.01 - 0.15, equivalent to 1 risk factor, 22%), moderate contextual risk (0.16 - 0.25, equivalent to 2 risk factors, 8.7%), and high contextual risk (> 0.25, equivalent to 3 or more risk factors, 20% ). These findings were very similar to the findings in the NICHD sample: 44% no risk, 21% low risk (1 risk factor), 13% moderate risk (2 risk factors), and 22% high risk (≥ 3 risk factors). For use in the analyses the cumulative risk scores were $Z$-standardized and outliers (≥ 3.29) were winsorized to the next highest score (3.08).

**Statistical analyses**

To examine whether environmental risk and structural variations in subcortical structures predicted attachment disorganization, we calculated Odds Ratios of attachment disorganization per standard deviation increase in cumulative contextual risk and gangliothalamic ovoid diameter. Non-disorganized infants were considered the reference group. We tested two models: Model 1 was adjusted for head circumference, and Model 2 was adjusted for other possible confounders (age at 6 weeks visit, birth weight, gestational age at birth, gender, parity, age of the mother, and duration of breastfeeding). To confirm findings from these analyses and to exclude possible threshold effects, we conducted linear regression analyses, using standardized cumulative contextual risk and standardized gangliothalamic ovoid diameter as predictors and attachment disorganization score as outcome. To exclude the possibility that our results merely reflected the general level of neuro-developmental functioning, we repeated these analyses after excluding infants classified as disorganized due to behaviors that may be neurobiologically determined ($n = 28$). We repeated analyses for boys and girls separately, and for both hemispheres separately. As an additional check, we examined whether total volume of the lateral ventricles as an index of general brain development predicted attachment disorganization at 14 months. Again, we tested the same two models as described above.

Finally, we tested whether gangliothalamic ovoid diameter predicted not only disorganized vs non-disorganized attachment, but possibly also predicted specific non-disorganized classifications (secure, insecure-avoidant and insecure-resistant). We conducted multinomial regression analyses to compare the three separate non-disorganized attachment classifications to the disorganized group.

**Table 2.** Gangliothalamic ovoid diameter at 6 weeks and the risk of attachment disorganization at 14 months

| | | Model 1: Attachment disorganization | | Model 2: Attachment disorganization | |
|---|---|---|---|---|---|
| **Total group** | **N** | **OR (95% CI)** | **p** | **OR (95% CI)** | **p** |
| Diameter of gangliothalamic ovoid (mm), *Z*-score | 626 | 0.73 (0.57; 0.93) | .02 | 0.73 (0.57; 0.94) | .01 |
| Cumulative contextual risk, *Z*-score | | 1.13 (0.92; 1.37) | .24 | 1.09 (0.87; 1.33) | .42 |
| **Dual indices excluded** | | | | | |
| Diameter of gangliothalamic ovoid (mm), *Z*-score | 591 | 0.71 (0.54; 0.94) | .02 | 0.70 (0.53; 0.94) | .01 |
| Cumulative contextual risk, *Z*-score | | 1.09 (0.87; 1.37) | .45 | 1.04 (0.82; 1.32) | .76 |

*Note*: Table 2 depicts results of binary logistic regression analyses. Not disorganized infants ($n = 497$) were used as the reference group. In the first analysis, the whole group of disorganized infants ($n = 132$) were the index group. In the second analyses infants classified as disorganized based on possible dual indices ($n = 35$) were excluded from the index group. Model 1: analyses adjusted for head circumference at 6 weeks. Model 2: analyses are adjusted for head circumference at 6 weeks, age at 6 weeks visit, birth weight, gestational age at birth, gender, parity, age of the mother, and duration of breastfeeding.
All continuous scores were standardized. Outliers (< -3.29, > 3.29) were excluded from the analyses.

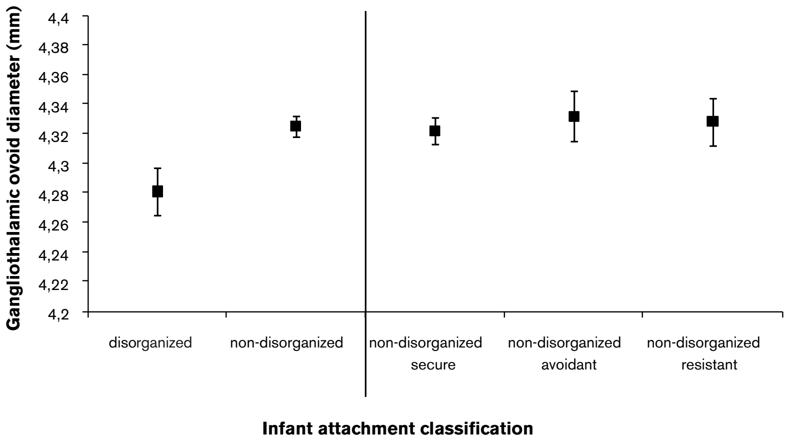
# Results

### Subcortical structures and infant attachment disorganization

We tested whether early variations in subcortical structures predicted infant attachment disorganization. First, we compared disorganized infants (D) to all non-disorganized classifications (A, B and C). Logistic regression analyses showed that a larger diameter of the gangliothalamic ovoid (per 1-*SD* increase in diameter) predicted a 25% lower risk of a disorganized attachment classification (*OR* 0.73, 95% *CI* 0.57 to 0.93, $p < .05$). This finding was confirmed in linear analyses, demonstrating that a larger gangliothalamic ovoid diameter six weeks postpartum predicted a lower attachment disorganization score at 14 months ($B = -.23$, 95% *CI* -0.42 to -0.04, $p < .05$). We tested two models: Model 1 was adjusted for head circumference and cumulative contextual risk, and Model 2 was adjusted for other possible confounders (age at 6 weeks visit, birth weight, gestational age at birth, gender, parity, age of the mother, educational level of the mother, and duration of breastfeeding, see Table 2). Results were essentially the same in both models. Furthermore, results were very similar in both genders and in left and right hemisphere.

Additionally we compared all separate non-disorganized classifications to the disorganized classification. Multinomial logistic regression analyses showed that gangliothalamic ovoid diameter significantly differentiated between the prediction of secure versus disorganized classification ($OR = 1.34$, 95% $CI$ 1.04 to 1.74, $p < .05$) and between avoidant and disorganized classification ($OR = 1.63$, 95% $CI$ 1.14 to 2.34, $p < .05$), but not between resistant and disorganized classification ($OR = 1.33$, 95% $CI$ 0.96 to 1.85, *ns*). The mean diameter of the gangliothalamic ovoid at 6 weeks across attachment classifications at 14 months can be seen in Figure 2.

**Figure 2.** Diameter of the gangliothalamic ovoid at 6 weeks of age across attachment classifications at 14 months




*Note:* Depicted are unadjusted means in mm. Error bars indicate the standard error of the mean. The non-disorganized group comprises secure, avoidant and resistant attachment classifications. Gangliothalamic ovoid diameter across the separate non-disorganized classifications is depicted in the right-hand half of Figure 2.

### Measures of general brain development and attachment disorganization

In order to test whether these differences might be due to general brain development, we repeated the analyses using the volume of the lateral ventricles as a predictor. The volume of the lateral ventricles at six weeks of age predicted neither disorganized classification ($OR$ 0.86, 95% $CI$ 0.67 to 1.09, *ns*) nor disorganization scores at 14 months ($B = -0.11$, 95% $CI$ -0.27 to 0.06, *ns*).

**Contextual risk and infant attachment disorganization**
Cumulative contextual risk was not significantly related to disorganized classification (see Table 2) or with ABCD-classification. However, higher contextual risk predicted a higher continuous disorganization score (Model 1: $B = .20$, 95% *CI* 0.05 to 0.36, $p = .01$; Model 2: $B = .15$, 95% *CI* -0.01 to 0.31, $p = .07$). Contextual risk did not interact with gangliothalamic ovoid diameter or volume of the lateral ventricles in predicting disorganized classification or score.

**Dual indices of attachment disorganization**
To exclude the possibility that our results merely reflected the general level of neurodevelopmental functioning, we conducted additional analyses in which infants classified as disorganized due to behaviors that may be neurobiologically determined ($n = 28$) were excluded. Results were essentially unchanged (see Table 2): A larger diameter of the gangliothalamic ovoid (per 1-*SD* increase in diameter) predicted a 29% lower risk of a disorganized attachment classification based on relationship characteristic behavior only ($OR = 0.71$, 95% *CI* 0.54 to 0.93, $p < .05$). We thus may conclude that our results are not an artifact of neurological impairments.

# Discussion

The current study suggests the involvement of basal ganglia and thalamus in attachment disorganization, since non-clinical volumetric differences in the gangliothalamic ovoid at six weeks postpartum predicted attachment disorganization at 14 months. We are aware that the study is quite exploratory, however, little is known yet about the neurobiology of infant attachment disorganization, e.g. not a single longitudinal MRI study in infants with subsequent attachment assessment has been conducted. The functions and connectivity of the structures we studied correspond well with the behavioral phenotype of disorganized attachment. Via cortico-striatal loops, the basal ganglia are a relay station between higher cortical regions, such as the prefrontal cortex, and lower motor areas. They are involved in voluntary motor action and have been conceptualized as a selection center that decides which behaviors to apply to achieve a certain set-goal (Redgrave et al., 1999). Attachment has been described as a behavioral system with the set-goal of achieving proximity to and contact with the protective attachment-figure (Bowlby, 1969/1982). In order to achieve the set-goal, attachment behavior like crawling, signing, calling etc. is applied. The breakdown of the ability select and execute goal-directed attachment behavior is the most salient characteristic of attachment disorganization (Main & Solomon, 1990). Smaller size of these structures may indicate an impairment of goal-directed attachment behavior and therefore contribute to the development of disorganized attachment relationships. Via cortico-striatal loops, putamen and caudate play an essential role in goal-directed learning (Horvitz, 2008) and have also been shown to be important in social learning (Harris & Fiske, 2010). Furthermore, the basal ganglia are involved in processes that may be more generally connected to the formation of attachment relationships, such as memory, facial recognition and reward (Grahn, Parkinson, & Owen, 2009; Redgrave et al., 1999). Early structural differences in the thalamus, which is one of the output structures of the basal ganglia, might affect the organization of attachment relationships via connections with the emotion centers of the limbic system (Kober et al., 2008).

Although not essential for the interpretation of the current findings, it is tempting to speculate about the origin of these early life variations in subcortical structures. Interindividual differences could be due to intrauterine influences or could be genetically determined. It is known that intrauterine influences such as placental circulation or prenatal stress affect the developing fetus (Field, Diego, Hernandez-Reif, 2006; Henrichs, Schenk, Roza, Van den Berg, Schmidt et al., 2009) and may also affect the development of the subcortical structures described in this study. Future studies may address this question and also whether such an effect might help to explain the association between prenatal stress, depression or anxiety and attachment disorganization independently of postnatal stress (Deave, Heron, Evans, & Emond, 2008).

Some molecular genetic studies have linked, for example, the dopamine D4 receptor gene (DRD4) to attachment disorganization. It has been argued that variations in the DRD4 7 repeat allele polymorphism makes infants more susceptible to environmental influences for better and for worse (Bakermans-Kranenburg & Van IJzendoorn, 2007). It is conceivable that genetic effects on attachment are mediated by variations in subcortical structures. Most neural pathways in the basal ganglia are dopaminergic, and these pathways are involved in attentional, motivational and reward mechanisms that are important in the formation of attachment relationships (Bakermans-Kranenburg & Van IJzendoorn, 2007). Furthermore, it has been shown that dopamine plays an important role in animal attachment learning in the face of frightening stimuli, which may also relate to human attachment disorganization (Barr, Moriceau, Shionoya, Muzny, Gao, et al., 2009; Sapolsky, 2009).

Our measure of general brain development did not predict attachment disorganization, which implicates that our findings are not due to a general neurological immaturity. On the other hand, attachment behavior consists of a number of complex behaviors, which cannot exclusively be explained by the differences in subcortical structures that we found in our study. Due to the limited possibilities of ultrasound imaging, we could not assess other structures that are of interest for attachment disorganization. Animal studies and studies in adults suggest a strong involvement of prefrontal structures or the amygdala (for a review see Coan, 2008). However, our results indicate for the first time that the development of disorganized attachment may have a neurological component. Considering that attachment theory posits that attachment behavior has evolved to ensure survival of the human offspring (Bowlby, 1969/1982) it makes sense that part of this behavior would be “hardwired” in the brain involving evolutionary older subcortical structures. To investigate the role of other brain regions for attachment disorganization, more sophisticated imaging techniques are indicated, which were not feasible in this sample of infants.

Evidence from genetic studies suggests that multiple genetic and contextual factors play a role in the development of attachment disorganization in a non-additive way (for a review see Bakermans-Kranenburg & Van IJzendoorn, 2007). The results of the current study indicate that structural neuro-developmental factors are also involved in the etiology of attachment disorganization and we may speculate how they interact with other factors that are known to play a role for attachment disorganization. For example, Barnett and colleagues (1999) suggested that neurobiological differences may predispose certain children to be more susceptible for experience factors. The current findings suggest that experience factors, indicated by cumulative contextual risk, and neurological factors are both involved in the etiology of attachment disorganization: While the original framework of Barnett and colleagues (1999) considered only clinical neurological deviations, the current study suggests that neurological variations within the normal range may play a role. Although cumulative contextual risk did not predict disorganized classification in the current study, in accordance with earlier findings in a low risk sample (Belsky & Fearon, 2002), it was related to higher continuous disorganization scores Our data do not support, however, an interaction- model of general contextual risk and early variations in subcortical structures. To test how early neurological predispositions may interact with genetic factors and more specific contextual factors such as disrupted parental behavior that have often been demonstrated to play a role in the development of disorganized attachment (Bakermans-

Kranenburg & Van IJzendoorn, 2007; Madigan et al., 2006) was beyond the scope of the current and should be addressed in future studies. High risk populations might be better suited than the current very low risk sample to study the interplay between neuro-developmental factors and disrupted parenting. It has previously been shown that extreme parental insensitivity was not related to attachment disorganization in low risk samples (Out, Bakermans-Kranenburg, & Van IJzendoorn, 2009).

The actual difference between disorganized and not disorganized infants in gangliothalamic ovoid diameter of is relatively small (0.04 mm corresponding to 1% of the diameter). Future research should address whether these structural differences relate to functional differences in processes critical for attachment formation. Another question that needs to be clarified is whether the current findings are specific to attachment disorganization or whether these early subcortical variations underlie general socio-emotional maladjustment. For example, a recent study from our study-group showed an association between smaller gangliothalamic ovoid diameter and internalizing problems at 18 and 36 months (Herba et al., 2010).

As a conclusion, the current study shows that early non-clinical neurobiological differences can predict infant attachment disorganization. Infants with a larger gangliothalamic ovoid at 6 weeks had a lower risk of attachment disorganization at 14 months. This finding may provide a new, neurological perspective on disorganized attachment, in addition to the common psychosocial explanations and might stimulate further studies that examine how neurobiological correlates and other genetic and contextual factors interact in the etiology of disorganized attachment.

# 9

# Discussion

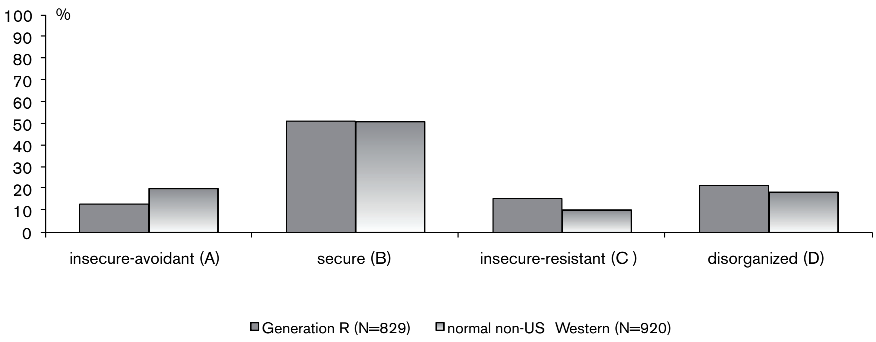
# Discussion

In the current series of studies, we examined environmental and biological factors that may explain individual differences in infant attachment quality in one of the largest attachment cohort study to date, the Generation R study.

**Distribution of attachment classification in the general population**

The Generation R Study is one of the largest studies to date examining infant attachment quality using the gold standard procedure, the Strange Situation (Ainsworth et al., 1978). This provided the opportunity to examine the distribution of attachment classifications in the general population and compare our findings to the distribution that was meta-analytically derived for non-US Western general population samples (Van IJzendoorn et al., 1999). The Strange Situation procedure was conducted with either infant-mother or infant-father dyads, depending on which parent accompanied the infant during the 14 months visit. If both parents were present, we asked the primary caregiver to participate in the Strange Situation. A total of 882 Strange Situations were completed. For 53 dyads (5.9%), no attachment classification could be determined due to technical (e.g. DVD-recording failed) or procedural (e.g. parent failed to complete the protocol) problems. Of the remaining 829 infants, 721 (87%) received an attachment classification with their mother, and 108 infants (13%) received an attachment classification with their father. The distribution of attachment classifications in infant-mother dyads was 49.1% secure, 13.3% insecure-avoidant, 15.1% insecure-resistant and 22.5% disorganized. In infant-father dyads the distribution was 62.0% secure, 9.3% insecure-avoidant, 17.6% insecure-resistant, and 11.1% disorganized. The total distribution is depicted in Figure 1 together with the normative distribution reported for normal, non-US Western samples ($N=920$) in the meta-analysis of Van IJzendoorn and colleagues (1999).

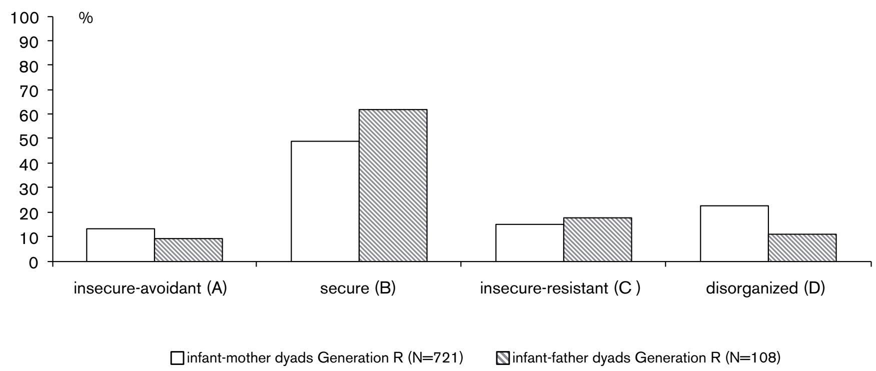
**Figure 1.** Distribution of attachment classifications




Distribution of attachment classifications varies slightly between the different studies described in this thesis due to different study populations. In the whole sample, the proportion of disorganized vs. not disorganized children as well as secure vs. insecure children is comparable to what has been described for normal non-US Western populations by Van IJzendoorn and colleagues (1999). However, the distribution of the organized insecure classifications differs somewhat from the meta-analytic findings, i.e. there were less insecure-avoidant and more insecure-resistant children in the current sample. It is unclear whether the differences in distribution of the different insecure classifications are a characteristic of the current study or are also found in other more recent non-US Western general population samples.

The distribution of attachment classifications in our sample as well as the normative distribution for non-US Western samples differ from the normative distribution found for general population samples in the United States as reported by Van IJzendoorn and colleagues (1999), i.e. 61% secure, 15% insecure-avoidant, 9% insecure-resistant and 15% disorganized. The distribution within the current sample is in accordance with the universality hypothesis, which predicts that all children will have a strong tendency to become attached and that the majority of children in normal samples will develop a secure attachment relationship. Nevertheless, culture specific differences in the distribution of the different insecure strategies might emerge. For example, as Van IJzendoorn and Sagi-Schwarz (2008) describe, if the suppression of negative emotions is required in a certain culture, avoidant attachment strategies may be more normative, because they increase inclusive fitness and general adaptation. Such cultural differences might exist between the United States and other Western countries and even between different Western countries. This should be taken into account when comparing distributions of attachment classifications to normative distributions. For infant-father dyads, no normative distribution is described yet, but the distribution may be different from the distribution in infant-mother dyads, as our findings suggest at least for highly involved fathers (see Figure 2).

**Figure 2.** Distribution of attachment classifications in infant-mother dyads and infant-father dyads




## Environmental factors

We studied two environmental factors that are often thought to be associated with attachment quality: 1) parental anxiety and depressive symptomatology, which are thought to be risk factors for attachment insecurity and disorganization even in non-clinical populations, and 2) breastfeeding, which is thought to foster attachment security.

The effects of maternal depression for the quality of early attachment relationships have frequently been studied (for a review see DeKlyen & Greenberg, 2008), however, with mixed results. Although some consensus has been reached that persistent and severe depressive symptoms undermine maternal sensitive responsiveness and are a risk factor for attachment insecurity and disorganization, findings vary greatly, probably due to differences in instruments used to measure attachment quality and depressive symptoms, as well as differences in the characteristics of the samples. In contrast with earlier studies that were often conducted in high risk or clinical groups, we found no association between maternal depression and infant attachment quality. Neither a maternal life-time diagnosis of depressive disorder, nor depressive symptoms during pregnancy and in the postpartum period were a risk factor for attachment insecurity or disorganization in our participants from the general population. A history of depression or anxiety was no risk factor for insecure or disorganized infant-father attachment either. In contrast, daughters of fathers with a history of depression or anxiety were more securely attached to their fathers than daughters of fathers with no psychiatric history. This rather unexpected finding might be explained by reporter-bias: secure fathers may be more inclined to honestly report a psychiatric history and might therefore be overrepresented in the group of secure dyads. Alternatively, this group of fathers reporting past but not current episodes of emotional disorders may be more self-reflective and parent differently. Our study of infant-father attachment also indicated that more sensitive responsive parental behavior was related to more attachment security, similar to what has been found for infant-mother dyads (for a meta-analysis see De Wolff & Van IJzendoorn, 1997). Interestingly, fathers with a history of depression or anxiety were not more sensitive than fathers with no psychiatric history, which means that the association between psychiatric history and attachment security was not mediated by sensitive responsiveness, but that the two factors were independent predictors of attachment security.

In our study on the effects of breastfeeding on maternal caregiving behavior and attachment quality, we found that longer duration of breastfeeding predicted more sensitive responsiveness in mothers as well as more secure and less disorganized infant-mother attachment. In this study, we could not replicate an association of maternal sensitive responsiveness and infant-mother attachment security. This implies that sensitive responsiveness did not mediate the association of breastfeeding duration and attachment security. Other factors, including hormonal pathways, other caregiving behaviors, and relationship characteristics need further study to explain the association between breastfeeding and attachment security.

### Biological factors

Our findings show that infant attachment quality is related to the functioning of physiological stress regulation systems, which may be less optimal in insecure-resistant and disorganized children. Insecure-resistant infants reacted more strongly to the mildly stressful Strange Situation Procedure

(Ainsworth et al., 1978) than infants with other classifications, as indicated by their larger increase in cortisol between the beginning and the end of the procedure. This reaction was even more pronounced in insecure-resistant children of mothers with a history of depression. In disorganized children, higher maternal depressive symptoms were related to lower resting vagal tone, which is also an indicator of less effective stress-regulation. This less optimal stress-regulation was also reflected by a flattened daily slope in cortisol production found in disorganized children.

These findings indicate that early social interactions may affect the functioning of physiological systems. Not much, however, is known about whether biological child characteristics might also play a role in the development of attachment relationships. In the first study to examine the effects of early structural neurobiological differences for attachment quality in human infants, we found that structural differences in subcortical structures were prospectively related to attachment disorganization. A smaller diameter of subcortical structures encompassing the gangliothalamic ovoid at six weeks of age was related to a higher risk of attachment disorganization at 14 months. Structural differences in the basal ganglia and thalamus may relate to functional differences in for example the selection and execution of goal-directed attachment behavior, which is disrupted in disorganized children. These findings provide a new, neurobiological perspective on the etiology of attachment disorganization.

## Determinants of infant attachment in the general population

Our findings do not completely converge with earlier findings concerning the determinants of infant attachment. Due to the important role of early attachment relationships for child socio-emotional development, many studies have addressed the question how individual differences in attachment quality develop. Across the past decades, ample empirical evidence has accumulated that infant attachment quality is determined by the quality of interactions between the child and his caregiver, supporting Mary Ainsworth's extension of Bowlby's theory of attachment (for a review see Belsky & Fearon, 2008). It is generally accepted that maternal sensitivity is causally related to attachment security, although there have also been studies that failed to replicate such an association (e.g. Murray, Fiori-Cowley, Hooper, & Cooper, 1996; Notaro & Volling, 1999; Seifer, Schiller, Sameroff, Resnick, & Riordan, 1996). In our studies, we could not replicate the link between maternal sensitive responsiveness and infant attachment security, maybe due to the relatively homogeneous sample or the somewhat contrived sensitivity assessment in a lab setting. However, we found that higher sensitivity in fathers predicted more secure infant-father attachment relationships. Attachment disorganization, on the other hand, is generally considered to be the result of fear in attachment relationships (Hesse & Main, 2006), although no studies have tested yet whether the link between frightening parental behavior and attachment disorganization is causal (see Belsky & Fearon, 2008, for a review). The association between frightening parental behavior and attachment disorganization was not included in the current series of studies.

In addition to these proximal determinants of attachment quality, research has addressed more distal factors that are thought to be important for attachment quality because they affect caregiver behavior and the quality of infant-caregiver interactions. These studies have often been conducted in high risk samples, such as the seminal Minnesota Longitudinal Study of Parents and their Children (e.g. Waters, Vaughn, & Egeland, 1980; Egeland & Farber, 1984; Carlson, 1998), or clinical samples (e.g. Lyons-Ruth, Connell, Grunebaum, & Botein, 1990; Murray et al., 1996). Findings from these studies indicate that severe and chronic risk factors such as clinical parental psychopathology, poverty, or single-parenthood are related to attachment insecurity and disorganization.

Because insecure and disorganized attachment also occur frequently in families that are not at an increased environmental risk, the current series of studies examined factors that may play a role for attachment quality in the general population. Our findings showed that some factors that might be involved in the development of attachment insecurity and disorganization in high risk or clinical studies, such as depressive symptoms (e.g. Carter et al., 2001; Field, 1992a; Lyons-Ruth et al., 1990), may not affect attachment security in the general population. A likely explanation for the absence of an association between maternal depressive symptoms and attachment quality is that depressive symptoms in the general population may not be invasive enough to alter maternal parenting behavior. This might be due to the severity of the symptoms, which is by definition less in general population samples than in clinical samples. Likewise, coping with depressive symptoms might be facilitated in many general population samples where additional risk factors are less frequent than in high risk samples, and social support is higher. Whereas single risk factors may not affect infant attachment in the general population, a combination of multiple risk factors, even less serious ones, may have negative effects. These risk factors may have additive effects in accordance with cumulative risk models (Greenberg et al., 1999; Rutter, 1999; Sameroff & Fiese, 2000) implying that developmental outcomes are predicted by the severity and variety of risk factors that a child encounters. Also, certain children may be more vulnerable for the negative effects of a risk factor, such as for example disorganized children were more strongly affected by maternal depressive symptoms than children with other classifications (see Chapter 4 and 5). The effects of risk factors identified in clinical or high risk populations may be non-significant in the general population because they are too weak or buffered by supportive factors. On the other hand, low risk population based samples might be better suited to identify factors enhancing attachment quality which may not play a role in high risk or clinical samples because their effects are too subtle and overshadowed by other more severe risk factors. Examples of such factors are breastfeeding and innate non-clinical neurobiological differences.

## The merit of large longitudinal attachment studies

Most of the studies concerning the determinants of infant attachment were conducted using relatively small samples that were not followed up over a longer period of time. Exceptions are the Minnesota Longitudinal Study, which has followed a cohort of 267 children and their parents since 1975, and the NICHD SECCYD who have followed more than 1000 children since the early 1990s. Thus, the Generation R Study, in which attachment is assessed in almost 900 one year-olds, is one of the largest studies to date to examine the determinants of infant attachment prospectively.

When the determinants of attachment quality are studied in retrospect at the time of the attachment assessment, findings might be confounded because the current experiences with the child may affect the way parents report about their own behavior and the behavior of the child in the past. In our studies, the measurement of attachment quality by observation and a prospective study design significantly reduce possible effects of recall bias on our findings. Another advantage of the prospective design is that temporal relations can be assessed. For example, earlier studies have shown that individual differences in attachment quality were related to neurobiological differences (for a review see Coan, 2008). However, it was generally assumed that early raising experiences affect neurodevelopment. We showed that the reverse might also be true by demonstrating that neurobiological differences at six weeks of age were prospectively related to differences in attachment quality at 14 months. Nevertheless, despite the prospective study design, causality cannot be directly inferred. Findings might be the result of indirect underlying causal factors, such as genetic factors that affect brain and thus attachment disorganization. The associations may also not be causal at all if an unknown third factor affects both the predictor and the outcome, which are in fact unrelated.

Due to the size of our sample, the power of our studies was sufficient to detect subtle effects that would not have been significant in smaller studies, such as the effect of breastfeeding duration on maternal sensitive responsiveness and infant attachment security and disorganization. Also, we were in the position to conduct more detailed analyses for example in the subgroups of disorganized attachment that have rarely been done before. Furthermore, null findings could not be explained by insufficient power, e.g., in our study about the effects of maternal depressive symptoms on infant attachment we had sufficient power (80%) to detect effect sizes corresponding to an Odds Ratio of 1.7 at $\alpha = .05$. This supports the conclusion that maternal depressive symptoms really did not affect infant attachment quality, which would have been more questionable had our results been derived from a smaller sample.

Results of earlier studies concerning the determinants of infant attachment have not always been unequivocal. For example, whereas some studies found an effect of maternal depressive symptoms on infant attachment quality, others failed to replicate this finding. Meta-analyses have tried to integrate the equivocal evidence to provide an overall picture of the determinants of infant attachment. Although meta-analyses are a very useful tool in summarizing the results of (smaller) single studies, large *N* single studies may still be warranted. In medical sciences, large trials usually follow meta-analyses to derive final conclusions about the effectiveness of a treatment. It has been shown that smaller studies often find larger effect sizes than large studies, and therefore, a meta-analysis of small studies may overestimate effects (e.g. Contopoulos-Ioannidis, Gilbody, Trikalinos, Churchill, Wahlbeck, & Ioannidis, 2005). Also, the included studies often vary greatly with regard to methods and sample composition, and this heterogeneity makes meta-analytic results on a limited set of small studies less reliable. Finally, although meta-analyses usually test for publication bias, meta-analytic findings might still overestimate effects because null-findings are less likely to be published (Ioannidis, 1998). Therefore, large, longitudinal single studies such as the current one, using repeated standardized assessments in a prospective design can add important contributions to the field of attachment research.

## Limitations

The studies described here were conducted within the context of the Generation R Focus Study. As described earlier, our study sample consists mainly of healthy, low risk families and is by definition limited to Caucasian Dutch participants. The initial response of Dutch women in the Generation R Study was about 68% which was somewhat higher than the overall response-rate of about 61% (Jaddoe et al., 2010). Of the women who were eligible for participation in the Focus Cohort, about 80% ($N = 1232$, Jaddoe et al., 2010) participated in the first measurement, a detailed ultra-sound exam in the third trimester of pregnancy, and 989 of these women participated in the home visit, during which the CIDI was conducted (see Chapter 2). Of these families, 881 infant-parent dyads participated at the 14 months visit and the Strange Situation Procedure. Non-response analyses indicated that both initial non-response and attrition were selective. As is usually the case in population based studies, healthier and less problematic families were more likely to participate, which further added to the low risk nature of our sample. For example, as described in Chapter 2, attrition analysis showed that families who stayed in the study had less parental psychopathology and higher educational levels than families who were lost to follow up. However, selective non-response is only a problem if the associations differ in the group of participants and the group that was lost to follow-up. Since outcome data are missing in the lost-to follow up group, it is not possible to test whether this was actually the case. Based on earlier studies and meta-analyses, it might be expected that effects of environmental factors on infant attachment quality are generally smaller in low risk samples than in high risk samples (e.g. Van IJzendoorn et al., 1999). However, the aim of the current project was to study determinants of infant attachment in “normal”, healthy families of which the current sample consisted. Furthermore, the homogeneous nature of this high functioning sample made it especially suited to study biological effects, as well as subtle environmental effects, because confounding by other risk factors was smaller than in high risk samples.

Effects of confounding, defined as a distortion of the apparent effect by an underlying third factor that is associated with both the predictor and the outcome, have to be considered. Although we were able to control for several confounding factors, such as SES, the presence of siblings, and parental psychopathology, other possibly confounders were not assessed, such as parental personality characteristics, child temperament, and parental attachment representation. Also, genetic factors might explain effects that we found, e.g. children of depressed parents might have a genetic predisposition for emotional maladjustment, which is expressed both in insecure attachment relationships and less effective physiological stress-regulation. Likewise, residual confounding may also affect the association between breastfeeding and maternal sensitive responsiveness and infant attachment, as would be the case if mothers who choose to breastfeed differ from mothers who choose not to breastfeed in personality traits that affect their choice to breastfeed as well as their parenting behavior and the attachment relationship.

The issue of confounding is closely related to the issue of causality that is discussed in each of the separate chapters. The prospective design, as discussed above, provides the most important criterion of causality, i.e. that the cause has to precede the effect in time (Rothman & Greenland, 1998). Nevertheless, causality cannot automatically be inferred from prospective associations. Associations may be the result of underlying confounding factors as discussed above. Also, reverse causality might be the case, as in Chapter 8, where child behavior problems might not be the result of parenting stress, but parenting stress might be the result of continuing misbehavior of the child. Intervention studies or (quasi-) experiments are needed to establish causality, but are not always ethical or feasible. However, the results of a large prospective study that are consistent with earlier findings from smaller studies may strengthen the confidence in possible causal pathways.

More specific limitations of the series of studies presented here may be that infant attachment was assessed with a slightly shortened version of the original Strange Situation protocol (Ainsworth et al., 1978) in order to make it fit into the schedule of the visit. The separations were shortened, but the critical reunion periods were left intact (for a detailed description see Luijk et al., 2010). In theory these differences may have affected the assessment of attachment quality. However, it might be expected that stress-levels of the children are lower due to the shorter separation, which might have led to an underestimation of insecurity or disorganization. However, as discussed above, the proportion of securely attached children and disorganized children found in the current study are comparable with earlier findings in non-US Western samples from the general population. The proportion of children for whom the SSP is expected to be most stressful (insecure-resistant and disorganized) is even at the higher end of what is typically found in low risk samples. By contrast, the absence of an association between maternal sensitive responsiveness and infant attachment security might be partly due to the situation in which sensitive responsiveness was assessed. Sensitive responsiveness is generally assessed in situations involving active interaction between mother and child, in this was not the case in one episode of sensitivity assessment, in which the child was sitting on the mother's lap watching a television show. However, meta-analyses have reported that the association between maternal sensitivity and infant attachment is robust but modest in size (De Wolff & Van IJzendoorn, 1997) which implies that there have been other studies that did not find such an association (e.g. Notaro & Volling, 1999; Seifer et al., 1996).

## Clinical implications and future directions

The quality of early attachment relationships can have long lasting consequences for the child's socio-emotional development (see DeKlyen & Greenberg, 2008 for a review). Insecure and disorganized attachment are risk factors for later emotional and behavioral problems that are relatively frequent even in an otherwise low risk environment. For example, as described in Chapter 8, we found that in families who experience higher levels of parenting stress, insecure and disorganized infant attachment is related to toddler emotional and behavioral problems. Securely attached children had low levels of emotional and behavioral problems, independently of parenting stress. These findings indicate that even in average families facing everyday stresses of family life, insecurely attached and disorganized children are more affected by normative stressors than securely attached children. Our findings that the physiological stress regulation capabilities of insecure-resistant and disorganized children were also less effective than those of securely attached children as described in Chapters 4 and 5 further support the assumption that insecure and disorganized children are less effective in dealing with stress, which in turn is thought to have long lasting consequences for behavioral and emotional adjustment.

Considering the importance of early attachment relationships for, among other things, the stress regulation capacities of the child, families may benefit from early interventions to enhance attachment security which might enable the child to deal more effectively with stressful situations, both behaviorally and physiologically. Different attachment strategies developed in infancy might even have specific consequences for emotional and behavioral development, as our last study (Chapter 8) showed. For example, we found that avoidant infant attachment, which is characterized by minimizing attachment behavior and direction of anger and frustration towards the environment, was related to aggressive behavior in toddlers from families with high parenting stress. This kind of information might be useful in the treatment of behavior problems in young children: Aggressive behavior may be partly due to behavioral strategies the child has developed in the interaction with an unresponsive parent in order to avoid further rejection, and interventions including the parent might target these dysfunctional interactive patterns.

Knowledge about the determinants of infant attachment in the general population may be used for the development of prevention and intervention programs to enhance attachment security. Intervention and prevention programs to enhance infant attachment security have mostly targeted parental behavior and factors affecting parental behavior. For example, it has been shown that relatively short intervention programs of up to 6 sessions focused on parental sensitivity are most effective in enhancing both sensitive parental behavior and attachment security (Bakermans-Kranenburg, Van IJzendoorn & Juffer, 2003). As the association between parental sensitive responsiveness and infant attachment is only moderately strong ($r = .24$, De Wolff & Van IJzendoorn, 1997), other parenting characteristics might also be important for attachment security. General population studies are especially suited to identify such factors that may positively affect attachment relationships, because strong environmental risk factors are absent. For example, as we have shown in Chapter 7, attachment relationships may benefit from longer breastfeeding. However, breastfeeding should not be promoted as a means to enhance infant-mother attachment quality before the findings are replicated and underlying mechanisms are better understood. Interestingly, the association between breastfeeding and attachment was not mediated by maternal sensitive responsiveness. This suggests that other aspects of breastfeeding might affect infant-mother attachment security, such as for example increased attunement due to close physical contact, or increased empathic concern due to higher levels of oxytocin, which is released during breastfeeding. The role of these factors for attachment security should be investigated in future studies.

Many previous studies on the determinants of infant attachment have been conducted with clinical or otherwise at risk samples, and those results may not necessarily apply to average families in the general population. For example, our findings show that factors known to affect the infant-parent attachment relationship at clinical levels, such as anxiety and depression (for meta-analyses see Atkinson et al., 2000 and Van IJzendoorn et al., 1999), were not related to attachment quality in otherwise healthy low risk families. This is good news for many parents who struggle with a “baby blues” or non-clinical anxiety that is frequent in new parents, or parents who have suffered from depression in the past but have been without symptoms for a longer time. Nevertheless, even in the general population parental depression might still affect child development in combination with other risk factors, as for example, depressive symptoms were related to less effective physiological stress regulation in insecure-resistant and disorganized children. Future studies should address how environmental risk factors interact in affecting infant attachment and how infant attachment interacts with other environmental risk factors in affecting the infant's stress regulation systems as this may have important consequences for later socio-emotional development.

Although the role of parental behavior is traditionally emphasized in the development of early attachment relationships, our results have made a start in studying possible neuro-developmental effects on infant attachment. We have shown that innate non-clinical structural differences in subcortical areas of the brain play a role for the development of disorganized attachment relationships, especially when strong environmental risk factors, such as maltreatment, are absent. Also, innate neurobiological differences might explain why interventions work for some children, but not for others. For example, it has been shown that attachment based interventions were effective in reducing cortisol levels only in children with the DRD4 7-repeat allele (Bakermans-Kranenburg, van IJzendoorn, Mesman, Alink & Juffer, 2008). These findings might inspire new studies concerning the neurobiology and genetics of attachment that might help to bridge the gap in the understanding of how attachment disorganization develops.

One other point worth mentioning here is that although insecure and disorganized attachment are known to be important risk factors for socio-emotional problems, they are not equivalent to diagnoses of attachment disorders that are used in clinical practice. In the DSM-IV, disruptions of early attachment relationships are included as "Reactive Attachment Disorder" (RAD). Although the description of RAD partly overlaps with behaviors characteristic for disorganized attachment, it appears that RAD and attachment disorganization are two different concepts. It is somewhat surprising that the wealth of knowledge from research using the concepts of attachment theory is not incorporated more strongly in clinical practice (DeKleyen & Greenberg, 2008; Van IJzendoorn & Bakermans-Kranenburg, 2003).

The main objective of the Generation R Study is to identify factors that determine why some children grow up healthy and others don't. In terms of mental health it is generally accepted that the risk of maladaptive development increases with the number of risk factors that a child is exposed to (e.g. Greenberg et al., 1999; Rutter, 1999; Sameroff & Fiese, 2000). The quality of early attachment relationships is considered to be one of these risk factors. In contrast with other risk factors, such as poverty, single parenthood, or clinical parental psychopathology, attachment insecurity and disorganization occur relatively often even in high otherwise low risk families and might therefore be a good target for interventions especially in average families from the general population in which other strong risk factors are absent. Although previous studies have shown that attachment quality is important for socio-emotional development (for a review see DeKlyen & Greenberg, 2008) and that interventions are effective in enhancing attachment quality, not much is known about possible long-term consequences of attachment based interventions (Bakermans-Kranenburg et al., 2003). Future studies should explore the effectiveness of attachment based interventions in reducing childhood emotional and behavioral problems. In the development of such interventions, it should be taken into account that different factors might be involved in low risk families than in families with clinical problems or otherwise high risk families.

# Appendices

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# Appendices

## Summary

# Summary

The formation of an attachment relationship, that is a stable emotional bond between infant and a potentially protective attachment figure (Bowlby, 1969/1982), is a developmental milestone in infancy. Based on their interactions with a caregiver, infants develop a working model of whether or not the caregiver will be available when needed. Securely attached infants are confident about the availability of their caregiver and can approach the caregiver for comfort and support in stressful situations. Insecure-resistant infants maximize their distress signals in order to get the attention of an inconsistently responsive caregiver. Insecure-avoidant infants have learnt that they might be rejected and thus minimize signs of distress to avoid further rejection. In disorganized children, the attachment strategy breaks down in stressful situations. This form of attachment is considered to be the most insecure form of attachment. It is thought to be the result of the paradoxical situation in which the caregiver is a source of fear and a source of comfort at the same time. The quality of early attachment relationships plays a crucial role in children's socio-emotional development. Insecure and disorganized attachment relationships are early risk factors for later emotional and behavioral problems. Secure attachment, on the other hand, predicts later social competence and resilience. This thesis, therefore aimed to extend the existing knowledge about the determinants of infant attachment quality in the general population. All studies presented in this thesis were conducted

within the Generation R study, a prospective longitudinal cohort study that follows infants and their parents from pregnancy onwards. Below, a brief summary of the main results per Chapter of this thesis is presented.

In Chapter 2, we addressed the question whether maternal depressive symptoms before and during pregnancy as well as in the postnatal period are related to infant-mother attachment insecurity or disorganization. Maternal depressive symptoms such as fatigue, loss of interest, and negative cognitions might affect her behavior towards the child and therefore have negative consequences for the infant-mother attachment relationship. We found that infants of mothers who had been depressed at some point in their life before the child was born, had no higher risk to be insecurely attached or disorganized than infants of mothers who had never been depressed. Likewise, elevated depressive symptoms during pregnancy and in the post-partum period were not related to a higher risk of attachment insecurity or disorganization. It has to be taken into account that the mothers we studied had non-clinical levels of depressive symptoms. Also, there were not many additional risk factors, such as poverty or single parenthood, and the women had high social support, which may have buffered the effects of depressive symptoms. These findings may be encouraging for many mothers who have been depressed at some point in their life or who struggle with elevated but non-clinical depressive symptoms during pregnancy and in the early post-partum period. More research is needed to study which protective factors may moderate the potentially disruptive impact of maternal depression on the developing infant-mother relationship in the general population.

In Chapter 3 we examined the role of anxiety and depressive symptoms for sensitive responsiveness of fathers and attachment quality in infant-father dyads. Here we found somewhat surprisingly that fathers who had been depressed or had had an anxiety disorder at some point in their lives before the child was born, had more secure attachment relationships with their children than fathers who had never had an anxiety or depressive disorder. In this study we also addressed the question whether sensitive responsiveness, which is the most important predictor of infant-mother attachment security, was also related to infant-father attachment security. Both empirical findings and a meta-analysis of 16 studies supported the hypothesis that more sensitive fathers have more securely attached children.

In Chapter 4, we examined associations of disorganized attachment and maternal depressive symptoms in the postnatal period on physiological stress-regulation systems of the infant. As an index for the functioning of these physiological stress-regulation systems, we measured the infants' heart-rate in resting state, which was used to calculated vagal tone, as an index of the basic functioning of the autonomic nervous system. Low baseline vagal tone may indicate less efficient stress-regulation capacities. We found that infants with either a disorganized attachment relationship or a mother with elevated postnatal depressive symptoms did not show lower vagal tone. However, in disorganized children, but not in non-disorganized children, higher levels of maternal depressive symptoms were related to lower vagal tone. This means that disorganized children were more vulnerable for the negative effects of maternal depressive symptoms on the child's physiological stress-regulation systems.

A different marker of the functioning of the infants' physiological stress regulation capacities was used in Chapter 5, i.e. cortisol, the so-called "stress-hormone". Cortisol was measured at home to assess the diurnal cortisol pattern, and before and after the Strange Situation Procedure during the 14 months visit at the Generation R research center to assess the infants' physiological reaction to this stressful situation. We found that disorganized children showed a more flattened diurnal cortisol pattern than non-disorganized children, which is thought to represent problematic physiological stress regulation. In addition, our results showed that insecure-resistant children had the largest increase in cortisol during the Strange Situation, especially when their mother had had a diagnosis of depression at some point in her life. Thus, these children were physiologically the most stressed by the Strange Situation Procedure.

Traditionally, the role of parental behavior in the development of infant attachment relationships is emphasized. However, disrupted infant-parent interactions only partly explain attachment disorganization. Therefore, the study presented in Chapter 6 examined whether early non-clinical neurobiological differences predicted later attachment disorganization. We focused on subcortical areas of the brain, i.e. the basal ganglia and the thalamus, which are included in the gangliothalamic ovoid. The basal ganglia are conceptualized as a selection center that decides which behaviors to apply to achieve a certain goal, an ability that is disrupted in disorganized infants. The thalamus may be involved in the development of attachment disorganization via connections with the emotion centers of the brain. We found that infants with a smaller gangliothalamic ovoid at 6 weeks of age had a higher risk of a disorganized attachment relationship at 14 months. This means that attachment disorganization may have a neurobiological component. Future studies may examine how neurobiological and environmental factors interact in the development of disorganized attachment relationships.

Chapter 7 examined the association of breastfeeding with maternal sensitive responsiveness and infant-mother attachment. Although a link between breastfeeding and attachment is intuitively appealing and there is empirical evidence for possible underlying mechanisms, surprisingly few studies have examined this link directly. In this study, we showed that longer duration of breastfeeding was related to higher maternal sensitivity, more attachment security and less attachment disorganization. Infants who were breastfed for at least 6 months had the most positive outcomes, and infants who were not breastfed at all had the most negative outcomes. However, even in the group of infants who were not breastfed at all, mean maternal sensitivity scores and attachment security scores were high enough, and attachment disorganization scores were low enough so there was no reason for concern in these children. Exclusivity of breastfeeding during the first two months was not related to maternal sensitivity or attachment security, however, infants who were exclusively breastfed when they were two months of age, had lower disorganization scores at 14 months, than infants who were not at all breastfed at two months of age.

Finally, we conducted a first study to examine the consequences of infant attachment for the development of emotional and behavioral development of children, which is presented in Chapter 8. We examined the role of infant attachment classification and parenting stress for toddler emotional and behavior problems. Our results showed that in families with low parenting stress, there was no difference in emotional or behavioral problems between the different attachment classifications. However, high parenting stress was related to more emotional and behavioral problems. This association was different for different attachment groups. Compared to securely attached children in families with high parenting stress, insecure-avoidant children were more aggressive, whereas disorganized children were more withdrawn. In contrast with the other attachment groups, securely attached children from families with high parenting stress did not have more behavioral or emotional problems than securely attached children from families with low parenting stress. This means that attachment quality in infancy influences the way parenting stress affects child emotional and behavior problems. Insecure attachment may be considered a risk factor, and attachment security a protective factor in the context of parenting stress.

In conclusion, the studies presented in this thesis show that some factors that are known to be related to insecure and disorganized attachment when they occur at clinical levels, such as anxiety and depression, were not related to attachment quality in otherwise healthy low risk families. This is good news for many parents who struggle with “baby blues” or non-clinical anxiety that is frequent in new parents, or parents who have suffered from depression in the past but have been without symptoms for a longer time.

These findings apply similarly to both mothers and fathers. Additionally, fathers also appear to be similar to mothers in the way that sensitive responsiveness serves to establish an attachment relationship, even though it has been suggested earlier that on other domains fathers might play a different role in child rearing than mothers.

Nevertheless, even in the general population parental depression might still affect child development in combination with other risk factors, as for example, depressive symptoms were related to less effective physiological stress-regulation in insecure-resistant and disorganized children. Our findings also show that attachment relationships of children growing up in a low risk environment may also benefit from parental behavior such as longer breastfeeding. Neurobiological factors may play a role in the development of attachment disorganization, especially in populations where strong environmental risk factors such as low SES are absent. Finally, our findings confirm and extend earlier results showing that attachment is important for children's socio-emotional development, not only in a high risk environment, but also in "normal" healthy families that experience the usual stresses related to raising a child. We found that in families where this parenting stress is relatively high, disorganized and insecurely attached children have more emotional and behavioral problems than securely attached children.

# Appendices

## Nederlandse samenvatting (Summary in Dutch)

# Samenvatting

## Het belang van vroege gehechtheidsrelaties

Het ontstaan van een gehechtheidsrelatie, een stabiel emotioneel band tussen een jong kind en een beschermende opvoeder, is een belangrijke stap in de sociaal-emotionele ontwikkeling van kinderen. Jonge kinderen moeten nog leren om met stressvolle situaties om te gaan en zijn afhankelijk van de hulp van anderen, vaak voornamelijk hun ouders. Gedurende hun eerste levensjaar leren kinderen in welke mate hun ouders beschikbaar zijn in stressvolle situaties. Veilig gehechte kinderen hebben geleerd dat de ouder beschikbaar is wanneer zij hem of haar nodig hebben en sensitief reageert op signalen van het kind. Dat wil zeggen, dat de ouder herkent wat het kind nodig heeft en hier tijdig en op de juiste manier op in gaat. Deze kinderen kunnen erop vertrouwen dat zij in stressvolle situaties hulp en troost kunnen vinden bij de ouder, en zullen dus het contact met de ouder zoeken wanneer zij hem of haar nodig hebben. Als de ouder niet of inconsistent reageert op de signalen van het kind, kan het kind dit vertrouwen in de ouder niet opbouwen. Onveilig-ambivalent gehechte kinderen weten nooit helemaal zeker of er wel hulp en troost van hun ouder beschikbaar zal zijn als dat nodig is. Deze kinderen maximaliseren hun gehechtheidsgedrag door veel nabijheid te zoeken, om zo de aandacht vast te houden van een inconsistente ouder. Door angst en onzekerheid over de beschikbaarheid van de ouder, zijn zij echter ook boos en overstuur en moeilijk te troosten. Onveilig-vermijdende kinderen hebben de ervaring dat de ouder ofwel niet, ofwel afwijzend reageert op hun signalen. Om afwijzing te voorkomen, minimaliseren onveilig-vermijdende kinderen hun gehechtheidsgedrag door nauwelijks te laten merken dat zij overstuur zijn of door zelf het contact met de gehechtheidspersoon te vermijden. De meeste kinderen ontwikkelen één van deze gehechtheidsstrategieën. Bij een kleine groep kinderen (10-20% in de normale bevolking) faalt de gehechtheidsstrategie in stressvolle situaties. Dit is karakteristiek voor gedesorganiseerde gehechtheid. Men gaat ervan uit dat dit voortkomt uit een tegenstrijdige situatie, waarin het kind de ouder tegelijkertijd als beschermend en als bedreigend ervaart. In een stressvolle situatie weet het kind vervolgens niet of hij toenadering moet zoeken of afstand moet houden van de ouder. Gedesorganiseerde gehechtheid wordt over het algemeen als de meest onveilige vorm van gehechtheid beschouwd.

## Dit proefschrift

De kwaliteit van de gehechtheidsrelaties van jonge kinderen speelt een belangrijke rol in de verdere sociaal-emotionele ontwikkeling: Veilig gehechte kinderen hebben later vaak betere sociale vaardigheden en kunnen beter omgaan met stressvolle situaties. Onveilig gehechte kinderen en vooral gedesorganiseerde kinderen hebben op latere leeftijd juist meer last van gedragsproblemen en van emotionele problemen. Het doel van dit proefschrift is daarom te onderzoeken welke factoren van invloed zijn op de kwaliteit van de gehechtheidsrelaties van jonge kinderen. Dit is onderzocht bij normale gezinnen die deel uitmaken van Generation R, een grootschalig, prospectief cohortonderzoek in Rotterdam. In dit geboortecohort worden kinderen en hun ouders vanaf de zwangerschap gevolgd om de groei, ontwikkeling en gezondheid van de kinderen te bestuderen. De studies die deel uitmaken van dit proefschrift zijn uitgevoerd binnen een subgroep van bijna 1000 kinderen en hun ouders van Nederlandse nationaliteit, waarbij binnen de eerste 3 jaar gedetailleerde metingen zijn verricht.

Bij deze kinderen is op de leeftijd van 14 maanden de kwaliteit van de gehechtheidsrelatie met één van de ouders in kaart gebracht door middel van een gedragsobservatie, de Vreemde Situatie Procedure. Hierbij bevinden ouder en kind zich in een onbekende spelkamer, waar na een paar minuten een onbekende persoon binnenkomt. Vervolgens verlaat de ouder twee keer kort de spelkamer en het kind blijft de eerste keer met de vreemde en de tweede keer alleen in de kamer achter. De ouder kan door een observatiespiegel blijven kijken naar het kind. Door deze voor het kind vreemde en licht stressvolle situatie wordt gehechtheidsgedrag opgeroepen op het moment dat ouder en kind worden herenigd. Veilig gehechte kinderen zoeken contact met de ouder en vinden hier troost zodat zij uiteindelijk weer kunnen spelen. Onveilig-ambivalente kinderen zoeken ook contact, maar blijven angstig en boos en zijn moeilijk te troosten. Onveilig-vermijdende kinderen laten nauwelijks merken dat zij overstuur zijn en vermijden het contact met de ouder. Bij gedesorganiseerde kinderen is geen duidelijk gedragspatroon te herkennen, zij vertonen tegenstrijdig en onverklaarbaar gedrag, zoals plotseling stilvallen, angstige of gedesoriënteerde gezichtsuitdrukkingen, of stereotype gedrag. Hier volgt een korte samenvatting van de belangrijkste resultaten van deze studies worden weergegeven.

**Emotionele klachten van de ouders en gehechtheid**

In Hoofdstuk 2 wordt onderzocht of depressieve klachten van de moeder vóór en tijdens de zwangerschap en in de postnatale periode gerelateerd zijn aan onveilige en gedesorganiseerde gehechtheid. Depressieve klachten, zoals vermoeidheid, interesseverlies en negatieve gedachtes kunnen het gedrag van de moeder naar het kind toe beïnvloeden en op die manier negatieve consequenties hebben voor de gehechtheidsrelatie tussen kind en moeder. Uit de resultaten bleek dat kinderen van moeders die voor de geboorte van het kind ooit depressief waren geweest geen hoger risico hadden op onveilige of gedesorganiseerde gehechtheid dan kinderen van moeders die nooit depressief zijn geweest. Ook depressieve klachten van de moeder tijdens de zwangerschap en in de eerste maanden na de geboorte hingen niet samen met een verhoogd risico op onveilige of gedesorganiseerde gehechtheid. Bij de interpretatie van deze resultaten moeten wij er wel rekening mee houden dat de depressieve klachten in dit onderzoek niet op klinisch niveau waren. Bovendien hadden de moeders in deze studie weinig andere problemen: zo was er bijvoorbeeld geen sprake van armoede en maar weinig moeders waren alleenstaand, zoals dat in veel eerdere onderzoeken naar het effect van depressieve klachten op gehechtheid wel het geval was. Ook hadden de moeders in ons onderzoek veel sociale steun. Deze factoren kunnen ervoor gezorgd hebben dat mogelijke negatieve effecten van depressieve klachten afgezwakt werden. Onze resultaten zijn wel bemoedigend voor veel moeders die ooit een depressie hebben gehad en moeders die tijdens of vlak na de zwangerschap last hadden van niet-klinische, depressieve klachten. Meer onderzoek is nodig naar beschermde factoren die de negatieve effecten van depressie op de gehechtheidsrelatie van moeder en kind in de algemene bevolking tegen kunnen gaan.

In Hoofdstuk 3 is de rol van angst en depressieve klachten op de sensitiviteit van vaders en de kwaliteit van de vader-kind gehechtheidsrelatie onderzocht. Uit dit onderzoek bleek, enigszins verrassend, dat kinderen van vaders die voor de geboorte van het kind ooit last hadden gehad van een depressie of een angststoornis, vaker veilig gehecht waren dan kinderen van vaders die nooit dit soort klachten hadden gehad. Verder is er gekeken of sensitiviteit voor de signalen van het kind, de belangrijkste voorspeller van veilige gehechtheid tussen kinderen en moeders, ook bij vader-kind koppels gerelateerd is aan veilige gehechtheid. Zowel ons eigen empirisch onderzoek als een meta-analyse van 16 eerdere onderzoeken liet zien dat sensitievere vaders inderdaad veiliger gehechte kinderen hebben.

**Depressie, gehechtheid en fysiologische stress regulatie**

In Hoofdstuk 4 is onderzocht of gedesorganiseerde gehechtheid en postnatale depressieve klachten van de moeder gerelateerd zijn aan de fysiologische stressregulatie capaciteiten van het kind. In een stressvolle situatie wordt het sympathisch zenuwstelsel geactiveerd en het parasympathisch zenuwstelsel gedeactiveerd, zodat het lichaam op de stressor kan reageren door te vechten of te vluchten. Na afloop van de stressvolle situatie wordt de stressreactie als het ware "uitgezet", ofwel gereguleerd, door activatie van het parasympathische zenuwstelsel. De hartslagfrequentie in rust geeft informatie over het functioneren van dit regulatiemechanisme. Verondersteld wordt dat een hoge hartslag in rust een teken is van een minder goed functioneren van het parasympathisch zenuwstelsel. Een andere maat voor het functioneren van het parasympathische zenuwstelsel is de cardiale vagale tonus, waarmee het parasympathische zenuwstelsel hartslagveranderingen reguleert. Men gaat ervan uit dat een lage vagale tonus in rust een teken is van minder efficiënte stressregulatie capaciteiten. Gedesorganiseerde kinderen kunnen in stressvolle situaties minder goed terugvallen op de ouder om troost te vinden. De vraag is, of dit zich ook uit in een minder efficiënt functioneren van de lichamelijke stressregulatie systemen. Uit de resultaten bleek geen verschil tussen gedesorganiseerde kinderen en niet gedesorganiseerde kinderen wat betreft het functioneren van de fysiologische stressregulatie systemen. Gedesorganiseerde kinderen bleken echter wel kwetsbaarder voor de negatieve effecten van depressieve klachten bij moeder op de fysiologische stressregulatie capaciteiten: postnatale depressieve klachten waren gerelateerd aan een lagere vagale tonus in rust bij het kind, maar alleen als de gehechtheidsrelatie tussen beiden gedesorganiseerd was. Bij kinderen die niet gedesorganiseerd waren, hadden depressieve klachten van de moeder geen verband met de vagale tonus. Dit houdt in dat de lichamelijke capaciteiten om stress reacties te reguleren minder goed ontwikkeld zijn bij gedesorganiseerde kinderen van moeders met postnatale depressieve klachten.

Een andere maat van fysiologische stressregulatie is in Hoofdstuk 5 gebruikt, namelijk het "stresshormoon" cortisol. Door de ouders werd thuis meerdere keren, verdeeld over een dag, speeksel afgenomen, waarmee een dagelijks patroon van cortisolproductie bepaald kon worden. Ook vóór en na de Vreemde Situatie Procedure werd speeksel afgenomen om te kunnen meten hoe het kind lichamelijk op deze licht stressvolle procedure reageerde. Uit de resultaten kwam naar voren dat gedesorganiseerde kinderen een afgevlakte dagelijkse cortisol productie curve hadden, waarvan wordt aangenomen dat het een teken is van niet optimale fysiologische stressregulatie capaciteiten. Verder bleek dat bij onveilig-ambivalent gehechte kinderen de cortisolconcentratie het meest toenam tijdens de Vreemde Situatie. Dit betekent dat onveilig-ambivalente kinderen van alle gehechtheidsclassificaties lichamelijk het sterkst reageerden op de stress van de Vreemde Situatie.

**Neurobiologische verschillen en gehechtheid**

De rol van de ouders voor de kwaliteit van de gehechtheidsrelatie wordt traditioneel benadrukt in de gehechtheidstheorie. Verstoringen in de interactie tussen jonge kinderen en ouders kunnen echter maar voor een gedeelte het ontstaan van gehechtheidsdesorganisatie verklaren. Om deze reden gaat het onderzoek beschreven in Hoofdstuk 6 na of vroege neurobiologische verschillen tussen kinderen gedesorganiseerde gehechtheid voorspellen. Hierbij hebben wij ons gericht op subcorticale gebieden van de hersenen, namelijk de basale kernen en de thalamus, die samen het 'gangliothalamische ei' genoemd worden. De basale kernen worden als beslissingscentrum beschouwd dat bepaalt welk gedrag vertoond moet worden om een bepaald doel te bereiken – een vaardigheid die bij gedesorganiseerde kinderen verstoord is. De thalamus zou een rol kunnen spelen in het ontstaan van gedesorganiseerde gehechtheid, omdat dit hersengebied veel verbindingen heeft met de emotiegebieden van de hersenen. Onze resultaten toonden aan dat het risico op gedesorganiseerde gehechtheid bij 14 maanden groter was, naarmate het gangliothalamische ei kleiner was op de leeftijd van 6 weken. Dit betekent dat gedesorganiseerde gehechtheid mogelijk mede verklaard kan worden door neurobiologische verschillen tussen kinderen. In toekomstige studies zal verder onderzocht moeten worden hoe neurobiologische factoren en omgevingsfactoren zoals opvoeding samenwerken bij het ontstaan van gedesorganiseerde gehechtheidsrelaties.

**Borstvoeding en gehechtheid**

In Hoofdstuk 7 wordt de relatie onderzocht van het geven van borstvoeding met sensitiviteit van de moeder en de kwaliteit van de moeder-kind gehechtheidsrelatie. Intuïtief lijkt een verband tussen het geven van borstvoeding en gehechtheid voor de hand liggend, maar er is weinig wetenschappelijk onderzoek gedaan naar dit verband. Uit ons onderzoek bleek dat moeders van 1-jarigen sensitiever waren naar hun kind toe naarmate zij langer borstvoeding hadden gegeven. Ook waren kinderen veiliger gehecht en minder gedesorganiseerd naarmate zij langer borstvoeding hadden gekregen. Hierbij bleken de kinderen die minstens 6 maanden gedeeltelijk of alleen maar borstvoeding hadden gekregen de meest gunstige uitkomsten te hebben en kinderen die nooit borstvoeding hadden gekregen de minst gunstige. Toch waren de mate van insensitiviteit van de moeder, en de mate van onveilige gehechtheid en desorganisatie ook in de groep van kinderen die nooit borstvoeding hadden gekregen niet zorgwekkend hoog. Wij hebben ook gekeken of er een verschil was tussen kinderen die in de eerste twee maanden uitsluitend borstvoeding kregen, kinderen die gedeeltelijk borstvoeding kregen en kinderen die helemaal geen borstvoeding kregen, Uit de resultaten bleek dat deze groepen niet van elkaar verschilden in sensitiviteit van de moeder en veiligheid van de gehechtheidsrelatie. Wel waren kinderen die uitsluitend borstvoeding hadden gekregen in de eerste twee maanden minder gedesorganiseerd dan de twee andere groepen.

**Gehechtheid en de ontwikkeling van emoties en gedrag**

Tenslotte is ook een studie naar de consequenties van gehechtheid bij 14 maanden voor emoties en gedrag op 3-jarige leeftijd uitgevoerd, waarvan de resultaten gepresenteerd worden in Hoofdstuk 8. Wij hebben de rol van gehechtheidsclassificatie en opvoedingsstress voor emotionele en gedragsproblemen bij peuters onderzocht. Hieruit bleken verschillende uitkomsten voor gezinnen met veel of met weinig opvoedingsstress. Bij gezinnen met weinig opvoedingsstress verschilden de vier gehechtheidsgroepen niet van elkaar wat betreft emotionele en gedragsproblemen. Bij gezinnen met veel opvoedingsstress daarentegen bleek dat veilig gehechte kinderen het minst last hadden van emotionele en gedragsproblemen. In gezinnen met veel opvoedingsstress waren onveilig-vermijdende kinderen agressiever en alle onveilig gehechte kinderen waren meer teruggetrokken dan veilig gehechte kinderen. Dit betekent dat de kwaliteit van de gehechtheidsrelatie van belang is voor de manier waarop opvoedingstress de ontwikkeling van emoties en gedrag van het kind beïnvloedt. Hierbij kan onveilige gehechtheid als een risicofactor worden beschouwd en veilige gehechtheid als een beschermende factor.

# Conclusie

Samenvattend kan worden gezegd dat factoren zoals angst en depressieve klachten, waarvan wij weten dat het op klinisch niveau risicofactoren zijn voor onveilige en gedesorganiseerde gehechtheid, bij de gezonde, laag risico gezinnen binnen ons onderzoek niet gerelateerd waren aan de kwaliteit van ouder-kind gehechtheidsrelaties. Dit is goed nieuws voor veel ouders die te kampen hebben met "baby-blues" of niet klinische angstklachten die vaak optreden bij ouders van jonge kinderen, en voor ouders die ooit last hebben gehad van depressie of angststoornissen, maar al een tijd zonder klachten zijn. Dit geldt zowel voor moeders als voor vaders. Ook bleek dat sensitiviteit bij vaders de veiligheid van de gehechtheidsrelatie met hun kind verhoogt. Dit komt overeen met wat voor moeders al uit eerder onderzoek bekend was, hoewel vaak gesuggereerd is dat vaders een andere rol spelen voor de ontwikkeling van het kind dan moeders.

Niettemin kan depressie nog wel een rol spelen voor de ontwikkeling van het kind in combinatie met andere risicofactoren. Uit ons onderzoek bleek bijvoorbeeld dat depressieve klachten van de moeder samenhangen met minder goede fysiologische stressregulatie capaciteiten bij gedesorganiseerde en onveilig-ambivalente kinderen. Verder tonen onze resultaten aan dat de gehechtheidsrelaties van kinderen die in een omgeving met weinig andere risicofactoren opgroeien, kunnen profiteren van het gedrag van de ouders, zoals het geven van borstvoeding. Neurobiologische factoren kunnen hierbij ook een rol spelen, met name voor het ontstaan van gedesorganiseerde gehechtheid. Tenslotte bleek uit onze resultaten dat in gezinnen met relatief veel opvoedingsstress meer emotionele en gedragsproblemen voorkwamen bij onveilig gehechte en gedesorganiseerde kinderen dan bij veilig gehechte kinderen. Deze bevindingen onderbouwen eerdere onderzoeken die hebben laten zien dat vroege gehechtheidsrelaties van belang zijn voor de sociaal-emotionele ontwikkeling van het kind, niet alleen in een risicovolle omgeving maar ook in "normale", gezonde gezinnen die de normale moeilijkheden meemaken die het opvoeden van een kind met zich mee brengt.

# Appendices

## About the author

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Anne Tharner was born on October 9th, 1978 in Nordhorn, Germany. She grew up in Neuenhaus, Germany, where she passed her secondary school in 1998. In the same year, she moved to the Netherlands and started to study psychology at the University of Amsterdam. During her studies, she spent a semester at the University of Otago, New Zealand, and did an internship at the Biopsychology lab of the Ruhr Universität Bochum, Germany. She obtained her master degree in 2003 at the University of Amsterdam with the programme group Brain & Cognition. In 2004, Anne started her PhD project at the Generation R study for the department of Child and Adolescent Psychiatry of Erasmus Medical Center Rotterdam in cooperation with the Centre for Child and Family Studies at Leiden University. While finishing her thesis, she worked as a teaching assistant at Leiden University in 2009 and 2010. In 2011, she started to work as a researcher at Leiden University.

## PhD Portfolio

| | |
|---|---|
| **Name PhD student:** | **A.Tharner** |
| **Erasmus MC Department:** | Kinder- en Jeugdpsychiatrie |
| | Generation R |
| **PhD period:** | 2004-2011 |
| **Promotor(s):** | Prof.dr. F.C. Verhulst |
| | Prof.dr. M.H. van IJzendoorn |
| | Prof.dr. M.J. Bakermans-Kranenburg |
| **Co-promotor:** | Dr. H. Tiemeier |

| **1. PhD training** | **year** | **workload (ECTS)** |
|---|---|---|
| **Research skills** | | |
| Netherlands Institute for Health Sciences (NIHES) | | 0.7 |
| Topics in evidence-based medicine | 2005 | 0.7 |
| Principles of research in medicine | 2005 | 0.7 |
| Health economics | 2005 | 0.7 |
| Introduction to public health | 2005 | 0.7 |
| Regression analysis | 2005 | 0.7 |
| Cohort Studies | 2005 | 0.7 |
| Study design | 2007 | 4.3 |
| Classical Methods for data-analysis | 2007 | 5.7 |
| Scientific English Writing | 2008 | 1.4 |
| **In-depth courses** | | |
| Attachment: State of the Art, Leiden University | 2005 | 5 |
| Workshop Attachment Assessment, University of Minnesota | 2007 | 5 |
| **National and international conferences, seminars and workshops – participation and presentation** | | |
| Voorjaarscongres van de Nederlandse Vereniging voor Psychiatrie, Amsterdam, the Netherlands. Oral presentation: "Maternal depressive symptoms and infant-mother attachment quality." | 2008 | 0.5 |
| Biennieal meeting of the Society for Research in Child Development (SRCD), Denver, Colorado, USA. | 2009 | |
| Poster presentation "Maternal depressive symptoms do not predict insecure or disorganized attachment in infants." | | 1 |
| Poster presentation " Maternal; depressive symptoms, infant autonomic functioning, and attachment classification." | | 1 |
| The Generation R Study Group research meetings | 2004-2009 | 1 |
| Attachment research meetings, Leiden University | 2009-2011 | 1 |

| 2. Teaching activities | year | workload (ECTS) |
|---|---|---|
| **Practicals, workshops and lectures** | | |
| Erasmus MC | | |
| VO.3 Workshops normal and pathological development of children. | 2008 | 0.5 |
| Erasmus University Rotterdam (EUR) | | |
| Faculty of Social Sciences (FSS), Institute of Psychology. Guest lecture "Infant Attachment – The Generation R Study." | 2008 | 0.5 |
| Leiden University, Education and Child Studies | | |
| Tutor | 2009/2010 | 2 |
| Teaching assistant at the following courses/practicals/workshops | | |
| Werkgroepen Inleiding in de pedagogische en onderwijswetenschappen | 2009/2010 | 3 |
| | 2010/2011 | 3 |
| Data-analyse met SPSS | 2009/2010 | 2 |
| Oefenonderzoek | 2009/2010 | 3 |
| Praktijkoriëntatie | 2009/2010 | 0.5 |
| Gesprekstechnieken | 2009/2010 | 2 |
| Werkgroepen Inleiding in de grondslagen van de pedagogische wetenschappen | 2010/2011 | 0.5 |
| Opvoedingsvoorlichting | 2009/2010 | 2 |
| Praktijk van empirisch onderzoek | 2009/2010 | 5 |
| | 2010/2011 | 5 |
| **Supervising Master's theses** | | |
| EUR FSS Institute of Psychology/Generation R | | |
| Maaike Nap, Thesis title: "Does mothers' expressed emotion assesses by the 3-minute speechsample during pregnancy, predict resistant behavior at 14 months of age? A pilot study." | 2005 | 3 |
| Shereen Kollmann, Thesis title: "Daycare and Infant Attachment." | 2007 | 3 |
| Veerle Meijer, Thesis title: "Daycare and Child Emotion Regulation Capacities." | 2007 | 3 |
| Zohrah Malik, Thesis title: "Daycare, attachment and executive functioning in early childhood." | 2008 | 3 |
| Yvonne Meijerink, Thesis title: "The impact of maternal prenatal psychological distress on mother-ifant attachment quality. The Generation R Study" . | 2008 | 3 |
| Linda Steenkamer, Thesis title: " The effect of infant attachment security on emotion regulation." | 2008 | 3 |
| Marije Frank, Thesis title: " Influence of disorganized mother-infant attachment on emotion-regulation behaviors in infancy" | 2008 | 3 |

**PhD Portfolio** (continued)

| 2. Teaching activities | year | workload (ECTS) |
|---|---|---|
| **Supervising Bachelor's theses** | | |
| Leiden University FSS, Department of Education and Child Studies | | |
| Naomi Boers, Thesis title: "Early infant-mother interaction and infant attachment." | 2010 | 2 |
| Milou Bol, Thesis title: "Ethnic socialization and the development of transracial adoptees." | 2010 | 0.5 |
| **Training of students** | | |
| Conducting observational and psychophysiological assessment procedures in infants (Strange Situation, neuromotor assessment, heart rate measures, saliva sampling) | 2005-2007 | 2 |
| Coding of observational assessments in prescholers (Berkeley Puppet Interview, executive functions) | 2007-2010 | 2 |
| 1 ECTS (European Credit Transfer System) is equal to a workload of 28 hours | | |

## List of publications and submitted manuscripts:

Dierckx, B., Tharner, A., Tulen, J.H.M., Jaddoe, V.W., Hofman, A., Verhulst, F.C., & Tiemeier, H. (*accepted for publication*). Spot the red herring: breastfeeding, fruitpurée, and infant autonomic functioning. *Pediatric Research*.

Dierckx, B., Tulen, J.H.M., Tharner, A., Jaddoe, V.W., Hofman, A., Verhulst, F.C., & Tiemeier, H. (2011). Low autonomic arousal as vulnerability to externalising behaviour in infants with hostile mothers. *Psychiatry Research*, *185*, 171-175.

Dierckx, B., Tulen, J.H.M., Van den Berg, M.P., Tharner, A. Jaddoe, V.W., Hofman, A., Verhulst, F.C., & Tiemeier, H. (2009). Maternal Psychopathology Influences Infant Heart Rate Variability: Generation R Study. *Psychosomatic Medicine*, *71*, 313-321.

Lucassen, N., Tharner, A., Van IJzendoorn, M.H., Bakermans-Kranenburg, M.J., Volling, B.L., Jaddoe, V.W., Hofman, A., Verhulst, F.C., Lambgregtse-Van den Berg, M.P., & Tiemeier, H. (*submitted*). Paternal Sensitivity and History of Depression/Anxiety Predict Infant-Father Attachment Security.

Luijk, P.C.M., Roisman, G.I., Tiemeier, H., Booth-LaForce, C., Van IJzendoorn, M.H., Belsky, J., Uitterlinden, A.G., Jaddoe, V.W., Hofman, A., Verhulst, F.C., Tharner, A. & Bakermans-Kranenburg, M.J. (*submitted*). Attachment genes? Associations of dopaminergic, serotonergic, oxytonergic and neuroplasticity candidate genes with attachment security and disorganization.

Luijk, P.C.M., Saridjan, N., Tharner, A., Van IJzendoorn, M.H., Bakermans-Kranenburg, M.J., Jaddoe, V.W., Hofman, A., Verhulst, F.C., & Tiemeier, H. (2010). Attachment, depression, and cortisol: deviant patterns in insecure-resistant and disorganized infants. *Developmental Psychobiology, 52 (5)*, 441-452.

Luijk, P.C.M., Tharner, A., Van IJzendoorn, M.H., Bakermans-Kranenburg, M.J., Jaddoe, V.W., Hofman, A., Verhulst, F.C., & Tiemeier, H. (*in press*). The Association between parenting and attachment is moderated by a polymorphism in the mineralocorticoid receptor gene: Evidence for differential susceptibility. *Biological Psychology*.

Luijk, P.C.M., Velders, F.P., Tharner, A., Van IJzendoorn, M.H., Bakermans-Kranenburg, M.J., Jaddoe, V.W., Hofman, A., Verhulst, F.C., & Tiemeier, H. (2010). FKBP5 and resistant attachment predict cortisol reactivity in infants: Gene-environment interaction. *Psychoneuroendocrinology*, *35*, 1454-1461.

Tharner, A., Dierckx, B., Luijk, P.C.M., Van IJzendoorn, M.H., Bakermans-Kranenburg, M.J., Van Ginkel, J.R., Moll, H.A., Jaddoe, V.W., Hofman, A., Hudziak, J.J., Verhulst, F.C., & Tiemeier, H. (*submitted*). The interaction between disorganized attachment and maternal depression predicts autonomic functioning in infants: Evidence for a cumulative risk model.

Tharner, A., Herba, C.M., Luijk, P.C.M., Van IJzendoorn, M.H., Bakermans-Kranenburg, M.J., Goveart, P.P., Roza, S.J., Jaddoe, V.W., Hofman, A., Verhulst, F.C., & Tiemeier, H. (*in press*). Subcortical structures and the neurobiology of infant attachment disorganization: a longitudinal ultrasound imaging study. *Social Neuroscience*.

Tharner, A., Luijk, P.C.M., Van IJzendoorn, M.H., Bakermans-Kranenburg, M.J., Jaddoe, V.W., Hofman, A., Verhulst, F.C., & Tiemeier, H. (*submitted*). Maternal depressive symptoms in the prenatal and early postnatal period do not predict infant-mother attachment quality in a large, population-based cohort study.

Tharner, A., Luijk, P.C.M., Van IJzendoorn, M.H., Bakermans-Kranenburg, M.J., Raat, H., Moll, H.A., Jaddoe, V.W., Hofman, A., Verhulst, F.C., and Tiemeier, H. (*submitted*). Milk and More? The Role of Breastfeeding for Maternal Sensitive Responsiveness and Infant Attachment.

Tharner, A., Luijk, P.C.M., Van IJzendoorn, M.H., Bakermans-Kranenburg, M.J., Jaddoe, V.W., Hofman, A., Verhulst, F.C., and Tiemeier, H. (*submitted*). Infant attachment, parenting stress and child behaviour at age three.

Wolff, N.J., Darlington, A.E., Hunfeld, A.M., Tharner, A., Van IJzendoorn, M.H., Bakermans-Kranenburg, M.J., Moll, H.A., Jaddoe, V.W., Hofman, A., Verhulst, F.C., Passchier, J., & Tiemeier, H. (*in press*). The influence of attachment and temperament on venipuncture distress in 14-month-old infants: The Generation R Study. *Infant Behavior & Development*.

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