Aggressive behavior in early childhood : The role of prenatal risk and self-regulation

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CHAPTER 3

The Mother-Infant Neurodevelopment Study (MINDS) – Leiden: background, design and study population

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Abstract

This paper describes the background, design, and sample characteristics of the Mother-Infant Neurodevelopment Study – Leiden, a longitudinal study investigating 1) mechanisms through which neurobiological, neurocognitive and social-environmental factors increase risk for emotional and behavioural problems in early childhood, 2) effects of an intensive home-visiting program for first-time mothers at high-risk on child neurobiological, neurocognitive and emotional and behavioural development, and 3) which factors (neurobiological, neurocognitive and social-environmental) predict variation in effects of the home-visiting program on child emotional and behavioural outcomes. A total of 275 families (128 low-risk and 147 high-risk) were included in the study. High-risk women were randomly assigned to the intervention (*n*=65) or high-risk control group (*n*=82). Six assessment waves were conducted within a four-year period. Demographic and mental health characteristics of the low-risk and high-risk group, collected during the first assessment at 27 gestational weeks, are presented. This study will help identifying specific biomarkers, precursors of neurocognitive functions and temperamental factors in infancy, facilitating the detection of children at risk for later emotional and behaviour problems. Furthermore, this study may yield insights into effective, targeted, and tailor-made components of prevention programs, ultimately reducing the psychological and economic costs of mental health problems to society.

Key words: High-risk, neurobiology, reflective functioning, infants, home-visiting program

Introduction

Children growing up in families struggling with multiple complex issues, including maternal psychiatric problems, substance (ab)use, single parenthood, and poverty, are at high risk for developing emotional and behavioural problems (Cabaj, McDonald, & Tough, 2014; Côté, Vaillancourt, LeBlanc, Nagin, & Tremblay, 2006; Hay, Mundy, et al., 2011; Huijbregts, Seguin, Zoccolillo, Boivin, & Tremblay, 2008). As these problems raise major public health concerns and increase costs to society, it is important to gain insight into developmental mechanisms and effectiveness of prevention approaches. Recent theoretical models have emphasized the complex interactions between neurobiological vulnerabilities and environmental risk factors (Beauchaine, Neuhaus, Brenner, & Gatzke-Kopp, 2008; Belsky & Pluess, 2009; Boyce & Ellis, 2005), and the mediating role of neurocognitive and neurobiological factors in the link between early adversity and emotional and behavioural outcomes (Van Goozen, Fairchild, Snoek, & Harold, 2007).

However, there are several important gaps in the current literature. First, most studies so far have involved toddlers, school-aged children and adolescents, and little is known about earlier manifestations of neurobiological and neurocognitive vulnerabilities, and how these might increase risk for emotional and behavioural problems later in life. This is particularly important given that the neurobiological systems underlying later emotional and behavioural regulation rapidly develop during the prenatal period and first years of life, resulting in increased sensitivity to environmental influences (Beauchaine et al., 2008; Laurent, Harold, Leve, Shelton, & Van Goozen, 2016). Prevention efforts initiated early in life are therefore presumed to be more effective (Beauchaine et al., 2008). Second, most longitudinal studies investigating the neurobiological and neurocognitive mechanisms underlying emotional and behavioural problems in early childhood involved community samples. Because evidence is accumulating that shows that different neurodevelopmental processes underlie emotional and behavioural development in normative versus high-risk or clinical samples (Beauchaine, 2001; Beauchaine et al., 2008), it is of critical importance to extend the current body of literature with studies focusing on high-risk samples in order to fully understand the mechanisms that are related to the development of emotional and behavioural problems.

The overarching aim of the Mother-Infant Neurodevelopment Study (MINDS) – Leiden study is to examine which neurobiological, neurocognitive and social-environmental factors increase risk or confer protection for developing emotional and behavioural problems in the first years of life in a heterogeneous sample of low- and high-risk families. Based on integrative models of the neurobiological bases of early-onset antisocial behaviour (Van Goozen et al., 2007),

and theories of differential susceptibility (Belsky & Pluess, 2009) and biological sensitivity to context (Boyce & Ellis, 2005), we considered neurobiological and neurocognitive factors as potential mediating and moderating mechanisms that lead to emotional and behavioural problems. We adopted a rigorous and systematic approach, assessing a wide range of social-environmental (i.e. maternal psychiatric problems, substance [ab]use, poverty, social support, parenting, maternal reflective functioning), neurocognitive (i.e. precursors of executive functioning, Theory of Mind, language, empathy) and neurobiological factors (i.e. autonomic nervous system and hypothalamic pituitary adrenal axis) that may either directly, indirectly, or in interaction increase risk for emotional and behavioural problems in young children.

Families at risk need substantial support to promote good enough care for their child. However, it is often difficult to engage these families in intervention programs. Home-visiting programs for first-time mothers at high-risk have the advantage of serving families at their home, thereby increasing the likelihood that they will (continue to) participate. Home-visiting programs have been found to be effective in improving maternal prenatal health behaviours (e.g. reductions in tobacco use), maternal life course (e.g. fewer rapid second pregnancies, returning to school/ seeking education), sensitive parenting behaviour and parenting attitudes, and child physical abuse (e.g. number of emergency room visits, injuries or ingestions treated, and accidents requiring medical attention) (Mejdoubi et al., 2014; Mejdoubi et al., 2015; Olds, Sadler, & Kitzman, 2007; Ordway et al., 2014; Sweet & Appelbaum, 2004). Further, positive effects of home-visiting programs have been reported for a wide range of child outcomes (Avellar & Supplee, 2013; Filene, Kaminski, Valle, & Cachat, 2013; Mejdoubi et al., 2015; Olds et al., 2007; Ordway et al., 2014; Peacock, Konrad, Watson, Nickel, & Muhajarine, 2013; Sweet & Appelbaum, 2004). For example, home-visiting programs have been found to positively affect cognitive development (e.g. academic and arithmetic achievement, intellectual functioning, executive functioning, receptive language), socio-emotional development (e.g. attachment security, social development, emotional vulnerability), and to reduce behavioural problems (e.g. externalizing and internalizing behaviour problems). Also, favourable results have been reported for birth outcomes (e.g. birth weight, gestational age) and physical health, although these effects have been less consistent among different home-visiting programs (Avellar & Supplee, 2013; Filene et al., 2013; Robling et al., 2016). Moreover, at 15 year follow-up, adolescents who had received home visitation early in life had fewer arrests and convictions, and committed fewer violations of probation (Olds et al., 1998).

Despite these promising results, the overall effect sizes of studies evaluating home-visiting programs are relatively small (Filene et al., 2013), and many studies

report non-significant findings (Avellar & Supplee, 2013). Currently, an important question is which factors predict this variability in the effects of home-visiting programs on child outcomes? While it is generally acknowledged that effectiveness of prevention programs may vary as a function of neurobiological and neurocognitive vulnerabilities (Beauchaine et al., 2008), there are no studies that have examined child neurobiological and neurocognitive factors as moderators of the effects of home-visiting programs. Moreover, surprisingly little is known about the effects of home-visiting programs on child neurobiological and neurocognitive development. Therefore, a second overarching aim of MINDS – Leiden was to evaluate the effects of an intensive home-visiting program for first-time mothers at high-risk on child neurobiological, neurocognitive and emotional and behavioural development, and to evaluate the predictive value of these child neurobiological and neurocognitive factors on the effectiveness of such a program.

Study aims

MINDS – Leiden is part of a large research program funded by the Dutch government called 'Brain & Cognition – Social innovation in health, education, and safety' (http://www.nwo.nl and http://www.nwo.nl/en/research-and-results/programmes/nihc/hcmi/index.html). The purpose of this Brain & Cognition program is to promote neurobiological and neurocognitive research to develop and improve intervention efforts aimed at reducing aggression and violence in society.

In the present study three important questions are addressed. First, which neurobiological and neurocognitive factors predict (directly, indirectly or in interaction with social-environmental factors) emotional and behavioural problems – specifically aggressive behaviour – in the first three-and-a-half years of life? Second, what are the effects of an intensive home-visiting program for first-time mothers at high-risk on neurobiological, neurocognitive and emotional and behavioural development in children in the first years of life? Third, which factors (neurobiological, neurocognitive and social-environmental) predict variation in effects of the home-visiting program on child emotional and behavioural outcomes? This paper describes the design of the study, the measures used, the intervention program and the sample characteristics.

Methods

Study design

The MINDS – Leiden study was designed as a longitudinal randomized control trial (see Figure 1 for an overview of the design of the study). Based on elaborate screening for the presence of risk factors during the first prenatal home visit (27 weeks gestation), pregnant women were assigned to either the high-risk (HR) or low-risk (LR) group (see *screening for risk factors* for a description of allocation criteria). Women in the HR group were randomly assigned to the high-risk intervention (HR-I) group (see *The intervention* for more details) or the high-risk control (HR-C) group. All participating families were followed over a period of approximately four years, consisting of six assessment waves, (the first assessment took place in the third trimester of pregnancy and the last assessment took place when the children were 42 months of age). A total of 65 families were included in the HR-I group. Families in the HR-I group took part in a home-visiting program starting within 2 weeks after the prenatal assessment until 30 months post-partum.

Recruitment

Recruitment of pregnant women took place between February 2011 and April 2015, via hospitals, midwifery clinics, prenatal classes, pregnancy fairs, and social workers. Dutch-speaking primiparous women between 17 and 25 years old with uncomplicated pregnancies were eligible to participate. Exclusion criteria were heavy drug addiction or severe psychiatric or psychotic disorder, an intelligence quotient (IQ) below 70, major acute or significant chronic illness in the mother or a disorder or syndrome in the child, which would affect normal development. We oversampled families from a high-risk background in order to obtain sufficient variance in risk factors that might influence children's early socio-emotional and cognitive development. This was done by collaborating with midwifery/obstetric clinics in areas with a low average social-economic status and/or by recruitment through social workers. All participating women provided written informed consent. The study was approved by the Medical Research Ethics Committee at the Leiden University Medical Centre (NL39303.058.12), and by the ethics committee of the Department of Education and Child Studies at the Faculty of Social and Behavioural Sciences, Leiden University (ECPW-2011/025).

Screening for risk factors

Classification to the HR-group was based on the following risk factors (Smaling et al., 2015; World Health Organization, 2005, 2016): 1) positive screening on current psychiatric disorder(s) or substance use (alcohol, tobacco and/or drugs)

during pregnancy; or 2) presence of two or more of the following risk factors: single status (biological father not involved), unemployment, financial problems, no secondary education, limited social support network (<4 individuals listed in network), and young maternal age (<20 years). In case only one risk factor was present - other than an indication for current psychiatric disorder(s) or substance use - women were discussed in a clinical expert meeting to determine whether placement in the HR-group was appropriate (*n*=6).

Positive screening on current psychiatric disorder(s) was established by the Mini-International Neuropsychiatric Interview – plus (M.I.N.I. - plus; Sheehan et al., 1997, Van Vliet, Leroy, & Van Megen, 2000) by screening for the following disorders: depressive disorder (current), dysthymic disorder (past 2 years), suicidality, mania (current), panic disorder (current and lifetime), agoraphobia (current), social phobia (current), other type of phobia (current), obsessive-compulsive disorder (current), generalized anxiety disorder (GAD; current), posttraumatic stress disorder (current), alcohol dependence and abuse (current and lifetime), drug dependence and abuse (non-alcohol, current and lifetime), attention-deficit/hyperactivity disorder (lifetime), and antisocial personality disorder (lifetime). Current is defined as 'in the past month' for all diagnoses except GAD, which has a 6-month time frame, and alcohol abuse/dependence and drug abuse/dependence for which a 12-month time frame is used.

The size of the social support network was established by using the Norbeck Social Support Questionnaire (NSSQ; Norbeck, Lindsey, & Carrieri, 1981, 1983). The presence of other risk factors (i.e. substance use during pregnancy, no secondary education, unemployment, financial problems, single status, and maternal age) were assessed by means of the Dutch translation of the 'Becoming a mother' questionnaire (Hay et al., 2011; Smaling et al., 2015).

Procedures

The study comprised of six assessment waves (see Figure 1). During the third trimester of pregnancy (T1), at 6 months (T2) and at 20 months (T4) post-partum 2-to-2.5 hour home visits were carried out by two female researchers. One leading researcher conducted all the tasks with the infant and guided the mother-infant interaction tasks, while a second researcher digitally recorded the whole session and administered the questionnaires to the mother. At 12 months (T3), 30 months (T5) and 42 months (T6), the mother-infant dyads visited the Baby lab at the Faculty of Social and Behavioural Sciences, Leiden University. The lab test sessions were carried out by one researcher, while a second researcher was seated behind a one-way screen, recorded the session and provided observational records.

Table 1 gives an overview of the main research areas of the study. In addition, Table 2 and give a detailed overview of instruments and its content used in the study. T1 included an interview regarding the emotional impact of the pregnancy to assess prenatal reflective functioning (RF), a structured interview to assess current psychiatric disorders, and various questionnaires to assess demographic information, mental and physical health, life style, social support, self-efficacy in the nurturing role, executive functioning, emotion regulation, life events, and antenatal attachment. T2 to T5 started with a free play session to measure maternal interactive behaviour. For T2, T3, and T5, this was followed by attachment of the cardiac monitoring equipment to the child to measure their autonomic nervous system (ANS) reactivity and regulation during mildly stressful events (see Table 2 and 3 for the paradigms that were used to measure stress reactivity and regulation). In addition, during the lab visits saliva samples were taken several times (before and after stress) from mother and child to measure hypothalamic pituitary adrenal (HPA)-axis functioning. Moreover, each wave consisted of various age-appropriate tasks to measure precursors of executive functioning, temperament and emotion, empathy, Theory of Mind, and language skills, and ended with the mother completing various questionnaires to assess demographic information and multiple mother (i.e. mental and physical health, obstetric characteristics, life style, social support, self-efficacy in the nurturing role, executive functioning, emotion regulation, life events, parenting cognitions and parenting stress) and child domains (language, temperament, aggression, behavioural problems, executive functioning) (see Table 1, 2 and 3 for more details). Mother-child interaction during normal, playful interaction, teaching tasks and following mildly stressful events was observed at T2 to T5. T4 also included an interview regarding maternal representations of the relationship with their child and the emotional impact of parenting to measure postnatal RF. At T6, children were assessed for approximately 1 hour in individual testing rooms, and then brought together with their mother and one or two other families for a simulated birthday party and a 20 minute free play session with peers, designed to provide an acceptable yet emotionally arousing setting in which to observe children's social behaviour (and specifically aggressive behaviour) with their peers.

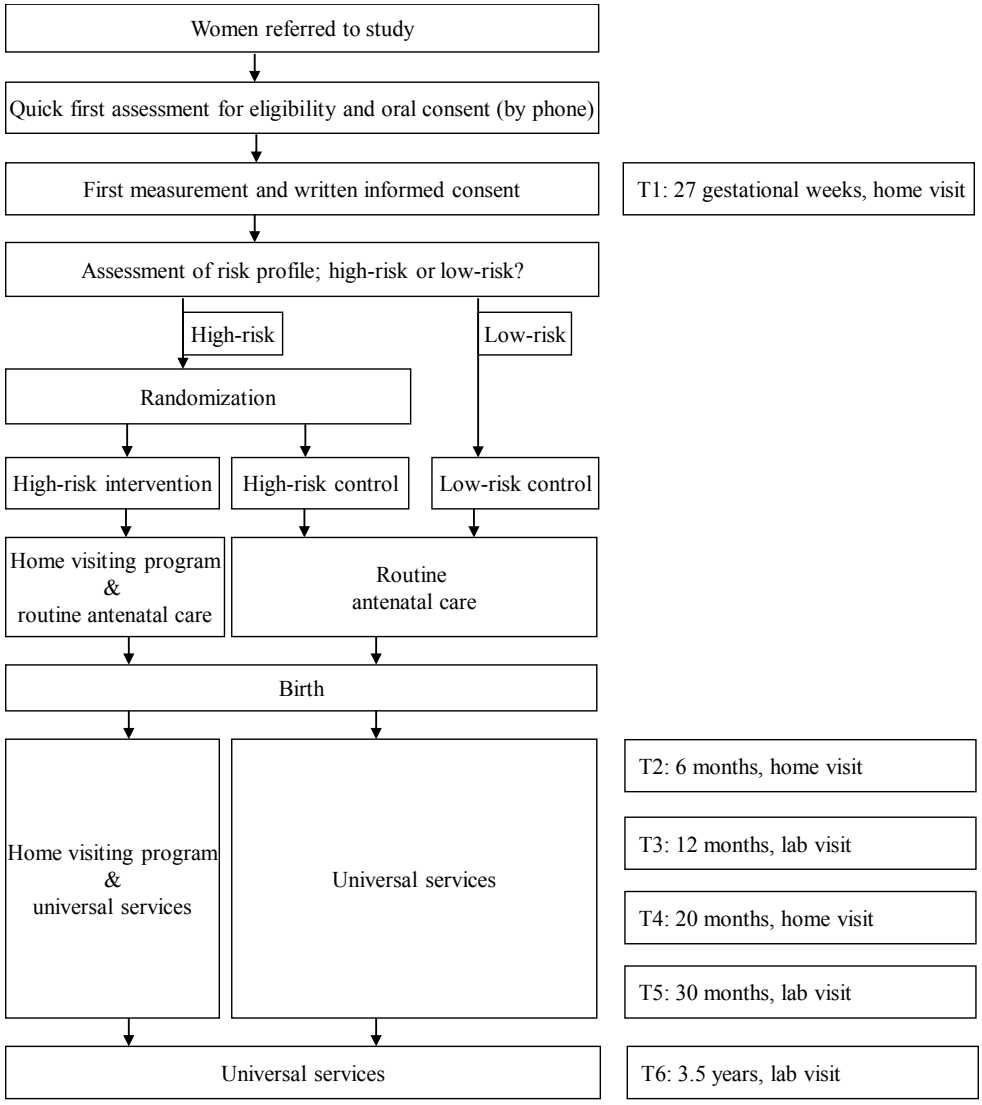

Figure 1. Design of the MINDS-Leiden study.

Table 1. *The main research areas of the MINDS- Leiden Study.*

Maternal variables	Wave 1: pregnancy	Wave 2: 6 months	Wave 3. 12 months	Wave 4. 20 months	Wave 5: 30 months	Wave 6: 42 months
Demographics	X	X	X	X	X	X
Reflective functioning	X			X		X
Mental and physical health	X	X	X	X	X	X
Life style	X	X			X	X
Social support	X				X	X
Self-efficacy in the nurturing role	X	X		X		
Executive functioning	X				X	
Emotion regulation	X				X	
Life events	X					X
Antenatal attachment	X					
Obstetric characteristics		X				
Parenting		X	X	X	X	X
Parenting stress					X	
IQ estimate		X				
Stress reactivity and regulation			X		X	

Note. IQ = intelligence quotient.

Table 1 cont.

Child variables	Wave 1: pregnancy	Wave 2: 6 months	Wave 3. 12 months	Wave 4. 20 months	Wave 5: 30 months	Wave 6: 42 months
Physical health		X	X	X	X	X
Cognitive development		X				
Stress reactivity and regulation		X	X		X	X
Language development			X	X	X	X
(Precursors of) executive functioning			X	X	X	X
(Precursors of) Theory of Mind			X	X	X	X
(Precursors of) empathy				X	X	X
Aggression		X	X	X	X	X
Behavioural problems				X	X	X
Temperament		X	X	X		
Peer social interaction						X

Table 2. *Research domains, instruments, and contents: mother.*

Domain (mother)	Instrument / data source	Content
Demographics, lifestyle, physical health & obstetric characteristics	'Becoming a mother'-questionnaire and 'Being a mother'-questionnaire (Hay, Mundy, et al., 2011; Smaling et al., 2015)	Key information regarding demographics, obstetric characteristics, life style, and physical health
Life events	List of Threatening Experiences – questionnaire (LTE-Q; Brugha & Cragg, 1990)	Stressful life events over the past year to self and close others, and whether they currently have impact
Social support	Norbeck Social Support Questionnaire (NSSQ; Norbeck, Lindsey, & Carrieri, 1981, 1983)	Functional variables (affect, aid, affirmation) and total network variables of social support (number of persons in the network, duration of relationships, frequency of contact), and loss of support within past year
	Multidimensional Scale of Perceived Social Support (MSPSS; Zimet, Dahlem, Zimet, & Farley, 1988)	Subjective assessment of social support adequacy
Self-efficacy in the nurturing role	Self-efficacy in the nurturing role scale (SENR; Pedersen, Bryan, Huffman, & Del Carmen, 1989)	Mothers' perceptions of their competence on basic skills required in caring for an infant
Mental health	Mini-International Neuropsychiatric Interview (MINI)– plus (Sheehan et al., 1997)	Screening for psychiatric disorders
	Beck depression inventory (BDI)-II (Beck, Steer, & Brown, 1996)	Intensity of depression
	State-Trait Anxiety Inventory (STAI; Spielberger, 2010; Spielberger, Gorsuch, & Lushene, 1970)	Indication of transient anxiety and tendency to experience general anxiety
	Aggression Questionnaire (Buss & Perry, 1992)	Verbal aggression, physical aggression, anger, and hostility
	Borderline personality checklist (Arntz et al., 2003; Giesen-Bloo, Arntz, & Schouten, 2005)	Severity of borderline-related symptoms during past month

Emotion regulation	Difficulties in Emotion Regulation Scale (DERS; Gratz & Roemer, 2004)	Clinically relevant difficulties in emotion regulation.
Antenatal attachment	Maternal antenatal attachment scale (MAAS; Condon, 1993; Van Bussel, Spitz, & Demyttenaere, 2010)	Quality of mother's affective experiences towards the foetus and intensity of preoccupation with the foetus
Reflective functioning	Pregnancy Interview (PI) – Revised (Slade, 2007; Slade, Patterson, & Miller, 2007) and Parent Development Interview (PDI) – Revised (Slade et al., 2003; Slade et al., 2005)	Parental reflective functioning
Parenting	Adapted version of the Mother Infant Coding System (Miller, McDonough, Rosenblum, & Sameroff, 2002) to code maternal behaviour during Free play, Teaching tasks, and Still-Face Paradigm (SFP; Tronick et al., 1978)	Maternal interactive behaviour (e.g. sensitivity, intrusiveness) with her child during various contexts.
	Parental Cognitions and Conduct Toward the Infant Scale (PACOTIS; Boivin et al., 2005)	Parental perceptions and behavioural tendencies towards infant
Parenting stress	Nijmeegse Ouderlijke Stress Index (NOSI; Abidin, 1990; De Brock, Vermulst, Gerris, & Abidin, 1992)	Parenting stress
IQ	WAIS-III-NL (Wechsler, 2005) – subtests Vocabulary, Matrix Reasoning, and Digit Span	Global indicators of intellectual functioning (IQ estimate) - mother
Executive functioning	Behavior Rating Inventory of Executive Function (BRIEF) – adult version (Roth, Isquith, & Gioia, 2005)	Difficulties in executive functioning in daily life
Stress reactivity and regulation – baseline, stress and recovery	Maternal response to mildly stressful situation (i.e. short mother-child separation and child exposure to fear paradigm (see child variables))	*Hypothalamic pituitary adrenal (HPA)-axis*: Cortisol and Alpha-amylase (saliva) *Subjective experience of stress (mother):* Visual Analogue Scale (VAS) (Lesage, Berjot, & Deschamps, 2012)

Table 3. *Research domains, instruments, and contents: child.*

Domain (child)	Instrument / data source	Content
Cognitive development	Infant Mental Development Index of the Bayley Scales of Infant Development (BSID), 2nd version (Bayley, 1993)	Global measure of infant cognitive development
Stress reactivity and regulation – baseline, stress and recovery	Stressors: - *Social*: Still Face Procedure (Mesman, Van IJzendoorn, & Bakermans-Kranenburg, 2009; Tronick et al., 1978) - *Frustration*: Laboratory Temperament Assessment Battery (Lab-TAB; Goldsmith & Rothbart, 1999a, 1999b): Car seat, Gentle arm restraint - *Fear*: Adapted version of unpredictable-mechanical-toy from the Lab-TAB (Baker, Shelton, Baibazarova, Hay, & van Goozen, 2013; Goldsmith & Rothbart, 1999a)	*Autonomic nervous system (child)*: Heart rate, pre-ejection period, skin conductance, respiratory sinus arrhythmia with the Vrije Universiteit Ambulatory Monitoring System (VU-AMS; De Geus, Willemsen, Klaver, & Van Doornen, 1995; Willemsen, De Geus, Klaver, Van Doornen, & Carrofl, 1996) *Hypothalamic pituitary adrenal (HPA)-axis*: Cortisol and Alpha-amylase (saliva) *Behavioural stress reactivity and regulation (child)*: observation (coding based on Lab-TAB)
Aggression	Cardiff Infant Contentiousness Scale (CICS; Hay et al., 2010)	Early manifestations of aggression
	Physical Aggression Scale for Early Childhood (PASEC; Alink et al., 2006)	Physical aggression
	Peer Interaction Coding System (PICS; Caplan, Vespo, Pedersen, & Hay, 1991; Hay, Nash, et al., 2011)	Peer aggression

Behavioural problems	Child Behavior Check List (CBCL) 1 ½ -5 year (Achenbach & Rescorla, 2000; Achenbach & Ruffle, 2000)	e.g. internalizing and externalizing behavioural problems
Temperament	Short versions of the Infant Behavior Questionnaire (IBQ; Rothbart, 1981) and Early Childhood Behavior Questionnaire (ECBQ; Putnam & Rothbart, 2006)	Dimensions of temperament (i.e. negative emotionality, effortful control)
(Precursors of) executive functioning	BRIEF – preschool version (Gioia, Espy, & Isquith, 2003)	Difficulties in executive functioning in daily life
	Music box (Goldsmith & Rothbart, 1999a)	Sustained attention
	Don't Paradigm (adapted from Kochanska, Tjebkes, and Fortnan (1998))	Infants' spontaneous restraint to maternal prohibition
	Self-restraint (Friedman, Miyake, Robinson, & Hewitt, 2011), and Inhibitory control tasks (Carlson & Moses, 2001)	Inhibitory control
	Snack task and Gift task (Kochanska, Coy, & Murray, 2001; Spinrad et al., 2007)	Delay of gratification
	Hide the pots (Bernier, Carlson, & Whipple, 2010), and Spin the pots (Hughes & Ensor, 2005)	Working memory
	Dimensional Change Card Sort (Zelazo, 2006)	Mental flexibility
(Precursors of) Theory of Mind	Pleasure-disgust task (Slaughter & McConnell, 2003)	Social referencing
	Discrepant desires tasks (Atance, Bélanger, & Meltzoff, 2010; Laranjo, Bernier, Meins, & Carlson, 2010; Repacholi & Gopnik, 1997)	Understanding of discrepant desires
	Early Social Communication Scales (ESCS) – subtask joint attention (Mundy et al., 2003)	Joint attention

	Visual Perspectives (Bigelow & Dugas, 2009; Carlson, Mandell, & Williams, 2004; Laranjo et al., 2010)	Visual perspective taking
	Subtest functional and symbolic imitation - Autism Diagnostic Observation Schedule (ADOS; Luyster et al., 2009)	Imitation
	False belief tasks (Bigelow & Dugas, 2009)	False belief
(Precursors of) empathy	Pain task (Young, Fox, & Zahn-Waxler, 1999; Zahn-Waxler, Robinson, & Emde, 1992)	Empathy
	Mishaps (Kochanska, Gross, Lin, & Nichols, 2002)	Guilt
	Emotion recognition task (Pollak, Cicchetti, Hornung, & Reed, 2000)	Emotion recognition
	Emotion eliciting film clips of ecologically valid situations (e.g. fear, sadness)	Social attention with the Tobii T120 eye-tracker
Language development	MacArthur communicative development inventory (Fenson et al., 2000)	Communicative skills in infants and toddlers
	Reynell Developmental Language Scales (Reynell, 1985), Peabody Picture Vocabulary Test (PPVT; Dunn & Dunn, 1997)	Receptive language skills
	Schlichting Expressive Language Test (Schlichting, Van Eldik, Lutje Spelberg, Van der Meulen, & Van der Meulen, 1995)	Expressive vocabulary skills

The intervention

Families in the HR-I group (n=65) participated in an intensive home-visiting program based on 'Minding the baby' (MTB) (Sadler et al., 2013; Slade et al., 2005; Slade, Sadler, & Mayes, 2005). MTB is an interdisciplinary home-visiting program developed at Yale University Child Study Center and Yale University School of Nursing (Slade et al., 2010). MTB focuses on young vulnerable first-time parents, primarily mothers, who are at high risk due to multiple complex issues, including psychiatric problems, poverty, young maternal age, single motherhood, or limited social support. MTB combines two well-researched early-intervention models; home visiting and infant-parent-psychotherapy, in order to meet the holistic, complex, multi-layered care needs of vulnerable families (Sadler et al., 2013). The program specifically aims to enhance maternal reflective functioning (RF) and the development of secure attachment relationships, as well as to address maternal (mental) health issues. RF refers to the mother's capacity to 'keep the baby in mind', to make sense of his/her internal states, emotions, thoughts, and intentions, as well as her own (Slade, 2002). Particularly in high-risk mothers, RF is often compromised, leading to disrupted interactions, insecure attachment relationships, and long term emotional difficulties. In the present study (see Table 3), RF skills were significantly lower among women in the HR-group compared to women in LR-group. In MTB, parents are encouraged to be curious, to try and figure out what the child needs or is thinking or feeling even in early infancy. RF is seen as a key to maternal sensitivity and plays an important role in the development of the child's capacity for Theory of Mind and adaptive socio-emotional development in young children (Ordway et al., 2014; Laranjo, Bernier, Meins, & Carlson, 2010; Sadler et al., 2013; Sadler, Slade, & Mayes, 2006; Slade, Sadler, & Mayes, 2005). Programs that are specifically aimed at improving parental RF in 'at-risk' parents indeed appear to improve RF-skills and parenting behaviour (Katznelson, 2014; Suchman et al., 2010). For a more detailed description of the conceptual framework underlying the MTB-model, see Sadler and colleagues (2013).

The MTB-program offers a treatment manual with a set of well-developed protocols and guidelines (Slade et al., 2010). At the same time, the program can be adapted to the individual needs of the family and the circumstances of each home visit. For implementation of the MBT-program in The Netherlands, one of the PI's (HS) and social workers of the MINDS-Leiden team were thoroughly trained in the basic constructs and techniques of the reflective parenting model used in MTB. This MTB 'Introductory training institute' provides the basis for implementation of the MTB-program in other settings. A difference between the original MTB and the intervention used in this study is that we chose to work only with clinical social workers ("coaches"), instead of alternating the home visits between a nurse

practitioner and clinical social worker. This decision has been based on the fact that in The Netherlands, mother and child pay regular visits to a paediatric nurse in the first four years of life. In the MTB-program, the visits by the nurse practitioner are mostly centered on health-related issues, which in The Netherlands are monitored by paediatric nurses at child health and welfare centres.

Home visits generally lasted about one hour, although at times of crisis home visits could be extended or increased in frequency. The home visits were conducted by a trained coach, starting during the last trimester of pregnancy until the child was 30 months old, and were scheduled weekly during the first year and continued two-weekly after that. Apart from the planned home visits, the coaches were available for their families when needed (by phone or 'WhatsApp'). The main objective of the coaches was to promote parental RF, support the mother-infant attachment relationship, and stimulate adequate parenting skills. Further, the coaches aimed to reinforce prenatal health care and health education, supported both mother's and child's health and development, helped mothers to extend or build a stronger social support network, educated mothers about the safety of their child, referred to a range of treatments as appropriate when psychiatric complaints were detected, and helped mothers negotiate issues involving legal, financial and housing problems. However, the coaches conferred regularly about their families during monthly supervision meetings, and maintained close contact with each other and their supervisor in case of crisis, or other family problems.

Group characteristics

Table 3 provides an overview of demographic and obstetric characteristics of the LR-and HR-groups. Compared to women in the LR-group, women in the HR-group were significantly younger, lower educated, had a lower income, were more often non-Caucasian and single, and had a smaller social support network (ps<.01). Further, pregnancies in the HR-group were more often unplanned, and women in the HR-group more often experienced miscarriages or had undergone abortion (ps<.05).

Among women in the LR-group (n=128), 9% (n=11) had one risk factor present, which was mostly limited social support (n=5), followed by single parenthood (n=2), young maternal age (n=2), unemployment (n=1) or no secondary education (n=1). In the HR-group, 64% of the women (n=94) had an indication for current psychiatric disorder(s), with 26% (n=38) having two or more diagnoses on the M.I.N.I.-plus. See Table 4 for an overview of the diagnoses on the M.I.N.I.-plus in the HR-group. Substance use during pregnancy was the second most frequent observed risk factor in the HR-group. Of the women who used substances during pregnancy, 33% (n=48) continued to smoke, 5% (n=8) drank alcohol, 1% (n=1) continued to use

(other) drugs, 2% (*n*=3) were smoking and drinking alcohol, 3% (*n*=5) were smoking and using drugs, and 1% (*n*=1) used all these substances (smoking, alcohol and drugs). Drugs used during pregnancy were cannabis (*n*=4), cocaine (*n*=1), methadone (*n*=1), and cocaine and cannabis (*n*=1).

Table 3. *Demographic characteristics of the low-risk and high-risk groups.*

	LR (*n*=128)		HR (*n*=147)		Group comparisons[a]
Variables	*M*	*SD*	*M*	*SD*	
Maternal age (years)	23.42	1.74	21.56	2.32	$F(1,273)=55.59^{***}$
Maternal education (% high[b])	41%		7%		$\chi^2(1)=44.10^{***}$
Monthly family income (euro's)	2,944.02	964.50	1,609.00	1,145.00	$F(1,273)=107.47^{***}$
Ethnicity (% Caucasian)	91%		76%		$\chi^2(1)=10.06^{**}$
Married or living with partner (%)	98%		61%		$\chi^2(1)=54.59^{***}$
First-time pregnant (%)	87%		76%		$\chi^2(1)=5.53^{*}$
Unplanned pregnancy (%)	23%		72%		$\chi^2(1)=65.15^{***}$
Expecting twins (%)	4%		5%		*ns*
Gestational weeks at assessment	30.03	3.77	29.91	3.68	*ns*
Size social support network	9.19	3.84	6.94	3.54	$F(1,273)=25.40^{***}$
Prenatal reflective functioning	4.27	1.03	3.53	0.86	$F(1,273)=42.58^{***}$
Number of risk factors	0.09	0.29	2.24	1.35	$F(1,273)=311.72^{***}$
Current psychiatric disorder(s) (%)	0%		64%		$\chi^2(1)=124.36^{***}$
Substance use pregnancy (%)	0%		44%		$\chi^2(1)=70.78^{***}$
Alcohol	0%		7%		$\chi^2(1)=7.36^{**}$
Tobacco	0%		39%		$\chi^2(1)=62.61^{***}$
(Other) drugs	0%		5%		$\chi^2(1)=6.25^{*}$
Single parenthood (%)	2%		21%		$\chi^2(1)=24.70^{***}$
Unemployed (%)	1%		24%		$\chi^2(1)=31.89^{***}$
No secondary education (%)	1%		9%		$\chi^2(1)=9.21^{**}$
Financial problems (%)	0%		25%		$\chi^2(1)=37.23^{***}$
Limited social support (<4 persons)	4%		12%		$\chi^2(1)=6.21^{*}$
Young maternal age (<20 years)	2%		20%		$\chi^2(1)=23.63^{***}$

Note: $^{*}p<.05$, $^{**}p<.01$, $^{***}p<.001$ [a]ANOVA or Chi-square test, [b]Maternal education (% high) represents percentage with a bachelor's or master's degree, LR = low-risk group, HR = high-risk group.

Table 4. *Overview of the current psychiatric problems in the HR-group.*

Current psychiatric problems*	N
Depressive disorder	17
Dysthymic disorder	8
Suicidality	11
Mania	1
Panic disorder	15
Agoraphobia	17
Social phobia	7
Other type of phobia	8
Obsessive-compulsive disorder	5
Generalized anxiety disorder	4
Posttraumatic stress disorder	4
Alcohol dependence / abuse	9
Drug dependence / abuse (non-alcohol)	18
Attention-deficit/hyperactivity disorder	7
Antisocial personality disorder	14

Note: N high-risk group = 147; * = positive screening based on the M.I.N.I.-plus (Sheehan et al., 1997; Van Vliet & De Beurs, 2007).

Discussion

This paper presented an overview of the background, methods and study population of the MINDS-Leiden study, a longitudinal study investigating social-environmental, neurobiological, and neurocognitive mechanisms predicting emotional and behavioural problems in young children and variation in effects of an intensive RF-based home-visiting program for first-time mothers with a high-risk background. The scope for changing behaviour is greatest in the early years because neurobiological systems involved in emotional and behavioural regulation are presumed to be most sensitive for environmental influences early in development (Beauchaine et al., 2008). The outcomes of this study may result in the identification of specific biomarkers, precursors of neurocognitive functions and temperamental factors in infancy, which directly, indirectly or interactively with social-environmental risk factors, may help to detect children who are at risk for later emotional and behaviour problems.

Home-visiting programs hold considerable promise for improving child outcomes (Avellar & Supplee, 2013; Filene et al., 2013; Olds et al., 2007; Peacock et al., 2013; Sweet & Appelbaum, 2004). From a socio-economic and ethical perspective, intervention programs should only be offered to those families who are expected to benefit and an alternative should be offered to those who are not expected to benefit. The outcomes of our study may result in a better understanding of the individual

(neurocognitive and neurobiological) factors that explain variation in effects of home-visiting programs. Ultimately, this may contribute to more efficient matching of families to intervention programs while at the same time provide relevant information to further enhance the effectiveness of the home-visiting program.

A considerable strength of the study includes the random controlled trial and the use of multi-method approach, including a combination of (semi-) structured interviews, questionnaires, behavioural observations, and physiological measures. An important aspect of the current study, compared to previous studies evaluating the effects of home-visiting programs (Olds et al., 2007; Ordway et al., 2014; Robling et al., 2016), is the use of both a high-risk and a low-risk control group when examining the effects of home-visitation, which allows us to more thoroughly determine the extent to which neurobiological and neurocognitive development in children in the HR-I group normalizes (as observed deviations in HR-children compared to LR-children throughout development may, in part, depend on their 'starting levels').

A limitation of this study is that we lack information about the number of subjects that refused to participate before the research team tried to contact them for scheduling the first assessment. This is due to our sampling strategy in which we relied on external parties for the recruitment of potential participants. It cannot be ruled out that non-participants may differ from participants in several respects, especially as participation in a longitudinal study with 6 assessments requires a strong commitment of the mothers and might be perceived as a burden. This may have resulted in the loss of more severe cases. For example, in our high-risk sample, only a small group of participants had three or more risk factors present (17%). We do have information about the women who were recruited by their healthcare provider and gave permission to contact them for partaking in the study, but declined participation when they were contacted (16%). The most common reasons for not participating were: too busy/too time-consuming, partner does not want to participate, personal problems, medical problems, or miscarriage.

A special point of interest is the potential loss of participants to follow-up over time. Although some loss to follow-up is inevitable, we used various strategies for maximizing retention in order to retain as many participants as possible. For example, mothers received gift certificates (respectively 15, 20, 25, 30, 35, and 25 EUR) and a present for their child after each assessment. After completion of the fifth assessment, they received a personalized DVD with video material from all five assessments. Also, over the course of the study regular contact was maintained by telephone calls after birth, birth- and birthday cards, and a newsletter (every 3 months). Travel expenses were covered for lab visits (wave three, five, and six). Moreover, we offered to pick mother and child up from their homes and drive them

to our baby lab when they had difficulties coming to the lab, and mothers in the HR-intervention group were often accompanied to the lab by their coach. With data collection for the first assessment completed, attrition rates between the first and second assessment were 5%. Therefore, we are optimistic that our strategies are working and our attrition rates in the long run will be limited.

At this moment, funding has been obtained for the first five waves of follow up, and we plan to seek funding for additional follow-up cycles. Now that the study is well underway, efforts are being made to disseminate the results of our study to obstetric care providers, health care workers, paediatricians and policymakers on a regular basis. Further, once we have gained insight into factors that predict the effectiveness of the home-visiting program, we will look for ways to implement the program in clinical practice. For this, we have already sought cooperation with health care organizations in the area of Leiden, The Hague, and Amsterdam.

Taken the potential restraints into account, we believe that this study program may provide detailed insight in the factors associated with (very) early child development and treatment success for interventions aiming to reduce and/or prevent emotional and behavioural problems. We hope that by effectively addressing behavioural problems from infancy onwards, improvements in (mental) health status (of children and their mothers), and public health policy and decision making may be achieved.