Chapter 1

General introduction
Preterm birth is a complication of pregnancy that is the leading cause of perinatal mortality and long-term morbidity. A child is born preterm if birth is before 37 weeks of gestation. Six to fifteen percent of all deliveries are preterm. Birth before 32 weeks of gestation, is defined as a very preterm birth. In the Netherlands, 1.5% of infants is born very preterm.

Children born very preterm also have low birth weights. Low birth weight is defined as a birth weight of 2500 grams or less, and very low birth weight and extremely low birth weight as birth weights of 1500 grams and 1000 grams or less, respectively. Low birth weight is not always a result of preterm birth, but can also be (partly) caused by intrauterine growth restriction. Preterm birth and low birth weight rates are rising in the last decades. Due to improving neonatal care mortality has decreased in the last decades, but (long term) morbidity has not decreased. Neurodevelopmental follow-up studies have become increasingly important for the evaluation of neonatal care. Very preterm born children are at risk for a wide range of impairments. Outcome studies initially focused on major handicaps (such as blindness, hearing loss, cerebral palsy, and mental retardation) revealing in the first few years of life. Focus has shifted to a broader range of less severe outcomes that became apparent in longer term follow-up.

The main aims of this thesis are 1) to describe the development of very preterm born children at the age of 5 on multiple developmental domains, and 2) to identify risk factors for developmental disabilities and for problems in the parental environment of very preterm born children at the age of 5.

Describing the developmental problems of very preterm born children and identifying risk factors for developmental disabilities may contribute to the identification of children who are especially at risk, and the evolvement of interventional programmes. It may contribute to the counselling of parents, both during and after hospitalization in the neonatal intensive care unit (NICU) and to the discussion about NICU treatment decisions.

**Developmental outcome of very preterm born children**

Research has shown that disabilities on multiple domains occur more often in very preterm born children than in term born children. Cerebral palsy is the most common major deficit that occurs in very preterm born children. As neonatal intensive care progressed though the last decades, rates went up at first because of the lowering mortality rates. In the last years, the rates of cerebral palsy in very preterm born children have dropped to approximately 5%. However, milder neurological problems (minor neurological dysfunction) occur in a much higher percentage of around 45%. Disabilities in motor functioning occur in as much as 30% of very preterm born children. Also behaviour is affected in very preterm born children, with higher degrees of subclinical behavioural
problems such as inattentive and withdrawn behaviour. Psychiatric disorders such as attention
deficit and hyperactivity disorder and autism spectrum disorders occur more often in very preterm
born children than in term born children. Intelligence scores are on average lower, and the
occurrence of mental disabilities is higher in very preterm born children as compared to term
born children. Other aspects of neurocognitive functioning, such as executive functioning and
attention are affected as well in very preterm born children.

Impact of preterm birth on parents and parent-child interaction
Premature birth and subsequent hospitalisation in the NICU are very stressful for parents and
can be traumatic. Even after hospital discharge, parents are still at elevated risk for distress.
Parents of children who are born with a biological vulnerability, like preterm born children, are
at risk of persistently perceiving their child as vulnerable as it grows up, which in turn is a risk
factor for child behaviour problems. Maternal posttraumatic stress symptoms are also associated
with subsequent mother-child interaction problems. Mother-child interaction problems are still
present in the second year of life of the preterm infant.

Risk factors for a disabling outcome
According to Aylward, ‘there are multiple factors that are associated with a biological risk
condition that add to the variability in neurodevelopmental outcome’. Severity of neonatal
course (e.g. number and type of medical procedures) and subsequent illnesses (e.g. chronic
lung disease and brain injury) are associated with long term outcome. Sociodemographic factors
(e.g. socioeconomic status) are also predictive of subsequent child functioning. According to
Deater-Deckard and Bulkley, ‘cognitive and social-emotional adaptation is a product of complex
transactions between biological and environmental risk and ameliorative factors that operate
within powerful family and cultural contexts’. Environmental risks include factors that have been
described earlier as consequences of preterm birth for parents (stress and perception of the child
as vulnerable) and problems in parent-child interaction.

Theoretical model
A theoretical model is used to organize this thesis. The theoretical model is based upon the
aforementioned paper by Deater-Deckard and Bulkley and is depicted in Figure 1.

In this model, both biological and environmental characteristics are taken into account as risk
factors for main child outcomes. Biological characteristics and child outcome are also defined as
possible risk factors for characteristics of the home environment. For example, declining cognitive
development of the 18 month old preterm born child is predictive of persisting higher parenting
stress.
figure 1. Theoretical model based on Deater-Deckard and Bulkley.

Purpose of the study
The main aims of this thesis were to describe the development of very preterm born children at the age of 5 on multiple developmental domains in comparison with term born controls, and identify risk factors for developmental disabilities.

On the basis of these aims and the theoretical model, the following research questions were formulated: 1) What is the prevalence of disabilities on the areas of neurology, motor functioning, behaviour, intelligence and broader neurocognitive functioning in 5 year old very preterm born children compared with term born children?, 2) Which biological and environmental risk factors for disabilities in developmental functioning of very preterm born children at the age of 5 can be identified?, and 3) How does the parental environment of very preterm born at the age of 5 compare with the parental environment of term born children and which risk factors for problems in the parental environment can be identified?

With the results of this study, we hope to be able to contribute to the improvement of care for very premature children and their parents. The following questions regarding the adjustment of clinical practices of follow-up and intervention on the basis of the results of this study were formed: 1) Which ages are optimal for follow-up assessment of very preterm children?, 2) Which developmental domains should be included in the follow-up of very preterm children?, and 3) What are possibilities for intervention aimed at improving developmental outcome in very preterm children?

Study design
The aforementioned research questions are addressed in a single center cross-sectional (and partly prospective) cohort study as part of the follow-up program of the Emma’s Children’s Hospital/ Academic Medical Centre, Amsterdam NICU. Two groups of 5 year old children participated in this
study, the preterm study group, and a group of term born children served as controls. The very preterm group consisted of a consecutive sample of children born < 30 weeks of gestation and/or with birth weights < 1000 grams. The term control group consisted of children born > 37 weeks of gestation and/or birth weights > 2500 grams. Of the preterm children, perinatal characteristics and follow-up data were gathered from birth to the corrected age of 5. At age 5, preterm and term-born children came to the hospital for two visits. During the first visit, mother-child interaction was assessed via a video observation, and intelligence, inhibition, sustained attention and visual-motor coordination were assessed by a child psychologist. During the second visit, neurologic and motor functioning were assessed by a trained pediatrician or child physiotherapist, and focused attention, working memory and face and emotion recognition were assessed by a developmental psychologist. Before the first assessment, parents and teachers filled in a questionnaire about the child’s behaviour, the child’s health and sociodemographic characteristics. During the first assessment, parents completed questionnaires about their own psychological and parenting stress and perception of their child’s vulnerability. For very preterm born children, perinatal risk factors were taken from the NICU database; for term born perinatal risk factors were assessed by parental questionnaire. For very preterm born children, data from follow-up assessments at the age of 2 and 3 regarding neurologic, motor, behavioural and cognitive development were also used for parts of this study.

Scope of the thesis

1) What is the prevalence of disabilities on the areas of neurology, motor functioning, behaviour, intelligence and broader neurocognitive functioning in 5 year old very preterm born children compared with term born children?

The first research question will be addressed in Chapter 2 and 3. Chapter 2 describes the occurrence and co-occurrence of developmental disabilities in preterm born children in comparison with term born controls. Previous research has shown that severe as well as mild disabilities occur in very preterm born children on many developmental domains. However, oftentimes developmental domains are investigated separately. As a result, co-occurrence of disabilities cannot be determined and an overview of global child functioning is lacking. In studies that aim to give an overview of several developmental domains oftentimes, don’t take into account motor functioning as a domain separate from neurological functioning. Evidence concerning the presence of behavioural disabilities is growing, but is predominantly only based on parent ratings of child behaviour. Intelligence has been studied extensively, but without differentiating between the different aspects of cognitive functioning, namely verbal intelligence, performance intelligence and processing speed. However, those different aspects of intelligence are clinically important separate indicators of cognitive functioning. Chapter 2 takes into account all these developmental domains: neurologic functioning, motor functioning, both parent- and teacher
rated behaviour, and different aspects of intelligence. In Chapter 3, outcomes of preterm and term born children are compared on a broad array of neurocognitive functions other than intelligence, namely processing speed, executive functioning, aspects of attention, visual-motor coordination as well as face and emotion recognition. Although the attention for specific neurocognitive functions is growing in the literature, all aforementioned neurocognitive functions have not been tested in one single group of preterm born children.

2) Which biological and environmental risk factors for disabilities in developmental functioning of very preterm born children at the age of 5 can be identified?

The second research question will be addressed in Chapter 2, 3, 4 and 5. In Chapter 2, risk factors for developmental disabilities are studied on the domains of neurology, motor functioning, behaviour and intelligence. Attention is given specifically to the interaction between biological risk factor preterm birth and the environmental risk factor socioeconomic status. Although research has shown that socioeconomic status is associated with less optimal developmental outcomes in preterm born children, it is not clear how socioeconomic status interacts with the risk of being born preterm. In Chapter 3, biological risk factors for neurocognitive dysfunction are identified, while taking into account socioeconomic status. Although the isolation of specific risk factors is important for the identification of children who are at risk, very few studies targeted risk factors for neurocognitive problems. In Chapter 4, risk factors for functioning on different aspects of intelligence from the perspective of follow-up at toddler age are investigated. In order to evaluate early follow-up, the prediction of the different aspects of intelligence by cognitive development and other domains of development at the age of 2 and 3 is investigated. The earlier a child and its family can be supported when cognitive problems are present, the better it is. It is unclear however, at what age cognitive development can be measured reliably, and to what extent cognitive development at a young age is associated with different aspects of cognitive functioning at school age. As a next step, it is explored whether biological risk in the perinatal period has its full impact on cognitive development in the first few years of life, or whether it can still have an additional impact between the age of 2/3 and the age of 5. Finally, it is explored whether impact of environmental risk can be found between the age of 2/3 and the age of 5. Although previous research has shown that environmental factors gain importance over the years, it has not been studied whether perinatal risk factors also play a longer term role in cognitive development. In Chapter 5, the risk factors for behaviour problems in very preterm and term born children are addressed. Both biological (perinatal and later medical) risk factors, and environmental risk factors (sociodemographic characteristics and parental stress) are investigated. Special attention is being paid to the subjective parental perception of child vulnerability as a risk factor for child behaviour, while taking into account true vulnerability of the child. Although research has shown that parental perception of child vulnerability can be a risk factor for behaviour problems in preterm...
born children, parental perception of child vulnerability has not been studied with all the other factors taken into account. Also, the differential role of maternal and paternal perception of child vulnerability is explored.

3) How does the parental environment of very preterm born at the age of 5 compare with the parental environment of term born children and which risk factors for problems in the parental environment can be identified?

The third research question will be addressed in Chapter 5 and 6. In Chapter 5, maternal and paternal perception of child vulnerability is compared between parents of preterm and term born children at the age of 5. Also, level of psychological stress and parenting stress is compared between parents of preterm and term born children at the age of 5. Although research has shown that stress levels in parents of preterm born children are heightened in the neonatal period and the months after, there is debate whether higher stress levels persist over the years. Chapter 6 focused on the quality of the interaction between mothers and their term or preterm born child. Although research has shown that in the first two years of life of the infant, quality of mother-child interaction is lower in preterm born children and their mothers than in term born children and their mothers, it is not clear whether this difference persists until school age. Furthermore, risk factors for problems in mother-child interaction are examined. The biological risk of preterm birth, the environmental risk of a low socioeconomic status, and risk factors in the child, namely developmental disabilities, are investigated. Because quality of mother-child interaction is predictive of later child development, it is important to identify mother-child dyads that are at risk for interaction problems and offer them support.
REFERENCE LIST


