Moderately preterm children need attention!

Behavior and development of moderately preterm born children at toddler age

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Matig te vroeg geboren kinderen: Aandacht gevraagd!
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(met een samenvatting in het Nederlands)

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Chapter 1

General Introduction

In the Netherlands, every 1 in 14 children (7.6%) is born preterm before 37 weeks of gestation, which results in around 13.000 children each year (Stichting Perinatale Registratie Nederland, 2014a). Although in some instances being born preterm might be better than staying in the womb for a longer period of time, for instance when the child is severely dysmature, most children will benefit from a longer period within the womb. Therefore, preterm birth places children at increased risk for short as well as long term problems.

First of all, despite technological advances and improvements in neonatal care during the last years (Saigal & Doyle, 2008), the mortality rate of the total group of preterm children is more than 30 times higher than in term born children (Stichting Perinatale Registratie Nederland, 2014a). This mortality rate is highest in the group of extremely preterm born children (i.e., gestational age 24-27 weeks; 24%) and lowest in moderately preterm born children (i.e., gestational age 32-36 weeks; 0.5%), which is, however, still almost 9 times higher than in term born children (Stichting Perinatale Registratie Nederland, 2014a). Next to a higher mortality rate, preterm children also experience more neonatal morbidity for which hospital admittance after birth is needed, varying from a few days until several months. Neonatal morbidity entails breathing difficulties, feeding difficulties, brain hemorrhage, infections, hypoglycemia, and hyperbilirubinemia (Fanaroff et al., 2007). As with the mortality rate, neonatal morbidity is most pronounced in extremely preterm children, but still elevated in moderately preterm when compared to term born children (Raju, 2012).

Important for later development is that when a child is born preterm, the brain is still immature, as around 90% of prenatal growth in brain weight occurs between 20 and 40 weeks of gestation (Kinney, 2006). Not only the weight of the brain increases dramatically; this is also a critical period in maturation of the structure of the brain (Kinney, 2006). Even though the brain of a preterm child continues to develop outside the womb, its development is likely to be disturbed by the change in environment. For instance, inside the womb brain development benefits from maternal thyroid hormones (e.g., De Escobar, Obregón, & Del Rey, 2004). Although thyroid hormones can be administered after preterm birth, this does not seem to have a beneficial effect on neurodevelopmental outcome at 2, 5½ and 10 years of age, except for children born before 28 weeks of gestation (Briet et al., 2001; Van Wassenaer et al., 1997; Van Wassenaer, Westera, Houtzager, & Kok, 2005). Furthermore, outside the womb the child is exposed to different sensory experiences, such as brighter light, louder sounds and often painful procedures. Research showed that these early experiences also affect brain function and brain structure (Als et al., 2004), which might influence later development of the children. Next to that, development of preterm children might also be influenced by parenting behavior, that is likely to be affected by the experience of preterm birth (Miles & Holditch-Davis, 1997).

On the long term, it has indeed been found that preterm children have an increased risk for behavioral, developmental and physical difficulties (Aarnoudse-Moens, Weisglas-

Kuperus, Van Goudoever, & Oosterlaan, 2009; Saigal & Doyle, 2008), which might be – at least partially – due to disturbed brain development.

Moderately preterm children

Until a decade ago, follow up studies mainly focused on very preterm children, born before 32 weeks of gestation. The vast majority of preterm born children (i.e., over 80%), however, is born moderately preterm between 32 and 36^{+6} weeks of gestation (Blencowe et al., 2012). Different definitions of moderately preterm have been used. While some researchers defined moderately preterm as being born between 32 and 36^{+6} weeks (e.g., Schermann & Sedin, 2004; Van Baar, Vermaas, Knots, De Kleine, & Soons, 2009), others make a distinction between moderately and late preterm children (e.g., Chyi, Lee, Hintz, Gould, & Sutcliffe, 2008; Ekeus, Lindström, Lindblad, Rasmussen, & Hjern, 2010). Moderately preterm is then defined as born between 32 and 33^{+6} weeks, and late preterm as born between 34 and 36^{+6} weeks. In the current dissertation, the first definition was adopted and moderately preterm was defined as being born between 32 and 36^{+6} weeks.

For a long time, it was believed that moderately preterm birth would not significantly affect later development of the children. However, even though the brain of a moderately preterm child is more mature than that of a very preterm born child, it is still immature: at 34 weeks of gestation, the brain weighs only 65% of the weight at full term (Kinney, 2006). Furthermore, at term age the brain of moderately preterm children was found to be still smaller and less mature than the brain of term born children (Walsh, Doyle, Anderson, Lee, & Cheong, 2014). This difference in brain development might have consequences for the development and functioning of moderately preterm children. Therefore, the first aim of this dissertation is to study differences in behavior and development of moderately preterm and term born children.

The last decade, an increasing number of studies focused on the long-term outcomes of school-aged moderately preterm children, showing that moderately preterm children are at risk for cognitive, behavior, and attention problems and have a greater need for special education (e.g., Talge et al., 2010; Van Baar et al., 2009). With this growing number of studies, a systematic review of these studies will give a better insight in the current state of knowledge regarding the long-term developmental outcomes of moderately preterm children. For this reason, an overview of the existing literature on behavior and development of moderately preterm children will be presented in this dissertation.

Although there is growing interest in the development of moderately preterm children, still relatively little is known regarding behavior and development during their first years of life. In general, during these first years of life, children develop at a rapid pace and the early experiences form the foundation for later functioning (Bornstein, 2014; Thompson, 2001). Furthermore, there is evidence that the school problems of very preterm born children at the age of 10 were already indicated at 2 years of age in the form of lower scores regarding cognitive functioning (Van Baar, Ultee, Gunning, Soepatmi, & De Leeuw, 2006). This indicates that developmental difficulties might be detected at an early age, which could facilitate early intervention and in turn reduce problems at later ages. Therefore, behavior and development of moderately preterm children at toddler age will be examined.

Attention capacities

One of the most prominent problems of *very preterm* children concern attention difficulties (e.g., De Kieviet, Van Elburg, Lafeber, & Oosterlaan, 2012; Mulder, Pitchford, Hagger, & Marlow, 2009). It has been suggested that especially these difficulties in attention capacities underlie the problems that preterm children experience in other domains, such as cognitive and school functioning (e.g., Davis & Burns, 2001). Attention capacities are needed in daily functioning and problems with attention capacities can have a wide range of consequences. For example, a review study showed that attention problems result in lower academic achievement, which can have a lifetime impact on employment possibilities, income, health, and wellbeing (Polderman, Boomsma, Bartels, Verhulst, & Huizink, 2010). It has also been shown that children with less attention skills are socially less competent (e.g., Andrade, Brodeur, Waschbusch, Stewart, & McGee, 2009; Bennett Murphy, Laurie-Rose, Brinkman, & McNamara, 2007). Social competence is needed to play with peers and establish relationships and on the long term, less socially competent children are at increased risk for bullying and neglect, which can have serious consequences up to adulthood (Andrade et al., 2009). These are just a few examples of the impact that attention problems can have and point to the importance of studying attention capacities in order to learn when and what kind of support children at risk for attention difficulties may need.

Already immediately after birth, attention capacities can be observed, for example when a newborn baby tries to focus on a face or on a brightly colored object, or stills when hearing an interesting sound (Brazelton & Nugent, 1995). Infants learn to pay attention to important persons and objects in their environment at a rapid pace. As such, the first years of life are very important in the development of attention, and are marked by an increasing ability to sustain and control attention (Ruff & Rothbart, 1996). For this reason, the second aim of this dissertation is to investigate attention capacities of moderately preterm children at toddler age.

Attention as a multi-dimensional construct

Attention in itself is a multi-dimensional construct with many different definitions. An influential theoretical model of attention is the model of Posner and Petersen (1990), which distinguishes three different attention systems: orienting, alerting, and executive attention. These three systems are supposed to be connected and interact with each other, but also have unique functions. The *orienting* system involves the ability to engage, disengage, and to shift attentional focus (Posner & Petersen, 1990). For example, when someone is presented a newspaper, the orienting system is responsible for focusing attention on a specific part of the newspaper and shifting between different parts. Brain areas involved in orienting are the parietal lobes, frontal eye fields, pulvinar, and superior colliculus (see Figure 1.1; Fan, McCandliss, Fossella, Flombaum, & Posner, 2005). Functioning of the orienting system improves largely during the first year of life and continues to develop up to mid childhood (Rueda & Posner, 2013; Ruff & Rothbart, 1996).

The *alerting* system is responsible for the ability to achieve and maintain a state of alertness (Posner & Petersen, 1990). Taking the same newspaper, the alerting system would be responsible for staying focused in order to be able to read and process the information of an article. The frontal and parietal cortices and the thalamus are involved in the alerting system (see Figure 1.1; Fan et al., 2005). While functioning of this system also improves vastly over the first year of life, with infants becoming alert more quickly and sustaining attention for a longer period of time (Ruff & Rothbart, 1996), development continues until childhood and early adolescence (Rueda & Posner, 2013).

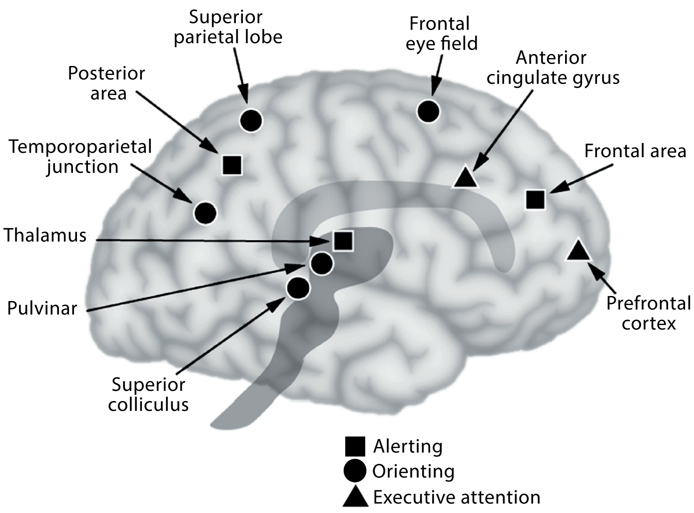

Figure 1.1. Brain areas involved in the three attention systems. Retrieved from Posner and Rothbart (2007).

Executive attention can be defined as more goal-directed and planned attention, as well as the ability to inhibit responses (Posner & Petersen, 1990). When reading that newspaper, an example of functioning of the executive attention system is controlling your own attention by ignoring other distracting information. The anterior cingulate and the frontal areas have an important role in executive attention (see Figure 1.1; Fan et al., 2005). Functioning of this system starts to develop by the end of the first year of life (Rueda & Posner, 2013; Ruff & Rothbart, 1996), and it continues to do so until at least early adolescence (Rueda & Posner, 2013).

Attention capacities and prematurity

Attention problems have been found in moderately preterm children (Perricone, Morales, & Anzalone, 2013; Potijk, De Winter, Bos, Kerstjens, & Reijneveld, 2012; Talge et al., 2010; Van Baar et al., 2009). Most of these studies used a general measure of attention problems. There are, however, indications that not all preterm children with attention difficulties are detected with the use of those general measures, as the problems they encounter are of a more specific nature (Davis, Burns, Snyder, & Robinson, 2007). Therefore, differences in specific attention capacities (i.e., functioning of the three attention systems) between moderately preterm and term born children at toddler age will be studied in this dissertation.

Measuring attention

There are different methods to assess attention capacities, such as questionnaires answered by parents, observations during play, or administration of (computerized) tasks. Different types of measures probably assess different aspects of attention, in different contexts as well. Questionnaires are often answered by parents, and usually cover attention capacities over a longer period of time in the home context. Observations and (computerized) tasks, in contrast, measure attention at only one moment in time and often in a lab situation, but these provide more objective information than parental reports. Thus far, it is unknown which method, or combination of methods, will provide the best impression of attention capacities in children. For this reason, in this dissertation, several methods will be used to measure attention capacities in moderately preterm and term born toddlers.

Task performance and eye-tracking technology

In young children, attention capacities are often assessed using looking behavior (Colombo, 2002). One way in which looking behavior in a systematic task can be assessed is by use of eye-tracking technology, which is more detailed and accurate than the use of human observers (Gredebäck, Johnson, & Von Hofsten, 2009). Eye-tracking technology was already used at the end of the 19th century by Edmund Huey in a study on how people read. His eye-tracking equipment was a contact lens placed on the eye with a hole that was attached to an aluminium pointer which moved when the eye was moving (Holmqvist et al., 2011). For years, researchers had to develop and build their own equipment just as Huey did, but in the 1970s, companies started to develop eye-tracking systems, which made eye tracking a more accessible tool for research (Holmqvist et al., 2011). After the need to use uncomfortable contact lenses to measure eye movements, in the 1990s it became possible to register eye movements without equipment in or around the eye using the 'automated corneal-reflection remote eye-tracking technique' (Holmqvist et al., 2011). This eye-tracking device sends out infrared light, which is reflected on the cornea of the eye. The reflection is recorded by cameras in the device, and the eye position is determined by the software.

The remote eye-tracking device is not attached to the head or the eyes, but integrated in a computer, making it suitable for use with young children. The automated corneal-reflection remote eye tracker has since been used successfully in several studies with infants and toddlers to study cognitive development. An example concerns the development of object representations (i.e., ability to remember an object that is temporarily out of sight; e.g., Bertenthal, Gredebäck, & Boyer, 2013). Another example is the study of anticipatory looking in infants: when a person is starting to perform an action with an everyday object, for example placing a cup to the mouth, anticipatory looking indicates that the child is already looking at the mouth of the person before the person is actually performing the action (e.g., Hunnius & Bekkering, 2010). With this paradigm, it can be studied at what age children have knowledge about the use of everyday objects. These are just a few examples of the application of eye tracking in the study of cognitive development of young children. In infants, eye tracking was also used to study attention capacities, for example by studying the ability to disengage and shift attention, or the development of selective attention (Amso & Johnson, 2008; Butcher, Kalverboer, Geuze, & Stremmelaar, 2002; Hunnius, Geuze, & Van Geert, 2006). However, less is known about the potential of eye tracking in studies of functioning of the orienting, alerting, and executive attention systems in toddlers.

Test batteries to measure attention

For preschool aged children, a few test batteries exist to measure functioning of the three attention systems: orienting, alerting and executive attention. The Early Childhood Attention Battery are eight (computerized) tasks that are suitable for 3- to 6-year-olds (Breckenridge, Braddick, & Atkinson, 2013). Orienting capacities are, for example, measured with the *visual search task* in which the child has to search for the red apples on a sheet of paper full of red apples, white apples and red strawberries. An example of a task to measure alerting capacities is the *visual sustained task* in which the child has to name or point to pictures of animals that are shown within a series of pictures. Executive attention is, for example, measured with the *verbal opposites task* in which a picture of a cat and a dog are shown and half of the time the child had to say "cat" when he or she saw the cat and "dog" when the dog was presented (non-conflict), but in the other half of the trials the child had to say the opposite, so "dog" when the cat was presented and "cat" when the dog was shown (conflict; Breckenridge et al., 2013).

For 5-year-olds, Berger, Jones, Rothbart, and Posner (2000) developed a test battery consisting of four computerized games. In the *orienting task*, used to measure functioning of the orienting system, the child is asked to feed the fish that are appearing in one of two tanks by touching the screen after a cue (darkening of one of the tanks), which could be right or wrong, was given. Functioning of the alerting system was measured using the *alert task* in which the child has to help the farmer to catch animals that run away by touching the screen when an animal is presented. The appearance of the animals is in half of the trials preceded by a warning sound. Executive attention is measured using two tasks, an example is the *pointing-stroop task*. In this task, a picture of a dog and a cat appear on the screen and an animal sound (e.g., meow) is heard. In compatible trials the child has to touch the animal that makes that sound, while in incompatible trials the opposite animal needs to be touched (Berger et al., 2000).

Unfortunately, for children under three years of age no such tasks were available to measure orienting, alerting, and executive attention capacities. Therefore, to accomplish the second aim of this dissertation (i.e., studying attention capacities of moderately preterm toddlers), an additional aim is to develop a test battery to measure attention capacities in toddlers using eye tracking.

Questionnaires

Another way of measuring attention is by the use of questionnaires answered by parents. The advantage of using questionnaires is that they are easy to administer and cover attention in everyday situations. For toddlers, however, no questionnaires were available designed specifically to measure attention capacities. Nevertheless, there are several questionnaires focusing on other domains that included questions about attention capacities. The Infant-Toddler Social and Emotional Assessment (ITSEA; Carter, Briggs-Gowan, Jones, & Little, 2003) included five questions with a 3-point-scale regarding attention. The Child Behavior Checklist 1½-5 (CBCL 1½-5; Achenbach & Rescorla, 2000) also includes five questions with a 3-point-scale regarding attention. The Nijmeegse Ouderlijke Stress Index (NOSI; De Brock, Vermulst, Gerris, & Abidin, 1992) has a 'distractibility' subscale including 12 questions with a 6-point scale. Finally, the Early Childhood Behavior Questionnaire (ECBQ; Putnam, Gartstein, & Rothbart, 2006) has two attention subscales: *attention focusing* and *attention shifting* that both contained 12 items with a 7-point-scale. For several reasons the ECBQ was chosen over the other questionnaires as measure in this dissertation. First, the ECBQ included 24 questions, divided in two subscales, to measure attention, while the ITSEA and CBCL had only five attention items, and the NOSI 12. Second, the answering scale of the ECBQ was broader than that of the ITSEA and CBCL (i.e., 7-point scale versus 3-point scale). With a broad scale we might be better able to detect (small) differences between the groups of children. Finally, although the NOSI also had a broad answering scale, the questions are more focused on how mothers perceive and cope with their child instead of the actual capacities their children show. Therefore, the ECBQ seemed to be the best choice.

Observations

Attention capacities of toddlers can also by measured by observing them. In contrast to questionnaires, this method is more time-consuming and it can be applied only on one or a few time points. In addition, it can be questioned if a child is showing his or her natural behavior while being observed. However, observers might be more objective and focused on the behaviors of interest than parents.

The setting of observations can vary in context (i.e., home or lab), duration (i.e., few minutes until few hours), situation (i.e., free play or performing tasks) and interaction partners (i.e., playing alone or together with a parent). In the current dissertation, the attention capacities of the child were observed in a lab setting when the child was interacting with his or her mother during both a free play and a task setting.

Predictors of cognitive functioning

Based on previous research, it is expected that moderately preterm children differ from term born children in cognitive functioning and attention capacities (e.g., Potijk et al., 2012; Van Baar et al., 2009). It has been suggested that attention capacities underlie cognitive functioning (e.g., Davis & Burns, 2001). Therefore, part of the final aim of this dissertation is to investigate whether attention capacities mediate the relation between gestational age and cognitive functioning. It is, however, unlikely that biological factors (i.e., gestational age) and child characteristics (i.e., attention capacities) alone can predict cognitive functioning. Although all children have a natural drive to develop, children do not grow up in isolation and their development will also be influenced by their environment (Thompson, 2001).

According to Sameroff's Unified Theory of Development (Sameroff, 2010), development is an outcome of the interplay between nature and nurture. He suggested that there are four models needed to understand human development (Sameroff, 2010). The first model is the *personal change model,* which is about learning how an individual child changes over time. This model includes both biological and psychological growth processes.

The second, *contextual model* is based on Bronfenbrenner's bio-ecological model (Bronfenbrenner, 1979), and implies that a child grows up in an environment that has direct and indirect influences on his or her development. This environment can be close to the child, such as parents, family, and peers, but also at more distance, such as the culture in which the child grows up. The parents are a very important part of the child's environment, as he or she spends a lot of time with them, especially during the first years of life. Furthermore, parents take care of and educate their children.

The third model is the *regulation model*, reflecting that development is an outcome of the dynamic interactions between the child and his or her environment. The child is not just passively influenced by the environment, but also shapes the environment, which then again influences the child. This results in a transactional influence of child and environment. Such transactional influence is also described by Vygotsky's *zone of proximal development* (Vygotsky, 1978). This *zone of proximal development* refers to the difference between the actual and the potential developmental level of the child. The actual developmental level of the child concerns activities the child can accomplish on its own. The potential developmental level of the child concerns the activities the child can only accomplish with guidance from others. The process with which parents can promote learning of their children is called *scaffolding* (Wood, Bruner, & Ross, 1976). Scaffolding implies that the parent adjusts his or her guidance to the developmental level of the child and provides just enough help to let the child accomplish the somewhat too difficult task (Wood et al., 1976). This specific guidance and regulation will facilitate the learning processes of the child and it is also based on the competencies of the child and the parent to adjust to each other.

The fourth model is the *representational model*, which implies that everyone has representations of their early environment and experiences, that form a background for the interpretation of new experiences and further shape one's development. An example of how such representations may work is shown in a study in which mothers rated temperament of their own child and of children from others (Seifer, Sameroff, Barrett, & Krafchuk, 1994). Results showed that the correlations between maternal ratings and ratings of independent observers were much higher when mothers rated children of others than when they rated their own child. These lower correlations were explained by the fact that the ratings of their own child were influenced by their representations of the child based on previous experiences, which might also influence how mothers behave and respond to their children. Sameroff proposes that combining these four models into a unified theory of development gives an overview of the processes involved in human development (Sameroff, 2010).

The unified theory of development underlies the studies in this dissertation. Especially with regard to the third aim, were a combination of the *personal change model* and the *contextual and regulation model* is used for studying the role of gestational age, attention capacities of the child (i.e., *personal change model*) and maternal stimulation (i.e., *contextual and regulation model)* on cognitive functioning of the child. Maternal stimulation is defined as the use of attention-directing behavior that stimulates the child to attend to certain objects or activities.

Study design

The studies described in this dissertation are part of the longitudinal study called the STAP Project (i.e., Study on Attention of Preterm children). In the STAP Project, a group of moderately preterm and a group of term born children were followed at 12, 18, and 24 months of age. There are several reasons to examine the children at these ages. First, previous research showed that between one and two years of age, the difference in cognitive functioning between very preterm and term born children enlarged, indicating that this might be a critical period in the development of preterm children (Van Baar et al., 2006). Next to that, regarding attention development, the period between 9 and 18 months of age is mentioned as an important transition phase during which children normally become increasingly able to focus their attention for a longer period of time and gain more control over their attention capacities (Ruff & Rothbart, 1996). For these reasons it is important to focus on the development of preterm children during the second year of life.

In the preterm group, age at all three measurement moments was corrected for prematurity. Age correction means that the age of the child is corrected for the number of weeks the child was born preterm. For example, a child that was born eight weeks premature is two years of corrected age eight weeks after his or her actual birthday. There is no consensus whether age should be corrected in this group of moderately preterm children. The reason that the corrected age was used in this dissertation is that this allows the preterm children, and their brain, the same amount of time to develop as a child that is born at term.

Selection criteria

Inclusion criterion was a gestational age of 32-36^{+6} weeks at birth for moderately preterm and ≥37 weeks for term born children. Exclusion criteria for both groups were tertiary Neonatal Intensive Care Unit (NICU) admittance, dysmaturity (birth weight below 10^{th} percentile according to Dutch references curves; Stichting Perinatale Registratie Nederland, 2014b), multiple birth, severe congenital malformations, antenatal alcohol or drug abuse by the mother, and chronic antenatal use of psychiatric drugs by the mother. These exclusion criteria were chosen because these factors might also be risk factors of developmental difficulties, next to preterm birth. For example, previous research showed that moderately preterm children that needed NICU admittance had worse cognitive outcomes than the children who did not (Baron, Erickson, Ahronovich, Baker, & Litman, 2011).

Measures

An overview of the study design is presented in Figure 1.2.

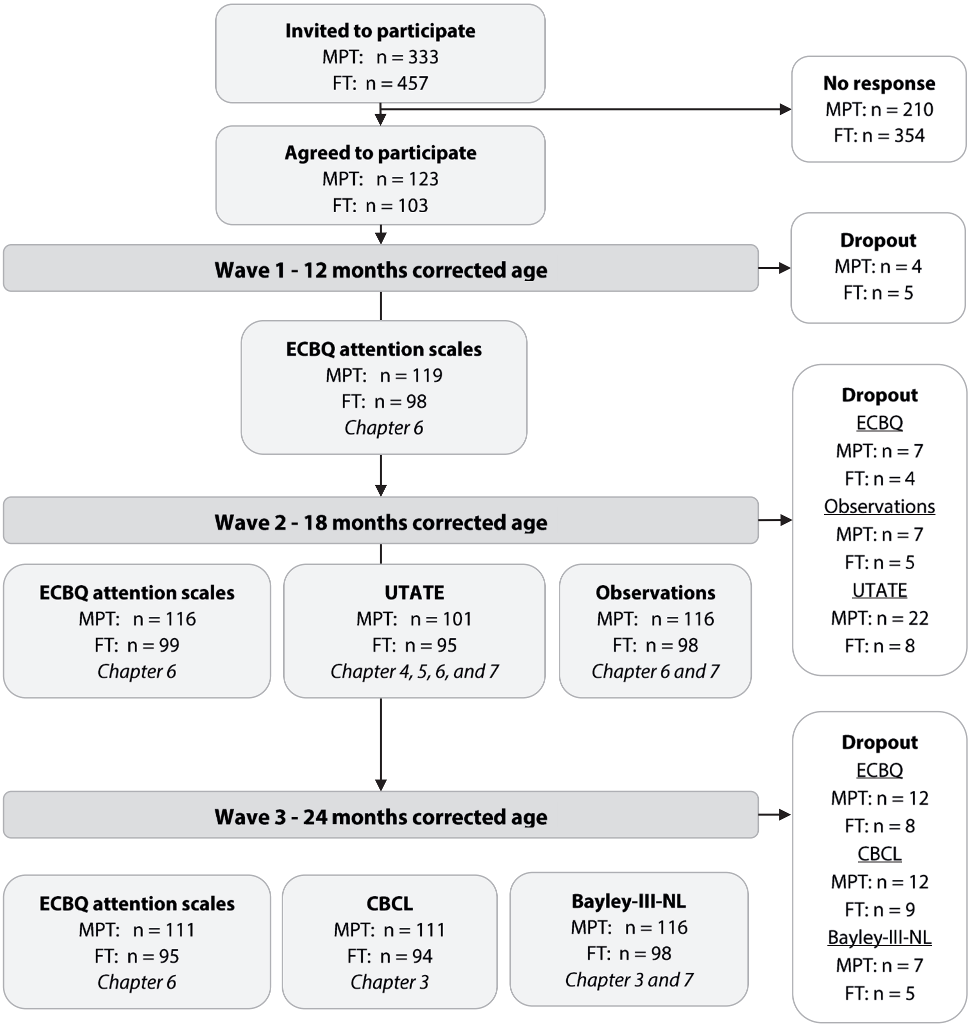

Figure 1.2. Flow chart of the study design
Note. MPT = Moderately preterm; FT = Full term.
Due to the use of repeated measures ANOVA, only children with complete data on the ECBQ at all three measurement waves were included in the analyses of chapter 6: MPT: n = 107, FT: n = 94.
Chapter 4 reports on a subsample of 16 FT children.
Chapter 5 reports on the FT sample.

Development

At 24 months of age, a developmental assessment was done with the Dutch version of the Bayley-III (Bayley, 2006), the Bayley-III-NL (Van Baar, Steenis, Verhoeven, & Hessen, 2014). The Bayley-III is the most widely used instrument to assess child development for children aged between 2 weeks and 3½ years (Steenis, Verhoeven, & Van Baar, 2012). It consists of five subtests: Cognition, Fine Motor, Gross Motor, Receptive Communication, and Expressive Communication. Recently, Dutch norms were developed and research showed differences between Dutch and United States norms, pointing to the importance of the use of population specific norms (Steenis, Verhoeven, Hessen, & Van Baar, 2015). Therefore, the Dutch version and scaled scores based on Dutch norms of the Bayley-III will be used in this dissertation. Scaled scores can vary between 1 and 19. Scores of 7 to 13 are considered normal, and a score below 7 indicates a (mild) developmental delay (Van Baar et al., 2014).

Behavior

Behavior problems of the children were assessed with the Child Behavior Checklist 1½-5 (CBCL 1½-5; Achenbach & Rescorla, 2000). Scores on this questionnaire give an indication of total, internalizing, and externalizing problem behavior. Furthermore, seven subcategories are distinguished: emotional reactivity, anxious/depressed behavior, somatic complaints, withdrawn behavior, sleep problems, attention problems, and aggressive behavior. The higher the scores a child has on the scales, the more behavior problems he or she has. Scores can also be categorized as *normal*, *borderline clinical*, and *clinical*. A borderline clinical score indicates that the behavior of the child needs attention, while a clinical score implies that the child might need treatment for his or her problem behavior.

Attention capacities of the children

Attention capacities were measured using different methods: questionnaires answered by mothers, observations during mother-child interaction, and an eye-tracking procedure.

Questionnaires

At 12, 18 and 24 months of age, mothers filled out the subscales *attention focusing* and *attention shifting* of the Early Childhood Behavior Questionnaire (ECBQ; Putnam et al., 2006). The ECBQ is developed to measure temperament of children aged 18 to 36 months. The precursor of the ECBQ, the Infant Behavior Checklist - Revised (IBQ-R; Gartstein & Rothbart, 2003), is only suitable until 12 months of age and does not include the same subscales as the ECBQ, complicating over time comparison. Based on the advice of the authors of the IBQ-R and ECBQ, we therefore decided to use the ECBQ attention subscales at all three ages. The subscale *attention focusing* was used as measure of the alerting attention system, and *attention shifting* as measure of the orienting attention system.

Eye-tracking procedure

At 18 months of age, an eye-tracking procedure was designed to measure orienting, alerting, and executive attention abilities of the children. The test battery was named the 'Utrecht Tasks for Attention in Toddlers using Eye Tracking' (UTATE). The UTATE consists of four different tasks: 1) *disengagement task*, 2) *face task*, 3) *alerting task*, and 4) *delayed response task*. Different aspects of looking behavior were coded during the four tasks measuring functioning of the three attention systems.

Observations

At 18 months of age, attention was measured using an observation of the child during the mother-child interaction. The *On-Task Persistence* item of the Coding Interactive Behavior (CIB) observational system (Feldman, 1998) was used as measure of the alerting attention system of the child.

Maternal attention-directing behavior

During the same mother-child interaction, maternal-attention directing behavior was observed. The Parental Attention Direction coding scheme (PAD; De Jong, Verhoeven, & Van Baar, 2016) was used, which was based on a coding scheme described in Landry, Smith, and Swank (2006).

With the PAD, the frequency of maternal maintaining and redirecting attention-directing behavior was coded. On the score sheet, 28 different behaviors or combinations of behaviors were distinguished, divided in physical behaviors, verbal behaviors, or a combination of verbal and physical. Examples of physical behavior are putting the child on the parents' lap or pointing. Verbal behaviors are, for example, saying "look…", asking "what is this", and praising. An example of a combination behavior is 'pointing, while giving instructions'. Most of the behaviors can be both maintaining and redirecting, based on the context in which mothers used it. The total number of maintaining and of redirecting behaviors were used as measures.

Aims and outline of this dissertation

In the current dissertation, three aims are addressed. First aim is to study behavior and development of moderately preterm children (Chapter 2 & 3). The second aim is to investigate differences in attention capacities between moderately preterm and term born children at toddler age (Chapter 4, 5 & 6). The final aim is to study the role of biological factors, child characteristics, and maternal stimulation in cognitive development of moderately preterm and term born children (Chapter 7).

The chapters consist of one review study and five empirical studies. In **Chapter 2**, a review of the existing literature on school outcome, cognitive functioning, behavior problems, and psychiatric disorders in moderately preterm children is presented. In **Chapter 3**, behavior and development of 24-month-old moderately preterm toddlers is compared with that of their term born peers. **Chapter 4** presents a pilot study in which a new instrument to measure attention capacities in toddlers - the Utrecht Tasks for Attention in Toddlers using Eye Tracking (UTATE) - is described and tested in a small sample. In **Chapter 5**, the factor structure of attention capacities of 18-month-old term born toddlers measured with the UTATE is examined. **Chapter 6** compares the attention capacities of moderately preterm and term born toddlers at 12, 18 and 24 months of age using a multi-method approach including questionnaires, observations and eye-tracking technology. In **Chapter 7** the role of gestational age, attention capacities and maternal stimulation in cognitive functioning is described in an integrated model. Finally, **Chapter 8** consists of a general discussion of the findings, as well as implications for clinical practice and recommendations for future research.

Chapter 2

School Outcome, Cognitive Functioning, and Behavior Problems in Moderate and Late Preterm Children and Adults: A Review

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Abstract

A large number of children (6 to 11% of all births) are born at a gestational age between 32 and 36 weeks. Little is known of long-term outcomes for these moderate and late preterm children. In this review, results of 28 studies on school outcome, cognitive functioning, behavior problems, and psychiatric disorders are presented. Overall, more school problems, less advanced cognitive functioning, more behavior problems, and higher prevalence of psychiatric disorders were found in moderate and late preterm born infants, children, and adults compared with full term peers. Suggestions for future research are discussed.

Acknowledgement of author contributions

Marjanneke de Jong performed search and study selection, drafted the initial manuscript, revised the manuscript and approved the final manuscript as submitted.

Marjolein Verhoeven reviewed and revised the manuscript and approved the final manuscript as submitted.

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Introduction

Many infants are born too soon and therefore are at risk for developmental problems. In 2007, 10.7% of all children in the USA (6.1% in The Netherlands; Stichting Perinatale Registratie Nederland, 2009) were born at a gestational age between 32 and 36 weeks, i.e., moderate (32-33 weeks) and late (34-36 weeks) preterm (Martin et al., 2010). This entails 84% of all preterm births. During the last two decades, the number of preterm births increased by almost 25%, with a 4% increase in very preterm births (i.e., below 32 weeks' gestation) versus a 30% increase in moderate and late preterm births (Martin et al., 2010). Hence, the number of children in this group especially has increased over the last 20 years. Although mortality rates are much lower (7.5 times) in these children than in very preterm children, these rates are almost 10 times higher than in full term children (Mathews & MacDorman, 2008). With respect to neonatal complications, moderate and late preterm infants experience fewer illnesses than very preterm infants, but they are at elevated risk for breathing and feeding difficulties, hypoglycemia, and hyperbilirubinemia compared with full term infants (Shapiro-Mendoza et al., 2008). Another risk factor results from the fact that the brain of moderate and late preterm children is still immature; at 34 weeks of gestation, the brain weighs only 65% of the weight at 40 weeks of gestation (Kinney, 2006). Despite the high prevalence and increased medical risk of moderate and late preterm birth, little is known of long-term developmental outcomes of these children. In this review, the available information on school outcome, cognitive functioning, behavior problems, and psychiatric disorders of infants, children, and adults born moderate or late preterm is presented.

Method

Search strategy and study selection

The Scopus database was searched until 23 June 2011, using the terms: "late preterm", "moderately preterm", and "moderate preterm". In addition, reference lists of selected articles were examined to find additional studies.

Studies were included if: 1) these were published after 1 January 2000; 2) gestational age of participants was between 32 and 36^{+6} weeks; and 3) these investigated school outcome, cognitive functioning, behavior problems or psychiatric disorders.

Results

Included studies

The three search terms resulted in 485 hits. Based on title and abstract, 449 studies were excluded. Thirty-six articles were read full text and 16 of these were excluded because outcome measures were beyond the scope of this review (n = 11) or because the studies did not concern empirical data collection and analyses (n = 5). In four of the included studies, gestational age of the participants differed slightly from our inclusion criterion (i.e., selected 31 and/or 37 weeks of gestation; Cheatham, Bauer, & Georgieff, 2006; Gray, Indurkhya, & McCormick, 2004; Moster, Lie, & Markestad, 2008; Nomura et al., 2009). Nevertheless, we decided to include these studies as most participants fell in our defined range of gestational age. An additional eight papers were included, based on the reference lists of the selected articles. Finally, a total number of 28 papers were included in this review.

Characteristics of included studies

Characteristics and results of the included studies are presented in Table 2.1. Regarding the participants, 17 studies focused on moderate and late preterm children (32-36 weeks of gestational age; Buchmayer et al., 2009; Chyi, Lee, Hintz, Gould, & Sutcliffe, 2008; Dalziel et al., 2007; Darlow, Horwood, Wynn-Williams, Mogridge, & Austin, 2009; Ekeus, Lindström, Lindblad, Rasmussen, & Hjern, 2010; Gray et al., 2004; Hillemeier, Farkas, Morgan, Martin, & MacZuga, 2009; Huddy, Johnson, & Hope, 2001; Kirkegaard, Obel, Hedegaard, & Henriksen, 2006; Lindström, Lindblad, & Hjern, 2009; Lindström, Lindblad, & Hjern, 2011; Moster et al., 2008; Nomura et al., 2009; Romeo et al., 2010; Schendel & Bhasin, 2008; Schermann & Sedin, 2004; Van Baar, Vermaas, Knots, De Kleine, & Soons, 2009), 10 focused on late preterm children (34-36 weeks of gestational age; Baron et al., 2009; Baron, Erickson, Ahronovich, Litman, & Brandt, 2010; Baron, Erickson, Ahronovich, Baker, & Litman, 2011; Cheatham et al., 2006; Gurka, Locasale-Crouch, & Blackman, 2010; Linnet et al., 2006; Morse, Zheng, Tang, & Roth, 2009; Petrini et al., 2009; Talge et al., 2010; Woythaler, McCormick, & Smith, 2011), and one focused on children born between 32-34 weeks of gestational age (Marret et al., 2007). Twenty-three studies investigated outcomes in infancy or childhood (0-15 years of age; Baron et al., 2009; Baron et al., 2010; Baron et al., 2011; Buchmayer et al., 2009; Cheatham et al., 2006; Chyi et al., 2008; Darlow et al., 2009; Gray et al., 2004; Gurka et al., 2010; Hillemeier et al., 2009; Huddy et al., 2001; Kirkegaard et al., 2006; Lindström et al., 2011; Linnet et al., 2006; Marret et al., 2007; Morse et al., 2009; Petrini et al., 2009; Romeo et al., 2010; Schendel & Bhasin, 2008; Schermann & Sedin, 2004; Talge et al., 2010; Van Baar et al., 2009; Woythaler et al., 2011), four studies reported outcomes in (young) adulthood (18-36 years of age; Dalziel et al., 2007; Ekeus et al., 2010; Lindström et al., 2009; Moster et al., 2008), and one reported on outcomes in both childhood and adulthood (Nomura et al., 2009). School outcome was investigated in seven

Table 2.1 Characteristics and results of included studies

Authors	Gestational age range (weeks) preterm	Subject characteristics	No. of subjects	School outcomes	Cognitive functioning [Mean (SD)/(range) or confidence interval]	Behavior problems and/or psychiatric disorders
Baron et al. (2009)	LPT: 34-36	3 years old; born in 2004-2005; complicated group (e.g. NICU admittance)	LPT: 60 FT: 35		LPT < FT: 105 (15.9) vs 112 (12.9)	
Baron et al. (2010)	LPT: 34-36	3 years old; born in 2004-2006; complicated group	LPT: 75 FT: 40		LPT < FT: 106 (15.0) vs 116 (10.3)	
Baron et al. (2011)	LPT: 35-36	3 years old ; born in 2004-2006; both complicated and uncomplicated groups	LPT: 118 (90 complicated; 28 uncomplicated) FT: 100		Complicated LPT (103-109) < FT (109-115) Uncomplicated LPT (104-115) = FT	
Buchmayer et al. (2009)	MPT/LPT: 32-36	0-10 years old; born in 1987-2002	MPT/LPT: 420 FT: 6207			Autism: OR=1.55
Cheatham et al. (2006)	LPT: 35-37	12 months; year of birth unknown	LPT: 29 FT: 20		LPT = FT: 97 (81-111) and 95 (77-112) respectively	
Chyi et al. (2008)	MPT/LPT: 32-36 MPT: 32 - 33 LPT: 34 - 36	5-10 years old; born in ~1993-1994	MPT: 203 LPT: 767 FT: 13671	Poor school outcomes: MPT: OR=1.0-2.0 LPT: OR=1.0-1.3 Need for help: MPT: OR=1.9-2.8 LPT: OR=1.1-1.4 Special education: MPT: OR=2.0-2.9 LPT: OR=1.2-2.1		
Dalziel et al. (2007)	MPT/LPT: 32-35	30 years old; born in 1969-1974	MPT/LPT: 126 FT: 66		MPT/LPT = FT: 103 (13.4) and 104 (12.2) respectively	MPT/LPT = FT for depression, anxiety, schizophrenia and attention deficit disorder

Table 2.1 Characteristics and results of included studies (continued)

Authors	Gestational age range (weeks) preterm	Subject characteristics	No. of subjects	School outcomes	Cognitive functioning [Mean (SD)/(range) or confidence interval]	Behavior problems and/or psychiatric disorders
Darlow et al. (2009)	MPT/LPT: 33-36	2 years old; born in 2001-2002; NICU admittance for MPT/LPT group	MPT/LPT: 112 FT: 94		MPT/LPT = FT: 90 (14.2) and 92 (11.0) respectively	Showing two or more out of five problematic behaviors: MPT/LPT (26%) > FT (20%)
Ekeus et al. (2010)	MPT/LPT: 33-36 MPT: 33-34 LPT: 35-36	18-19 years old; born in 1973-1976; male conscripted for military service	MPT: 1088 LPT: 3981 FT: 94821		MPT (4.8) and LPT (4.9) < FT (5.1)	
Gray et al. (2004)	MPT/LPT: 31-37 MPT: 31-34 LPT: 35-37	3, 5 and 8 years old; born in 1985	MPT: 435 LPT: 262			~20% of MPT/LPT had clinical scores on CBCL
Gurka et al. (2010)	LPT: 34-36	4.5-15 years old; born in 1991; low risk group (e.g. no serious illness)	LPT: 53 FT: 1254	Special education: OR=1.3	LPT = FT	LPT = FT on CBCL
Hillemeier et al. (2009)	MPT/LPT: 33-36	9 and 24 months; born in 2001	MPT/LPT: 1224 (592 singletons, 632 multiple births) FT: 7173 (6570 singletons, 603 multiple births)		Scoring in lowest 10%: 9 months: OR=2.4 (singletons), 3.6 (multiple births); 24 months: OR=0.9 (singletons), 1.3 (multiple births), NS	
Huddy et al. (2001)	MPT/LPT: 32-35	7 years old; born in 1990	MPT/LPT: 117	School problems: MPT/LPT (~30%) > population (10-20%) Special education: MPT/LPT (4%) > population (1.7%) Need help at school: ~25% of MPT/LPT		Abnormal hyperactivity scores: MPT/LPT (parents: 18%, teachers: 18.8%) > population norm (10%)

Table 2.1 Characteristics and results of included studies (continued)

Authors	Gestational age range (weeks) preterm	Subject characteristics	No. of subjects	School outcomes	Cognitive functioning [Mean (SD)/(range) or confidence interval]	Behavior problems and/or psychiatric disorders
Kirkegaard et al. (2006)	MPT/LPT: 33-36	9-11 years old; born in 1990-1992	MPT/LPT: 169 FT: 3081	Spelling difficulties: OR=1.6 Reading difficulties: OR=1.2		
Lindström et al. (2009)	MPT/LPT: 33-36	23-29 years old; born in 1973-1979	MPT/LPT: 2037 FT: 450165			Psychiatric disorders: OR=1.3 Neuropsychiatric disorders (e.g. ADHD): OR=2.1
Lindström et al. (2011)	MPT/LPT: 33-36 MPT: 33-34 LPT: 35-36	6-19 years old; born in 1987-2000	MPT/LPT: 56650 FT: 813606			ADHD: MPT: OR=1.4 LPT: OR=1.3
Linnet et al. (2006)	LPT: 34-36	All children born in 1980-1994 diagnosed with HKD and control children	LPT: 37 cases, 544 controls. FT: 456 cases, 12365 controls.			HKD: OR=1.8
Marret et al. (2007)	MPT: 32-34	5 years old; born in 1997	MPT: 788		Scores < 85: MPT (~24%) > population (15%)	
Morse et al. (2009)	LPT: 34-36	0-5 years old; born in 1996-1997; low risk group (<3 days hospitalization)	LPT: 7152 FT: 152661	School related problems (e.g. grade retention, special learning needs): OR=1.1-1.3		

Table 2.1 Characteristics and results of included studies (continued)

Authors	Gestational age range (weeks) preterm	Subject characteristics	No. of subjects	School outcomes	Cognitive functioning [Mean (SD)/(range) or confidence interval]	Behavior problems and/or psychiatric disorders
Moster et al. (2008)	MPT/LPT: 31-36 MPT: 31-33 LPT: 34-36	20-36 years old; born in 1967-1983	MPT: 6363 LPT: 31169 FT: 828227		Mental retardation: MPT: OR=2.1 LPT: OR=1.6	Schizophrenia: MPT: OR=1.4 LPT: OR=1.3 Disorders of psychological development, behavior, and emotion: MPT: OR=1.4 LPT: OR=1.5 Autism: NS
Nomura et al. (2009)	MPT/LPT: 33-37	7-8 and 27-33 years old; born in 1960-1964	MPT/LPT: 226 FT: 1393	Reading: MPT/LPT < FT Spelling: MPT/LPT < FT Arithmetic: MPT/LPT < FT (age 7-8 years) This is associated with lower educational attainment in adulthood	MPT/LPT < FT; 89 (11.8) vs 94 (11.6)	
Petrini et al. (2009)	LPT: 34-36	0-5.5 years old; born in 2000-2004	LPT: 8341 FT: 128955		Developmental delay/ mental retardation compared: OR=1.4	
Romeo et al. (2010)	MPT/LPT: 33-36	12 and 18 months old; born in 2005-2006; low risk group (e.g. no serious illness)	MPT/LPT: 61 FT: 60		MPT/LPT < FT [at 12 months 92 (9.3) vs 100 (8.7) and at 18 months 88 (9.9) vs 98 (8.1)], only when age was not corrected for prematurity	

Table 2.1 Characteristics and results of included studies (continued)

Authors	Gestational age range (weeks) preterm	Subject characteristics	No. of subjects	School outcomes	Cognitive functioning [Mean (SD)/(range) or confidence interval]	Behavior problems and/or psychiatric disorders
Schendel and Bhasin (2008)	MPT/LPT: 33-36	3-10 years old; born in 1981-1993	MPT/LPT: 26319 FT: 241888		Mental retardation: OR=1.9	Autism: MPT/LPT =FT
Schermann and Sedin (2004)	MPT/LPT: 32-36	10 years old; born in 1986-1989; NICU admittance for preterm group	MPT/LPT: 82 FT: 72		MPT/LPT < FT; 101 (12.9) vs 109 (14.4)	
Talge et al. (2010)	LPT: 34-36	6 years old; born in 1983-1985	LPT: 168 FT: 168		LPT = FT; 101 (SE=1.3) and 102 (SE=1.3) respectively	Internalizing problems: LPT > FT Externalizing problems: LPT>FT (slightly) Attention problems: LPT>FT
Van Baar et al. (2009)	MPT/LPT: 32-36 MPT: 32 – 33 LPT: 34 - 36	8 years old; born in 1996-1998; low risk group (e.g. no NICU admittance)	MPT/LPT: 377 MPT: 62 LPT: 315 FT: 182	Special education: MPT/LPT (7.7%) > FT (2.8%) MPT (9.7%) = LPT (7.3%) Grade retention: MPT/LPT (19%) > FT(8.8%) MPT (30%) > LPT (17%)	MPT/LPT < FT; 105 (14) vs 108 (15)	Internalizing problems: MPT/LPT > FT Externalizing problems: MPT/LPT = FT Attention problems: MPT/LPT > FT Behavior problems: MPT < LPT
Woythaler et al. (2011)	LPT: 34-36	24 months old; born in 2001	LPT: 1200 FT: 6300		LPT < FT, 126 (10.3) vs 128 (10.4) Percentage < 70: LPT (21.2%) > FT (16.4%)	

Note. MPT = moderate preterm; LPT = late preterm; FT = full term; OR = odds ratio; NS = non-significant; CBCL = Child Behavior Check List; ADHD = attention deficit/ hyperactivity disorder; NICU = neonatal intensive care unit; HKD = hyperkinetic disorder.

studies (Chyi et al., 2008; Gurka et al., 2010; Huddy et al., 2001; Kirkegaard et al., 2006; Morse et al., 2009; Nomura et al., 2009; Van Baar et al., 2009), cognitive functioning in 19 (Baron et al., 2009; Baron et al., 2010; Baron et al., 2011; Cheatham et al., 2006; Dalziel et al., 2007; Darlow et al., 2009; Ekeus et al., 2010; Gurka et al., 2010; Hillemeier et al., 2009; Marret et al., 2007; Moster et al., 2008; Nomura et al., 2009; Petrini et al., 2009; Romeo et al., 2010; Schendel & Bhasin, 2008; Schermann & Sedin, 2004; Talge et al., 2010; Van Baar et al., 2009; Woythaler et al., 2011), behavior problems in six (Darlow et al., 2009; Gray et al., 2004; Gurka et al., 2010; Huddy et al., 2001; Talge et al., 2010; Van Baar et al., 2009), and psychiatric disorders in seven (Buchmayer et al., 2009; Dalziel et al., 2007; Lindström et al., 2009; Linnet et al., 2006; Moster et al., 2008; Schendel & Bhasin, 2008).

School outcome

All seven studies found an increased risk for school problems for moderate and late preterm children compared with full term children. Compared with full term children, they were at 1.3-2.8-fold increased risk for attending special education (Chyi et al., 2008; Gurka et al., 2010; Huddy et al., 2001; Van Baar et al., 2009) and had repeated grades between 1.3 and 2.2 times more often at 5-10 years of age (Morse et al., 2009; Van Baar et al., 2009). Three studies focused on specific school abilities in 5-10 year-olds and found lower scores for moderate/late preterm children on reading, spelling, and arithmetic compared with full term children (Chyi et al., 2008; Huddy et al., 2001; Nomura et al., 2009). A higher risk for reading and spelling difficulties was also found in the preterm children at age 9-11 years (Kirkegaard et al., 2006). With regard to educational attainment in adults, it was found that individuals born moderate or late preterm had more learning-related disabilities at age 7, which was related to lower educational attainment in adulthood (Nomura et al., 2009).

Cognitive functioning

Five studies investigated cognitive functioning in infancy (0-24 months of age; Cheatham et al., 2006; Darlow et al., 2009; Hillemeier et al., 2009; Romeo et al., 2010; Woythaler et al., 2011). One of these found lower developmental scores for preterm children compared with full term children at 24 months of age (not corrected for prematurity; Woythaler et al., 2011). In a longitudinal study by Romeo et al. (2010), a delay in cognitive functioning was found for children born at 33-36 weeks compared with full term children at 12 and 18 months of age. These group differences were no longer significant when age was corrected for prematurity. Two other studies that corrected age for prematurity also found no differences in scores between moderate/late preterm and full term children at 12 and 24 months of age (Cheatham et al., 2006; Darlow et al., 2009). Hillemeier et al. (2009) performed a longitudinal study in which cognitive functioning was investigated at 9 and 24 months of age (corrected for prematurity). They found a two-fold higher risk for scoring in the lowest 10% in moderate/late preterm children compared with full term children at 9 months of age, but this difference was no longer seen at 24 months of age.

Different results emerge from 11 studies concerning cognitive functioning in moderate/late preterm children at 3-15 years of age (Baron et al., 2009; Baron et al., 2010; Baron et al., 2011; Gurka et al., 2010; Marret et al., 2007; Nomura et al., 2009; Petrini et al., 2009; Schendel & Bhasin, 2008; Schermann & Sedin, 2004; Talge et al., 2010; Van Baar et al., 2009). Two studies on large samples of more than 100,000 and 300,000 children found an increased risk of 1.3-1.9 for mental retardation (i.e., IQ scores <70) in moderate/late preterm children compared with full term children (Petrini et al., 2009; Schendel & Bhasin, 2008). In line with this, the preterm children were twice as likely to score <85 on an IQ test than their full term peers at age 5, 6, and 10 (Marret et al., 2007; Schermann & Sedin, 2004; Talge et al., 2010). In two of these studies (at ages 5 and 6 years), no differences were found between mean scores of moderate/late preterm and full term children (Marret et al., 2007; Talge et al., 2010), which suggests a different distribution in scores with more moderate/late preterm children showing developmental delay than in the population. Six studies did find differences in mean IQ scores between moderate/late preterm and full term children aged 3-10 years, with preterm children scoring below their full term peers (Baron et al., 2010; Baron et al., 2011; Nomura et al., 2009; Schermann & Sedin, 2004; Van Baar et al., 2009). Medical risk of the children regarding their need for neonatal intensive care unit treatment seemed to differ between these six studies. Three of these studies only investigated moderate/late preterm children with a high medical risk (Baron et al., 2009; Baron et al., 2010; Schermann & Sedin, 2004), one included only low risk children (Van Baar et al., 2009), and another study did not report any neonatal characteristics regarding high or low risk (Nomura et al., 2009). Baron et al. (2011) showed that medical risk might be important, as they found lower scores for late preterm children only in those children that were at high risk, but not for low risk children. Gurka et al. (2010) also found no differences in mean IQ scores between low risk late preterm and full term children in their longitudinal study following children from 4 to 15 years of age.

Results regarding cognitive functioning in adulthood are somewhat inconsistent (Dalziel et al., 2007; Ekeus et al., 2010; Moster et al., 2008). An increased risk for mental retardation was found in adults born moderate/late preterm compared with adults born at full term in a large epidemiological study (Moster et al., 2008). Ekeus et al. (2010) also found slightly lower scores on a general intellectual performance test used for the military service in 18-19 year old preterm born men, compared with full term. By contrast, Dalziel et al. (2007) found no differences between moderate/late preterm and full term born adults at 30 years of age regarding their scores on the Wechsler Abbreviated Scale of Intelligence.

Behavior

Behavior problems as reported by parents and teachers

Six studies examined the prevalence of behavior problems in moderate/late preterm children as reported by parents and teachers (Darlow et al., 2009; Gray et al., 2004; Gurka et al., 2010; Huddy et al., 2001; Talge et al., 2010; Van Baar et al., 2009). A longitudinal study showed that at age 3, 5 and 8 years, ~20% of the preterm children scored in the clinical range of the Child Behavior Check List total problem scale as reported by their parents; twice as much as the expected 10% (Gray et al., 2004). Likewise, Darlow et al. (2009) found that parents reported slightly more behavior problems in 2-year-old preterm compared with full term children, as indicated by the presence of two or more out of five problem behaviors (i.e., poor positive affect, frequent negative affect, poor attention, highly active, low self-confidence). Teachers of 6-year-old children reported more internalizing behavior and attention problems, and slightly more externalizing behavior in late preterm children compared with full term children (Talge et al., 2010). Similarly, in the study by Van Baar et al. (2009), both mothers and teachers reported more internalizing behavior and attention problems in moderate/late preterm children compared with full term children at 8 year of age. Next to that, mothers reported more symptoms of hyperactivity in moderate/late preterm children than in full term children. At 7 years of age, Huddy et al. (2001) also found that parents and teachers rated moderate/late preterm children more often as being hyperactive, but did not report higher levels of emotional symptoms, conduct problems, peer problems, or prosocial behavior for these children. A longitudinal study investigating children between 4 and 15 years of age found no differences in parent-reported externalizing, internalizing, aggressive, and anxiety/depressive behavior between a small group of late preterm (n = 53) and a large group of full term children (n = 1254; Gurka et al., 2010).

Prevalence of psychiatric disorders

Seven studies reported on the prevalence of psychiatric disorders (Buchmayer et al., 2009; Dalziel et al., 2007; Lindström et al., 2009; Lindström et al., 2011; Linnet et al., 2006; Moster et al., 2008; Schendel & Bhasin, 2008). Lindström et al. (2009) found a 30% higher risk for psychiatric disorders in moderate/late preterm adults compared with full term adults, especially in the domain of organic/neuropsychiatric disorders. Moster et al. (2008) found a 30-40% higher risk for schizophrenia and 40-50% higher risk for psychiatric disorders in moderate/late preterm adults compared to full term adults, including developmental, behavioral, and emotional disorders.

Three studies reported the prevalence of autism in large samples (Buchmayer et al., 2009; Moster et al., 2008; Schendel & Bhasin, 2008). Buchmayer et al. (2009) found a 50% increased risk for autism in moderate and late preterm children compared with full term children, whereas the other two studies found no differences in prevalence of autism (Moster et al., 2008; Schendel & Bhasin, 2008). Two studies examining the prevalence of attention deficit/hyperactivity disorder (ADHD) or hyperkinetic disorder (HKD) in large samples both reported a higher risk (30-80%) for these disorders in moderate/late preterm children (Lindström et al., 2011; Linnet et al., 2006). On the other hand, Dalziel et al. (2007) found no negative effect of moderate/late preterm birth on the presence of attention deficit disorder, as well as depression, anxiety, and schizophrenia in adulthood. It should, however, be noted that the sample used in this study was relatively small (126 preterm and 66 full term adults) compared with the above-mentioned studies, which were all epidemiological (Lindström et al., 2009; Lindström et al., 2011; Moster et al., 2008) or nested case-control (Buchmayer et al., 2009; Linnet et al., 2006; Schendel & Bhasin, 2008) designs.

Discussion

The aim of this review has been to gain more insight into long-term developmental outcomes of moderate and late preterm children, specifically in school outcome, cognitive functioning, behavior problems, and psychiatric disorders. Based upon the 28 studies included in this review, we conclude that moderate/late preterm children show more school problems, have lower IQ scores, and more behavior problems than their full term peers. For psychiatric disorders it is concluded that especially ADHD is more frequently reported for these preterm children; concerning autism, inconsistent findings have been reported.

The first explanation for the developmental problems of moderate/late preterm children lies in their immature (brain) development at birth. At 34 weeks of gestation, the brain weighs only 65% of the weight at 40 weeks of gestation (Kinney, 2006), so a lot of the 'hardware' brain tissue still has to grow during this period. In addition, other organs of the preterm infant, such as the lungs and the heart, have to adapt to extrauterine life at an earlier stage of development, which may stress brain development.

Correction for prematurity is important, as it provides at least the same amount of time for moderate or late preterm children to develop as could be used by full term children. This correction for prematurity explained the differences in results of several studies done in infancy from 0 to 2 years of age (Cheatham et al., 2006; Darlow et al., 2009; Hillemeier et al., 2009; Romeo et al., 2010; Woythaler et al., 2011). Lower scores on developmental tests were found for moderate/late preterm children compared with full term children only when age was not corrected for prematurity. However, when age was corrected and both groups of children could be considered equally mature, differences in developmental tests were no longer visible. The contrasting finding of Hillemeier et al. (2009), that at 9 months of age moderate/late preterm children performed worse than full term children even after age correction for prematurity whereas no group differences appeared at 24 months, may be very important. It might be that differences between the preterm and full term born children are larger at younger ages (<12 months). This suggests a different developmental pattern for young moderate or late preterm infants. Further research is needed on such developmental trajectories of these infants over the first years.

Moderate and late preterm children were found to be at risk for school problems and low scores on IQ tests. This might result from the regulation difficulties, or more specifically from attention difficulties involved in ADHD symptoms (Van Baar et al., 2009). In very preterm children, attention difficulties were repeatedly found (Landry, 1995; Rose, Feldman, & Jankowski, 2001), and differences in attention capacities were suggested as a mechanism partially explaining cognitive and school problems (Van De Weijer-Bergsma, Wijnroks, & Jongmans, 2008). In this review it was found that ADHD symptoms and attention problems are more common in moderate/late preterm children (Lindström et al., 2011; Linnet et al., 2006; Van Baar et al., 2009). The first years of life are very important in the development of attention capacities (Ruff & Rothbart, 1996). Neurological maturation is one of the factors influencing the development of attention capacities. Important brain development takes place between 32 and 37 weeks' gestation and preterm children cannot benefit from the neurobiological processes (e.g., related to maternal thyroid hormone exchange) during this period in the womb. Attention capacities of moderate and late preterm children should be studied in detail and compared with the development of processes in attention of full term children.

Not all moderate/late preterm children actually show developmental problems. The finding that a higher percentage of these children had an IQ score <85 compared with full term children, although mean scores on a standardized intelligence test did not differ between the preterm and full term children (Marret et al., 2007; Talge et al., 2010), indicates differences within the moderate/late preterm group. Even within the moderate/late preterm group gestational age may be important. In only two studies included in the review were differences between moderate and late preterm born children discussed or analyzed (Chyi et al., 2008; Van Baar et al., 2009). Chyi et al. (2008) found that the moderate preterm children showed more difficulties than the late preterm children. Van Baar et al. (2009) found that moderate preterm children more frequently repeated a grade, but also found that late preterm children showed more behavior problems than moderate preterm children. Hence, further study in relation to a further differentiation of gestational age, as well as in relation to different developmental outcomes, is necessary.

Another factor of influence might be differences in neonatal complications that may have occurred. Some of the preterm children needed neonatal intensive care treatment and are considered to be at high medical risk. Looking at the studies that investigated specific samples of high or low medical risk children, it seems that high risk moderate/late preterm children in particular score lower on standardized intelligence tests than full term children (Baron et al., 2009; Baron et al., 2010; Baron et al., 2011; Gurka et al., 2010; Schermann & Sedin, 2004; Van Baar et al., 2009). In general, not much attention has been paid to the importance of specific neonatal complications and the medical treatments in relation to developmental outcome of moderate or late preterm children. Future research could focus on the association between medical treatments (e.g., for hypoglycemia or infections), caretaking habits during the hospital stay (e.g., caregiving or kangarooing by parents, Newborn Individualized Developmental Care and Assessment Program (NIDCAP) or individualized caretaking), or hospital discharge routines and developmental outcome.

Another factor in explaining differences within the preterm group might be parent-child interaction and the quality of caregiver stimulation. Regarding very preterm infants, it was found that individual differences in cognitive development at infant and toddler age could be explained by maternal behaviors such as the amount of stimulation provided (Landry, Smith, Miller-Loncar, & Swank, 1997). Further research is needed on the influence of parent-child interaction on the development of moderate and late preterm children.

Only a few studies investigated cognitive functioning in adults born moderate or late preterm and comparison between these is hampered by their differences in selection criteria. As these studies showed inconsistent results, more research is needed before any conclusions on outcome in adulthood can be drawn. A general problem with studies on adults born preterm is that they were treated a long time ago (in these studies from 1967 to 1983). Information on the quality of their functioning may not be appropriate any more for infants treated with the current medical techniques and nursing methods. Nevertheless such information may provide some insight into developmental trajectories and the severity of problems in developmental outcome.

A strength of this review is that it presents an overview of long-term outcome of moderate and late preterm birth across the life span on the domains of school, cognitive, and behavioral functioning. Furthermore, the focus was not solely on late preterm (34-36 weeks) infants but also included studies investigating children born after 32-33 weeks of gestation. A limitation may be that the focus was on recent findings, as only studies published after 2000 were included. Secondly, the included studies varied in design and sample size (varying from 29 to 56,650 moderate preterm children). Finally, year of birth of the samples varied strongly across the studies from 1960 to 2006. Because quality of neonatal care increased a great deal during the last several decades, year of birth might influence the outcome for moderate and late preterm children. However, this review shows no clear association between developmental outcome and year of birth.

A clinical implication of the information from this review is that careful follow-up monitoring of moderate and late preterm children is required to provide early intervention when needed and to try to reduce the amount of school and behavior problems. Selective intervention, perhaps based on early indications of insufficient attention capacities, might be worthwhile.

In conclusion, moderate and late preterm children are at risk for school problems, lower cognitive functioning, behavior problems, and psychiatric disorders. Future research should focus on developmental trajectories over the first years. Also the associations between medical treatments, caretaking practice during the hospital stay in the neonatal period, hospital discharge routines and developmental outcome need to be studied in greater detail. Research should focus on attention capacities of moderate and late preterm children, as well as on differences within the group and factors explaining these differences. Intervention programs based on improvement of attention skills could be worthwhile. Finally, consequences of moderate and late preterm birth in adulthood might be subject of study. In short: moderate and late preterm children need attention!

Chapter 3

Behavior and Development in 24-Month-Old Moderately Preterm Toddlers

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Abstract

Objective: Moderately preterm children (gestational age 32-36^{+6} weeks) are at risk of cognitive and behavior problems at school age. The aim of this study was to investigate if these problems are already present at the age of 2 years. **Study design:** Developmental outcome was assessed at 24 months (corrected age) with the Bayley-III-NL in 116 moderately preterm (M=34.66±1.35 weeks' gestation) and 99 term born children (M = 39.45±0.98 weeks' gestation). Behavior problems were assessed with the Child Behavior Checklist. **Results:** With age corrected for prematurity, moderately preterm children scored below term peers on Receptive Communication skills (11.05±2.58 vs 12.02±2.74, p=0.02). Without correcting age for prematurity, moderately preterm children scored below term born peers on Cognition (8.97±2.11 vs 10.68±2.35, p<0.001), Fine Motor (10.33±2.15 vs 11.96±2.15, p<0.001), Gross Motor (8.47±2.55 vs 9.39±2.80, p=0.05), Receptive Communication (10.09±2.48 vs 12.02±2.74, p<0.001) and Expressive Communication (10.33±2.43 vs 11.49±2.51, p=0.005) skills. Compared with term peers, more moderately preterm children showed a (mild) delay (i.e., scaled score < 7) in gross motor skills with age uncorrected for prematurity (20.7% vs 11.2%, p=0.04). Moderately preterm children had more internalizing behavior problems than term children (44.76±8.94 vs 41.54±8.56, p=0.03). No group differences were found in percentages of (sub)clinical scores. **Conclusion:** At the age of 2 years, uncorrected for prematurity, differences in cognition, communication, and motor development were present in moderately preterm children compared with term born peers. After correcting age for prematurity, a difference was only found for receptive communication skills. In addition, moderately preterm children show more internalizing behavior problems.

Acknowledgement of author contributions

Marjanneke de Jong designed the study, coordinated the data collection, carried out the analyses, drafted the initial manuscript, revised the manuscript and approved the final manuscript as submitted.
Marjolein Verhoeven designed the study, reviewed and revised the manuscript and approved the final manuscript as submitted.
Carole A. Lasham assisted in data collection, reviewed the manuscript and approved the final manuscript as submitted.
Clemens B. Meijssen assisted in data collection, reviewed the manuscript and approved the final manuscript as submitted.
Anneloes L. van Baar conceptualized and designed the study, reviewed and revised the manuscript and approved the final manuscript as submitted.

Introduction

Worldwide, 11.1% of all pregnancies end in preterm delivery before 37 weeks of gestation, of which 84% are born moderately preterm after a gestational age (GA) between 32 to 36 weeks and 6 days (Blencowe et al., 2012). Although to a lesser extent than very and extreme preterm children, moderately preterm children still have more neonatal complications than term born children, such as respiratory distress, hypoglycemia and feeding problems (Shapiro-Mendoza et al., 2008). Long-term follow-up studies have shown that these children are at increased risk of cognitive, school and behavior problems at (pre)school age (De Jong, Verhoeven, & Van Baar, 2012). Little is known about developmental and behavioral outcomes in moderately preterm children in their first 2 years of life, even though this may be a period during which the first signs of developmental delay appear. The aims of the current study are to investigate developmental and behavioral outcomes of 24-month-old moderately preterm children compared with term born peers.

Few studies have compared developmental outcomes (i.e., cognitive, motor and/or communication skills) of moderately preterm with term born toddlers at this early age, using developmental tests. These studies showed inconsistent results, with some studies finding poorer outcomes for moderately preterm children (Hillemeier, Farkas, Morgan, Martin, & MacZuga, 2009; Morag et al., 2013; Nepomnyaschy, Hegyi, Ostfeld, & Reichman, 2012; Romeo et al., 2010; Voigt, Pietz, Pauen, Kliegel, & Reuner, 2012; Woythaler, McCormick, & Smith, 2011), while others found no differences (Blaggan et al., 2014; Cheatham, Bauer, & Georgieff, 2006; Darlow, Horwood, Wynn-Williams, Mogridge, & Austin, 2009; Hillemeier et al., 2009; Morag et al., 2013; Romeo et al., 2010). The inconsistencies in these findings are most likely a result of the use of age correction for prematurity or not. Age correction is infrequently used in moderately preterm children, especially in the late preterm subgroup (i.e., GA of 34-36 weeks). Most studies that found group differences did not correct age for prematurity (Morag et al., 2013; Nepomnyaschy et al., 2012; Romeo et al., 2010; Woythaler et al., 2011), while the studies that found no differences did correct the ages (Blaggan et al., 2014; Cheatham et al., 2006; Darlow et al., 2009; Morag et al., 2013; Romeo et al., 2010). Two studies did find differences with scores based on corrected age (Hillemeier et al., 2009; Voigt et al., 2012). Hillemeier et al. (2009) found that moderately preterm children had double the risk for scoring in the lowest 10% at 9 months of age, but by 24 months of age there was no increased risk in the moderately preterm children. Voigt et al. (2012) found a difference, with lower scores for moderately preterm children, with a medium effect size at 24 months of age. In the current study, differences between moderately preterm and term born toddlers will be determined for corrected as well as uncorrected age.

Despite growing evidence that moderately preterm children show more problem behavior at (pre)school age (De Jong et al., 2012; Gray, Indurkhya, & McCormick, 2004; Potijk, De Winter, Bos, Kerstjens, & Reijneveld, 2012; Van Baar, Vermaas, Knots, De Kleine, & Soons, 2009), no studies have been published that have determined the prevalence of behavioral problems in this group at toddler age using standardized measures such as the Child Behavior Checklist (CBCL 1½-5; Achenbach & Rescorla, 2000). In this study, standardized and up-to-date assessments were performed in moderately preterm and term born children at 2 years of age in order to compare functioning of both groups.

Method

This study is part of an ongoing longitudinal project on the development of Dutch moderately preterm children, the STAP Project (i.e., Study on Attention of Preterm children). Parents of moderately preterm (32-36 weeks' gestation) and term born (≥37 weeks' gestation) children were invited by letter by their pediatrician or midwife to participate in the study when their child was 10 months old. Children were born between March 2010 and April 2011 in nine hospitals in and around Utrecht. For both groups, exclusion criteria were dysmaturity (birth weight below 10th centile according to Dutch reference curves; Stichting Perinatale Registratie Nederland, 2014b), multiple birth, severe congenital malformations, antenatal alcohol or drug abuse by the mother, and chronic antenatal use of psychiatric drugs by the mother. We also excluded children admitted to a tertiary neonatal intensive care unit (NICU), according to the admission criteria of the official guidelines from the Dutch Society for Obstetrics and Gynecology and the Dutch Pediatric Association, as this might be a specific subgroup. In the Dutch population in 2012, NICU treatment was needed in 29% of the children born after 32-33 weeks and only in 7% of infants born after 34-36 weeks (Stichting Perinatale Registratie Nederland, 2013).

Informed consent was given by the parents. The children received a gift after the visit and parents received travel expenses.

Measures

Developmental level

At 24 months of age, corrected for prematurity, a trained examiner performed the Dutch version of the Bayley-III, the Bayley-III-NL (Steenis, Verhoeven, & Van Baar, 2012) to assess the developmental level of the children.

The Bayley-III-NL consists of five subtests: Cognition, Fine Motor, Gross Motor, Receptive Communication and Expressive Communication. Scaled scores based on Dutch norms were used, which vary between 1 and 19 with a mean of 10 and a SD of 3. Scores of 7-13 are considered normal; a score below 7 indicates a (mild) developmental delay (Van Baar, Steenis, Verhoeven, & Hessen, 2014), and is therefore seen as a clinically relevant score in this study. The reliability and validity of the Bayley-III-NL is good (Van Baar et al., 2014).

Behavior

Prior to the visit to the test location, mothers completed the Dutch version of the CBCL 1½-5 (Achenbach & Rescorla, 2000) to assess the child's behavior problems. The CBCL 1½-5 consists of 100 items with descriptions of behavior problems for which the mother indicates to what extent this fits the child now or in the past 2 months (*not/never*, *somewhat/sometimes* and *very/often*). The T-scores of the total problem scale, as well as the T-scores on the two broadband scales (i.e., internalizing and externalizing behavior) and the seven subscales (i.e., emotional reactivity, anxious/depressed behavior, somatic complaints, withdrawn behavior, sleep problems, attention problems and aggressive behavior) were used. For total problems and the broadband scales, T-scores below 60 are considered normal, between 60 and 64 is seen as borderline clinical, and 64 or higher as clinical scores (Achenbach & Rescorla, 2000). For the subscales, scores below 65 are considered normal, between 65 and 70 borderline clinical, and 70 or higher as clinical scores (Achenbach & Rescorla, 2000). Subclinical and clinical scores are considered as clinically relevant scores in this study. The reliability and validity of the CBCL 1½-5 is good (Achenbach & Rescorla, 2000).

Neonatal and background characteristics

Neonatal characteristics regarding hypoglycemia, phototherapy, oxygen requirements, and length of hospital stay were based upon the discharge letters in the hospital files. Background characteristics, such as maternal education level, maternal age at birth, and ethnic origin of the child, were provided by the parents using a short questionnaire.

Data analysis

Group differences in scores were investigated using (Multivariate) Analyses of Covariance ((M)ANCOVAs). Group differences in percentages of clinically relevant scores were investigated with logistic regression analyses. Analyses were adjusted for background characteristics that differed between the groups. (Multivariate) Analyses of Variance and Pearson's correlations were used to explore the relationship between neonatal characteristics and outcome measures within the moderately preterm born group.

Power analysis using G*Power showed that to test a group difference with a medium effect size (Cohen's f2 = 0.15), a significance level of $\alpha = 0.05$ and a power of 0.80, using a MANCOVA with seven dependent variables, a sample of in total 104 was needed, with 52 children in each group (Faul, Erdfelder, Lang, & Buchner, 2007). Partial η^2 was used as effect size estimate, with 0.01 indicating a small effect size, 0.06 a medium effect size, and 0.13 and above a large effect size (Cohen, 1988).

Results

Of the 333 parents of moderately preterm children that were eligible for this study in the participating hospitals, 123 consented (37%). The participating moderately preterm children did not differ from non-participants in GA, birth weight, number of days in hospital, additional oxygen requirement, phototherapy requirement, gender and percentage of first-born children. A slightly higher incidence of hypoglycemia was observed in non-participants (11.2% vs 4.9%, $\chi^2 = 3.76$, $p = 0.05$). For the 457 eligible term born children, parents of 103 children (23%) consented to participate. The participating term born children did not differ from non-participants in gender, GA, birth weight, number of days in hospital, additional oxygen requirement, phototherapy requirement, hypoglycemia, and percentage of first-borns. The distribution of GA in weeks of both the preterm and term born sample did not differ significantly from that in the general Dutch population (Stichting Perinatale Registratie Nederland, 2013).

Complete data was available for 116 (94%) moderately preterm children and for 99 (96%) term born children. Sample characteristics are shown in Table 3.1. The groups differed in maternal education level and maternal age at birth, with more low and medium educated mothers and younger mothers in the moderately preterm group. Therefore, we controlled for maternal education level and maternal age at birth in all analyses concerning group differences.

Developmental outcomes

The average scaled scores and the percentage of children with a (mild) developmental delay, which reflects a score below 7 on the subtests of the Bayley-III-NL, are presented per group in Tables 3.2 and 3.3, respectively. For the moderately preterm group, the results are presented separately for corrected and uncorrected age (for prematurity).

Group differences using age corrected for prematurity

A MANCOVA of the five subtests of the Bayley-III-NL showed no overall difference between moderately preterm and term born children on the scaled scores after correcting age for prematurity and adjusting for maternal education level and maternal age at birth. However, moderately preterm children scored significantly lower than full term peers regarding Receptive Communication with a small effect size. No group differences were found in the percentages of children with a mild developmental delay, see Table 3.3.

Group differences using uncorrected, chronological age

When age was not corrected for prematurity, the MANCOVA showed a significant difference between moderately preterm and term born children. Moderately preterm children scored

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Table 3.1 Neonatal and demographic characteristics of the participants

	Term born GA 37-41 weeks (n = 99)	Moderately preterm GA 32-36 weeks (n = 116)	
Neonatal characteristics			
GA in weeks			
Mean (SD)	39.45 (0.98)	34.66 (1.35)	
32 weeks (%)		10.3%	
33 weeks (%)		11.2%	
34 weeks (%)		17.2%	
35 weeks (%)		24.1%	
36 weeks (%)		37.1%	
37 weeks (%)	4.0%		
38 weeks (%)	11.1%		
39 weeks (%)	32.3%		
40 weeks (%)	40.4%		
41 weeks (%)	12.1%		
Birth weight in grams			
Mean (SD)	3575 (460)	2575 (508)	
Range	2795-5330	1420-3850	
Days in hospital			
Mean (SD)	0.42 (1.01)	12.00 (9.84)	
Range	0-6	1-42	
Need for oxygen[a] (%)	0%	22.4%	
Phototherapy (%)	0%	35.3%	
Hypoglycemia (%)	0%	5.2%	
Demographic characteristics			**p Value[b]**
Age in months[c]			
Mean (SD)	23.71 (0.52)	23.60 (0.63)	0.20
Range	23-25	23-27	
Gender (% boys)	45.5%	57.8%	0.07
First born (%)	51.5%	62.9%	0.09
Ethnic origin (% Dutch)	95.9%	96.5%	0.42
Maternal age at birth (years)			
Mean (SD)	32.52 (4.20)	31.04 (4.43)	0.01
Range	20-43	21-41	
Maternal educational level			
Low[d]	3.0%	7.8%	
Medium[e]	12.1%	35.3%	<0.001
High[f]	84.8%	56.9%	

Note. [a]That is, additional oxygen right after birth, nasal cannula and/or continuous positive airway pressure (CPAP; n = 17); [b]ANCOVAs used for child age and maternal age. χ^2 tests used for gender, first born, ethnic origin, and maternal educational level; [c]Age at Bayley-III assessment; [d]no education, elementary school, special education or lower general secondary education; [e]high school or vocational education; [f]College, university or higher
ANCOVAs = analyses of covariance; GA = gestational age.

Table 3.2 Developmental outcomes of the children on the Bayley-III-NL

	FT N = 98	MPT - Corrected age N = 116			MPT - Uncorrected age N = 116		
	Mean (SD)	Mean (SD)	p Value[a]	Effect size[b]	Mean (SD)	p Value[a]	Effect size[b]
Cognition	10.68 (2.35)	10.01 (2.27)	0.26	0.01	8.97 (2.11)	<0.001	0.09
Fine motor	11.96 (2.15)	11.34 (2.06)	0.09	0.01	10.33 (2.15)	<0.001	0.11
Gross motor	9.39 (2.80)	9.26 (2.78)	0.88	0.00	8.47 (2.55)	0.05	0.02
Receptive communication	12.02 (2.74)	11.05 (2.58)	0.02	0.03	10.09 (2.48)	<0.001	0.11
Expressive communication	11.49 (2.51)	11.15 (2.54)	0.59	0.001	10.33 (2.43)	0.005	0.04

Note. MANCOVA results for corrected age: Wilks' $\Lambda = 0.96$, $F_{5,206} = 1.80$, $p = 0.11$, partial $\eta^2 = 0.04$;
MANCOVA results for uncorrected age: Wilks' $\Lambda = 0.83$, $F_{5,206} = 8.26$, $p < 0.001$, partial $\eta^2 = 0.17$.
[a]Compared to full term group; [b]Partial η^2; analyses are adjusted for maternal education level and maternal age at birth.
FT = full term, GA 37-41 weeks; GA = gestational age; MANCOVA = multivariate analyses of covariance; MPT = moderately preterm, GA 32-36 weeks.

Table 3.3 Percentage of children with a (mild) developmental delay (i.e., scaled score <7) on the Bayley-III-NL

	FT	MPT - Corrected age				MPT - Uncorrected age			
			OR	(95% CI)	p Value[a]		OR	(95% CI)	P Value[a]
Cognition	3.1%	4.3%	0.89	(0.19 to 4.15)	0.89	8.6%	2.19	(0.56 to 8.63)	0.26
Fine motor	2.0%	0.9%	0.48	(0.04 to 6.36)	0.57	5.2%	2.13	(0.40 to 11.44)	0.38
Gross motor	11.2%	15.5%	1.61	(0.69 to 3.73)	0.27	20.7%	2.30	(1.03 to 5.13)	0.04
Receptive communication	2.0%	4.3%	2.07	(0.37 to 11.56)	0.41	6.9%	3.52	(0.69 to 17.82)	0.13
Expressive communication	6.1%	4.3%	0.48	(0.13 to 1.75)	0.26	7.8%	1.03	(0.33 to 3.17)	0.96

Note. [a]Compared to full term group; analyses are adjusted for maternal education level and maternal age at birth.
FT = full term, GA 37-41 weeks; GA = gestational age; MPT = moderately preterm, GA 32-36 weeks.

significantly below term born children on all subtests, that is, Cognition, Fine Motor skills, Gross Motor skills, Receptive Communication and Expressive Communication with small to medium effect sizes. A higher percentage of moderately preterm children showed a (mild) developmental delay regarding gross motor skills (see Table 3.3). No group differences were found for the other subtests.

Behavioral outcomes

The CBCL T-scores are presented in Table 3.4. Moderately preterm children did not differ from term born children in total problem scores. A MANCOVA with the T-scores of the internalizing and externalizing scale also showed no significant group difference. However, moderately preterm children did have significantly higher internalizing behavior scores. No

Table 3.4 Behavioral outcomes of the children

	T score Mean (SD)				% (sub)clinical				
	FT N = 94	MPT N = 111	p Value	Effect size[a]	FT (%)	MPT (%)	OR	(95% CI)	p Value
Total problems	43.34 (8.56)	46.06 (7.87)	0.08	0.02	3.2	5.4	1.37	(0.31 to 6.02)	0.68
Internalizing problems	41.54 (8.56)	44.76 (8.94)	0.03	0.03	1.1	5.4	3.70	(0.41 to 33.09)	0.24
Externalizing problems	46.80 (8.68)	48.80 (8.11)	0.24	0.01	4.3	9.0	1.88	(0.54 to 6.54)	0.32
Subscales									
Emotionally reactive	51.43 (2.98)	52.60 (4.59)	0.12	0.01	1.1	4.5	3.70	(0.40 to 34.22)	0.25
Anxious/ depressed	50.46 (1.55)	50.74 (1.88)	0.53	0.002	0	0	-	-	-
Somatic complaints	52.15 (4.23)	53.68 (5.49)	0.18	0.01	3.2	10.8	2.26	(0.58 to 8.83)	0.24
Withdrawn	51.87 (3.34)	52.23 (3.51)	0.70	0.001	1.1	0.9	0.76	(0.04 to 15.14)	0.86
Sleep problems	51.99 (4.09)	52.13 (3.89)	0.89	0.00	2.1	1.8	0.53	(0.06 to 4.43)	0.55
Attention problems	52.68 (4.58)	53.46 (5.26)	0.88	0.00	4.3	6.3	1.06	(0.28 to 4.04)	0.93
Aggressive behavior	52.28 (3.58)	52.86 (4.60)	0.35	0.004	0	3.6	-	-	-

Note. [a]partial η^2; analyses are adjusted for maternal education level and maternal age at birth; ANCOVA results of the total problems score: $F_{1,201} = 3.15$, $p = 0.08$, partial $\eta^2 = 0.02$; MANCOVA results of the internalizing and externalizing scale: Wilks' $\Lambda = 0.98$, $F_{2,200} = 2.54$, $p = 0.08$, partial $\eta^2 = 0.03$; MANCOVA results of the subscales: Wilks' $\Lambda = 0.98$, $F_{7,195} = 0.59$, $p = 0.76$, partial $\eta^2 = 0.02$.
ANCOVA = analysis of covariance; FT = full term, GA 37-41 weeks; GA = gestational age; MANCOVA = multivariate analysis of covariance; MPT = moderately preterm, GA 32-36 weeks.

differences were found in externalizing behavior problems. A MANCOVA with the T-scores of the seven subscales of the CBCL showed no group differences. No group differences were found in the percentages of children with (sub)clinical scores, see Table 3.4.

Neonatal characteristics in relation to outcome measures within the moderately preterm group

The analyses described above were repeated comparing only late preterm born children (i.e., GA 34-36 weeks, n = 91) with the term born group. All results remained the same (data not presented).

Within the moderately preterm group, GA (as continuous variable), birth weight and days in hospital were not related to developmental outcomes (using chronological age and corrected age) or behavioral outcomes; Pearson's correlations between these neonatal characteristics and the Bayley-III or CBCL scores were not significant and varied between 0.001 and 0.17, except for the correlation between birth weight and the sleep problems subscale of the CBCL that was significant with a small effect size ($r = 0.19$, $p = 0.05$). No differences on behavioral and developmental outcomes were found between children who required additional oxygen and those who did not. Also, no differences were found between the 41 children who received phototherapy and those who did not, and between the 6 children who had hypoglycemia and those who had normoglycemia.

Discussion

This study on outcome of moderately preterm children at 2 years of age showed that using uncorrected, chronological age, resulted in lower scores for cognitive, motor and communication skills, compared with scores of term born children. Even for the (large) subgroup of only late preterm children these results were found. This is in line with previous studies that used uncorrected age (Morag et al., 2013; Romeo et al., 2010; Woythaler et al., 2011). When we did correct age for prematurity, the group differences generally were not statistically significant, although, overall, preterm children had lower scores than their term born peers. Moderately preterm children did not differ from term born peers in cognitive and motor skills when age-corrected scores were analyzed, which is in accordance with some previous studies at infant and toddler age (Blaggan et al., 2014; Cheatham et al., 2006; Darlow et al., 2009; Hillemeier et al., 2009; Morag et al., 2013; Romeo et al., 2010). However, even after correcting age for prematurity, a significant difference was found, showing that moderately preterm children scored somewhat below term born peers on receptive communication skills. It is difficult to compare these results with previous studies, as in most previous studies regarding prematurely born toddlers (Cheatham et al., 2006; Darlow et al., 2009; Hillemeier et al., 2009; Nepomnyaschy et al., 2012; Romeo et al., 2010; Voigt et al., 2012; Woythaler et al., 2011), language skills were not assessed by a separate subtest, except for the study by Morag et al. (2013), that found no difference between moderately preterm and term born children after correcting age for prematurity.

Little consensus exists whether correcting age for prematurity is needed in moderately preterm children and if so, until what age. This study showed that correcting age for prematurity influences the findings, even in the subgroup of late preterm children. It is, however, as yet unknown which score (i.e., corrected or uncorrected for prematurity) is most predictive for later functioning. A few studies examined the predictive value of both corrected and uncorrected scores in very preterm children with inconsistent results (Rickards, Kitchen, Doyle, & Kelly, 1989; Siegel, 1983; Sugita, Iai, Inoue, & Ohta, 1990). In two studies (Siegel, 1983; Sugita et al., 1990), no difference in predictive validity of corrected and uncorrected scores was found. In contrast, Rickards et al. (1989) reported that the corrected scores were most predictive of later outcomes. Further research is needed to investigate the predictive value of corrected and uncorrected scores in moderately preterm children.

The percentage of children showing a developmental delay was not higher in the moderately preterm group for most of the subtests, except for gross motor skills when age was uncorrected for prematurity. For both groups, the percentage of children showing a developmental delay was lower than expected for all subtests, except for gross motor skills. In addition, the mean scores of all subtests, except gross motor skills, were higher than the normative means. This might be explained by the fact that a sample of relatively highly educated mothers participated in this study and term born healthy children of higher educated mothers have been found to show higher Bayley-III scores (Van Baar et al., 2014).

Moderately preterm 24-month-olds were found to show somewhat more internalizing behavior problems than full term peers. No differences between levels of externalizing behaviors were found. Despite these higher mean levels of problem behavior, moderately preterm children did not show a higher risk of (sub)clinical scores than term born children. Our findings are partly in accordance with the study of Potijk et al. (2012), who found significantly higher problem scores for 4-year-old moderately preterm children on all scales of the CBCL. It might be that the behavior problems of moderately preterm children increase with age, as several studies showed at preschool (Gray et al., 2004; Potijk et al., 2012) and school age (Gray et al., 2004; Talge et al., 2010; Van Baar et al., 2009) that moderately preterm children had a higher risk of subclinical scores for total behavior problems (Gray et al., 2004; Potijk et al., 2012), internalizing behavior (Talge et al., 2010; Van Baar et al., 2009), externalizing behavior (Potijk et al., 2012), attention problems (Talge et al., 2010) and somatic complaints (Potijk et al., 2012).

A careful interpretation of our findings is important, as the mean scores of both groups of children, for both developmental outcome and behavior problems, were within the normal range. A statistically significant difference of one point on the scaled score of the Bayley-III-NL, which was found for receptive communication skills after correcting age for prematurity, is not immediately clinically significant. Additionally, the effect sizes of the group differences were found to be small, except for uncorrected age scores. Group differences with medium to large effect sizes need immediate attention from professionals in order to try to reduce the developmental and behavioral problems found. Small sized group differences might, however, also be important, as these could be early indicators of later, more serious difficulties, having an effect on their functioning at school. Further study of development of these moderately preterm children from toddler age onwards is therefore needed to fully evaluate these findings.

The analyses in our study were adjusted for maternal education level. In our sample, more mothers of moderately preterm children had a low or medium education level than mothers of term born children. This is in accordance with population based studies showing that lower maternal education level is a risk factor for premature birth (Morgen, Bjork, Andersen, Mortensen, & Nybo Andersen, 2008; Petersen et al., 2009). Correcting for maternal education level might therefore also lead to overcorrection. However, the number of low educated mother was small in both our moderately preterm and term born sample, which is a limitation of this study.

The relationship between neonatal characteristics and long-term developmental outcome measures was explored to investigate if indications for specific subgroups could be found. Comparison of late preterm born children (i.e., GA 34-36 weeks) with the term born group showed the same results as for the total group of moderately preterm children: even late preterm children differed from term born children on several aspects of development and behavior. With respect to other neonatal characteristics, no relationships were found between GA, birth weight, days in hospital, need for additional oxygen, and developmental and behavioral outcomes. As only a small percentage of the children had problems like hypoglycemia (5.2%) clearly indicated in their hospital discharge letters, our study had only limited power to find any differences between the subgroups of children with and without problems such as hypoglycemia. Therefore, when the focus needs to be on such neonatal problems in moderately preterm children, future studies should be specifically designed to examine these problems.

A final remark is that in this study, only moderately preterm children who were relatively healthy and did not need tertiary NICU admittance, were selected. However, in the Netherlands 10.2% of all moderately preterm children are admitted to the NICU (Stichting Perinatale Registratie Nederland, 2013). This specific subgroup might be at an even higher risk of developmental and behavioral problems, and therefore these children should also be studied in the future.

In conclusion, at 2 years of age, uncorrected for prematurity, moderately preterm children differed from their term born peers in cognitive, motor and communication skills. With age corrected for prematurity, they differed from their term born peers only on receptive communication skills. Already at 2 years of age, moderately preterm children show more internalizing behavior problems than term born peers. Although only subtle differences were found in this study, these findings may still be an indication for later difficulties of moderately preterm children in academic functioning and socioemotional development.

Chapter 4

Introduction of the Utrecht Tasks for Attention in Toddlers using Eye Tracking (UTATE): A Pilot Study

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Abstract

Attention capacities underlie everyday functioning from an early age onwards. Little is known about attentional processes at toddler age. A feasible assessment of attention capacities at toddler age is needed to allow further study of attention development. A new instrument has been developed, consisting of four tasks intended to measure the attention systems of orienting, alerting, and executive attention using eye-tracking technology: the Utrecht Tasks of Attention in Toddlers using Eye Tracking (UTATE). A pilot study in which the UTATE was tested in 16 Dutch 18-month-old toddlers, showed that the instrument was feasible and generated good quality data. A first indication of sufficient reliability was found for most of the variables. It was concluded that the UTATE could be used in further studies, that would also need to evaluate the reliability and validity of the instrument in larger samples.

Acknowledgement of author contributions

Marjanneke de Jong designed the study, performed the data collection, carried out the analyses, drafted the initial manuscript, revised the manuscript and approved the final manuscript as submitted.

Marjolein Verhoeven designed the study, reviewed and revised the manuscript and approved the final manuscript as submitted.

Ignace T.C. Hooge prepared the eye-tracking data for analyses, assisted in data analyses, reviewed and revised the manuscript and approved the final manuscript as submitted.

Anneloes L. van Baar conceptualized and designed the study, reviewed and revised the manuscript and approved the final manuscript as submitted.

Introduction

Everyone needs certain attention skills on an everyday basis; to learn about the social and physical context, to accomplish complicated tasks, and to solve problems and adapt to the environment. Attention-related problems hinder daily functioning and could therefore have important negative consequences, such as poor school performance (e.g., Duncan et al., 2007) and social incompetence (e.g., Bennett Murphy, Laurie-Rose, Brinkman, & McNamara, 2007). Early detection of attention problems in infancy or at toddler age could result in support and stimulation in order to improve attention capacities (Atkinson & Braddick, 2012). However, standardized and objective measurement tools of attention capacities in early childhood are scarce. In this pilot study, we present a detailed description of a newly developed instrument to assess attention capacities in toddlers using eye-tracking technology: the Utrecht Tasks for Attention in Toddlers using Eye Tracking (UTATE).

An important indicator of attention capacities in young children is looking behavior (Colombo, 2002). The challenge, however, is to reliably and accurately assess these looking behaviors and the underlying attention capacities. Previous research often used human observers to assess looking behavior (e.g., Rose, Feldman, & Jankowski, 2001; Rose, Feldman, & Jankowski, 2009). This method is very time consuming and might result in observer bias (Oakes, 2012). In contrast, eye tracking techniques provide an opportunity to get detailed and accurate information on looking behavior in young children (Gredebäck, Johnson, & Von Hofsten, 2009). In addition, the detection rate of eye-movements is quicker, and the relationship between the stimuli presented and the response given, can be checked more precisely. The use of eye-tracking techniques might result in better replication of measurements and studies.

With the introduction of the automated corneal-reflection eye-tracker technology, it became possible to use eye-tracking measurements in young children (Aslin & McMurray, 2004). As the quality of the data is dependent on the calibration of the eye-tracking device, specific challenges arise when eye tracking is used with young children. In addition, data may easily become missing due to movements of the child (Oakes, 2012). Nevertheless, this method has been successfully used to assess attention capacities in infants under 12 months of age (e.g., Butcher, Kalverboer, & Geuze, 2000). Eye-tracking technology has also been used with toddlers to investigate anticipatory looking and goal-directed gaze shifts (e.g., Gredebäck, Stasiewicz, Falck-Ytter, Rosander, & Von Hofsten, 2009; Paulus, Hunnius, & Bekkering, 2011). However, information is still scarce concerning the potential of eye-tracking technology to assess attention capacities in toddlers in particular.

Theoretically, attention can be divided into three attention systems: orienting, alerting, and executive attention (Posner & Petersen, 1990). Although assumed to be interconnected, these systems are also understood to have unique functions. The *orienting system* is responsible for the capacity to orient to a target (Posner & Petersen, 1990). It involves the ability to engage, disengage, and to shift attention focus. Transposed to looking behavior, functioning of the orienting system is often assessed by determining how long a child visually orients at a particular stimulus before looking at something else. Another indicator of orienting is whether the child is capable of shifting its gaze between stimuli (Van De Weijer-Bergsma, Wijnroks, & Jongmans, 2008).

The second attention system, the *alerting* or *vigilant system*, concerns the ability to achieve and to maintain a state of alertness (Posner & Petersen, 1990). In toddlers, functioning of the alerting system has been assessed by measuring the ability to sustain attention, as represented through continued looking at the stimuli (Van De Weijer-Bergsma et al., 2008). The ability to achieve a state of alertness can be measured by comparing the reaction times to a stimulus in trials in which someone is made alert, for example by a signaling sound, and trials in which no signaling sound is used.

Executive attention is the third attention system that can be distinguished theoretically. It is defined as goal-directed, planned attention, and the ability to inhibit behavior (Posner & Petersen, 1990). In contrast to the first two systems, this system is based on internal or voluntary control of attention, instead of exogenous control, which is the case in both the orienting and alerting system (Sheese, Rothbart, Posner, White, & Fraundorf, 2008). For toddlers, no tasks were available to measure executive attention (Van De Weijer-Bergsma et al., 2008). As the dorsolateral prefrontal cortex is involved in executive functions, tasks that measure functioning of this brain area, such as the delayed response task, were used as indirect measures of functioning of the executive attention system in infants (Van De Weijer-Bergsma et al., 2008).

No studies or assessment instruments were available that examined functioning of the three attention systems simultaneously in children under three years of age. Therefore, a test battery that collects objective and standardized data is needed. In the current study, a new test battery of four eye-tracking tasks was developed to assess attention capacities in toddlers: the Utrecht Tasks for Attention in Toddlers using Eye Tracking (UTATE). Four existing tasks focusing on attention capacities by observing children's looking behavior, were adapted for use with eye-tracking technology. In addition, the tasks were adapted for use with 18-month-old toddlers. The aim of this pilot study was to describe the four tasks and the potential outcome measures in detail. It is evaluated whether the UTATE indeed is feasible for use with 18-month-old toddlers. In addition, the quality of the data is studied by evaluating the amount of variable position error (i.e., noise) during fixations in relation to the size of the stimuli, which might be a problem when using eye tracking (Holmqvist et al., 2011). Finally, it is evaluated whether the eye-tracker measures indeed show individual variation in the children's looking behaviors during the tasks. Only if these goals would be attained, further studies with the UTATE to first assess its validity and reliability and later to perform actual studies that focus on attention capacities of toddlers, were considered to be worthwhile.

Method

Participants

The sample consisted of 16 Dutch 17- and 18-month-old children, M = 17.62 months, SD = .50, 50% boys. The children were born full term (i.e., gestational age 37-42 weeks) with a birth weight >2500g. Parents and children were recruited via the hospitals where the children were born.

The medical ethical committee of the Utrecht Medical Center approved this study as part of a larger study on visual attention capacities of young children. Informed consent was given by the parents. The children received a small gift after the visit and travel expenses of the parents were refunded.

Apparatus

The Tobii T60 Eye Tracker with an integrated 17-inch TFT screen was used, with a resolution of 1280 by 1024 pixels (Tobii Technology, Stockholm, Sweden). E-prime 2.0 software (Psychology Software Tools, Pittsburgh, PA) was used to present the stimuli on the screen.

Procedure

The procedure took place in a small, almost dark, and sound-proofed room. See Figure 4.1 for a visualization of the setup. To make the room less dark (and so less frightening to the children) without distorting the eye-tracking measures, a light bulb was oriented towards the ceiling. The children were placed into a car seat in order to keep them in a sitting position and somewhat constrain them in their movements. The car seat was positioned at a distance of approximately 65 cm from the eye tracker monitor. One of the parents was sitting next to the child and a little to the back, for safety reasons (i.e., to prevent the child climbing out of the chair) and to make the child feel more at ease in the experimental setting. If the child refused to sit in the car seat before or during the experiment, the child was placed on the parent's lap. The test computer, from which the experiments were started, was placed on a desk behind a curtain to prevent the child from seeing the examiner. If more than one parent was present, the second parent was seated next to the experimenter, behind the curtain. The face of the children was recorded with a video camera behind the eye tracker to be able to check the behavior of the child during the procedure.

A nine-point calibration was used, in which a movie clip of a bouncing ball accompanied by sound was presented at nine different points on the screen (i.e., left, middle, and right at

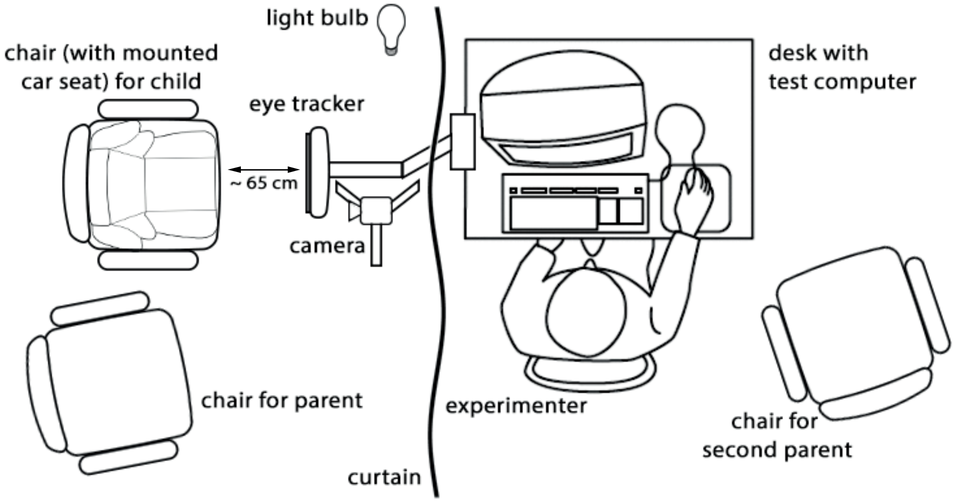

Figure 4.1. Visualization of the lab situation

the top, center, and bottom of the screen; Hunnius & Bekkering, 2010). Calibration was accepted when the child looked at seven or more of the calibration points. Otherwise several points were recalibrated. After calibration, four tasks were presented in the following fixed order: 1) disengagement task, 2) face task, 3) alerting task, and 4) delayed response task. The whole procedure took about 18 minutes to complete.

At the beginning of the procedure, before starting the calibration, the parent was told that the procedure included four different tasks in which several pictures were shown, sometimes accompanied by sound. The parent was told to be quiet, unless the child asked for a verbal response. Next to that, the parent was instructed not to direct the attention of the child to the screen when the child looked away. The child was not verbally instructed beforehand.

Eye-tracker tasks

A visualization of the four tasks is shown in Figure 4.2.

Disengagement task

This task is an adaptation of the disengagement task described by Butcher et al. (2000). Stimuli were colorful pictures with a size of 6° by 6°. First, one stimulus was presented at the center of the screen accompanied by a signaling sound to attract the child's attention (i.e., first phase). After 2000ms a second stimulus appeared on the screen either on the left or right side from the central stimulus with a distance of 3.8° between the stimuli (i.e., second phase). After 5000ms both stimuli disappeared and after an inter-trial interval [ITI]

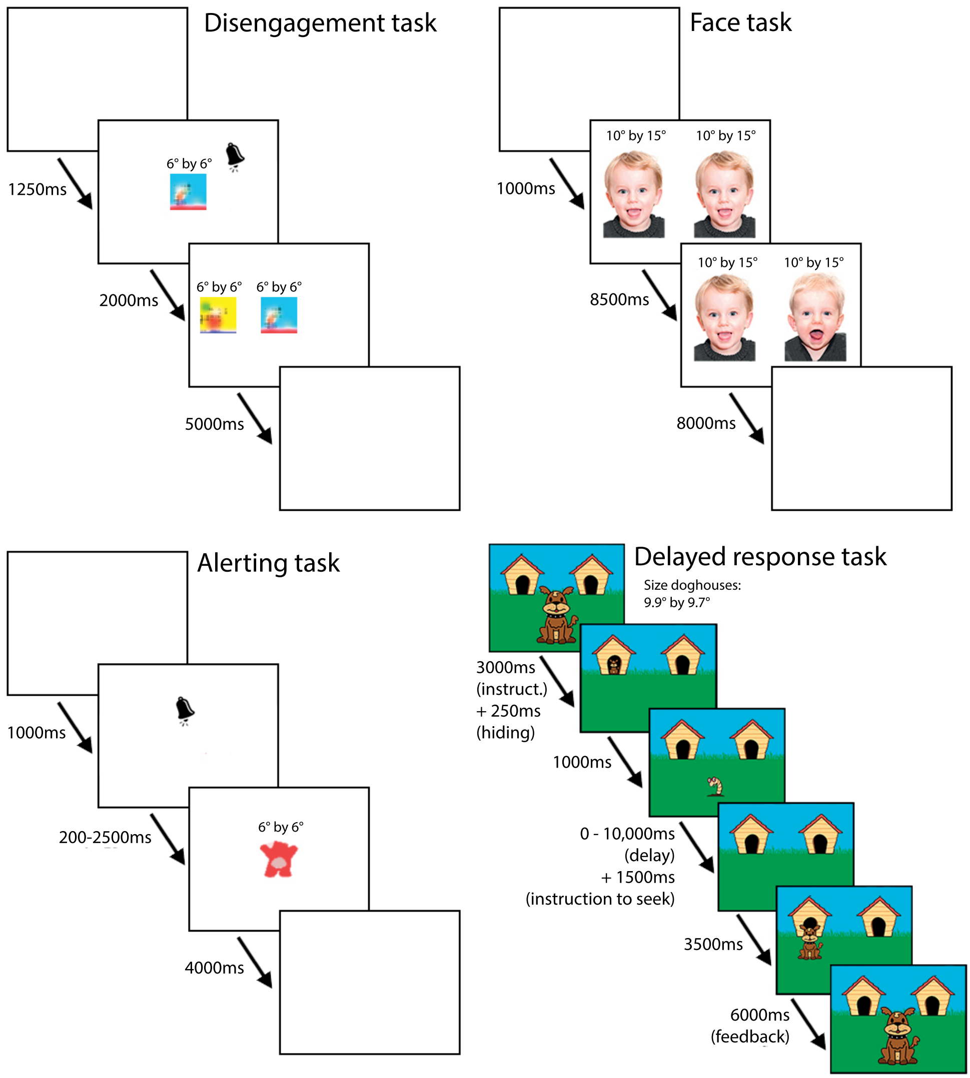

Figure 4.2. Visualization of timing and size of the stimuli in the different tasks

of 1250ms the next trial started. The task consisted of 20 trials in which the position of the peripheral stimuli was assigned randomly (half of the time at the left and half of the time at the right side from the central stimulus).

Five outcome measures from the disengagement task were intended to measure functioning of both the orienting and alerting system. Functioning of the orienting system was intended to be measured by: 1) *mean dwell time*, 2) *transition rate*, 3) *proportion of correct refixations*, and 4) *latency*. The *mean dwell time* is the average duration of the dwells per child averaged across participants. Duration of a dwell (i.e., *dwell time)* is the sum of all fixation durations during one visit in an area of interest [AOI], as defined by the researcher, from entry to exit (Holmqvist et al., 2011). *Mean dwell time* includes dwells during the first and the second phase of the trial at both the central and the peripheral stimuli. *Transition rate* is the number of transitions during the second phase of the trial divided by the *total dwell time* in the second phase of the trial. A *transition* is "the movement from one AOI to another" (Holmqvist et al., 2011). Because the number of transitions is influenced by the total amount of time the children actually looked at the stimuli (i.e., *total dwell time*), which is a measure of functioning of the alerting system, we controlled for the amount of time the child looked at the stimuli and used the *transition rate* as measure. A *correct refixation* means that the participant refixated from the central stimulus to the peripheral stimulus after the peripheral stimulus is presented, which reflects the ability to disengage and correctly orient to a target. *Latency* is the average time between appearance of the peripheral stimulus and fixation on the peripheral stimulus in trials in which the participant correctly refixated. Shorter *latencies* represent faster transitions. If a child did not look at the central stimulus when the peripheral stimulus appeared, this trial was not taken into account for determining the proportion of correct refixations and the average latency. More *correct refixations*, shorter *latencies*, shorter *mean dwell times,* and higher *transition rates* are thought to be indicative of better functioning of the orienting system (Colombo, 2002; Rose, Feldman, & Jankowski, 2002).

An additional outcome measure was expected to measure functioning of the alerting system by assessing the amount of sustained attention, which represents maintenance of a state of alertness: *total dwell time*. The *total dwell time* is the sum of the duration of all dwells per child averaged across participants. *Total dwell time* includes dwells during the first and the second phase of the trial on both the central and the peripheral stimuli. Longer *total dwell times* might reflect better sustained attention, hence a better functioning alerting system.

Face task

The face task is based on the 'Rose task' described by Rose et al. (2001; 2009). Stimuli were pictures of children's faces (16 different faces presented in 8 fixed sets) with a size of 10° by 15°. First, two identical stimuli (i.e., faces) were presented concurrently for 8500ms with a distance of 5.5° between the stimuli (i.e., familiarization phase). Next, one of the stimuli changed into a new stimulus (i.e., test phase). Both stimuli stayed on the screen for another 8000ms. ITI was 1000ms. The task consisted of 8 trials and the position of the new stimulus was randomly assigned (half of the time at the left and half of the time at the right side of the screen).

In the face task, three outcome measures were presumed to measure functioning of both the orienting and alerting system. Functioning of the orienting system was intended to be measured by: 1) *mean dwell time*, and 2) *transition rate*. Shorter *mean dwell times* and higher *transition rates* might be indicative of better functioning of the orienting system (Colombo, 2002; Rose et al., 2002). *Mean dwell time* includes dwells at both stimuli during both the familiarization and the test phase. *Transition rate* is based on the transitions and the total dwell time during both the familiarization and the test phase.

One variable was intended to indicate the amount of sustained attention: *total dwell time*. *Total dwell time* includes dwells at both stimuli during both the familiarization and the test phase. Longer *total dwell time* might reflect better sustained attention.

Alerting task

The alerting task is an adaptation of the alerting task described by Berger, Jones, Rothbart, and Posner (2000). The response type of this task was changed from touching behavior into looking behavior for use with the eye tracker. The stimulus was a picture of a bear appearing in one of eight different colors with a size of 6° by 6°. The stimulus was presented at the center of the screen for 4000ms, and the ITI was 1000ms. The experiment consisted of eight different trial types, which each appeared four times, leading to a total of 32 trials. Two variables varied between trial types: 1) a warning signal (i.e., a ringing sound) preceding the appearance of the stimulus or not (signal and no-signal trials); 2) the interval between the warning signal (or start of trial in no-signal trials) and appearance of the stimulus (200ms, 500ms, 1000ms or 2500ms). During the warning signal (or silence in the no-signal trials; duration in both cases 1000ms) and the interval (200-2500ms), the screen was white. First, to familiarize the child with the task, four practice trials were administered in which a signal preceded the appearance of the stimulus, and the stimulus followed after 200ms. Next, 32 trials were administered in semi-random order: four series of the eight different trial types were presented in which the order of trial types within the series was randomly assigned. The eight colors of the bears were randomly assigned, but the same color could not appear in two consecutive trials.

In the alerting task, the *difference between latencies* in the no-signal and signal trials was intended to measure of functioning of the alerting system. *Latency* is the average time between appearance of the stimulus and fixation on this stimulus. Larger *differences between latencies* in the no-signal and signal trials, with longer latencies in no-signal trials than in signal trials, are presumed to be indicative of better functioning of the alerting system. Another measure intended to measure functioning of the alerting system is *total dwell time*. *Total dwell time* includes dwells at the stimulus during the presentation of the stimulus. Longer *total dwell times* might reflect better sustained attention.

Delayed response task

The delayed response task is an adapted version of the task described by Diamond and Doar (1989). First, a dog and two doghouses were presented respectively at the center, the left top side, and right top side of the screen. The dog houses had a size of 9.9° by 9.7° and the distance between the dog houses was 5.5°. Before the first trial, an introduction was given during which a voice-over told the child that the dog wants to play hide-and-seek: "*Zie je dit hondje? Hij wil verstoppertje met je spelen. Doe je met hem mee?*" (i.e., "*Do you see this dog? He wants to play hide-and-seek with you. Will you play along?*"; duration 6000ms). At the start of each trial, the voice-over says that the dog is going to hide now: "*Het hondje gaat zich nu verstoppen. Goed opletten!*" (i.e., "*The dog is going to hide now. Pay attention!*"; duration 3000ms). The dog then moves to one of the two dog houses (250ms) and disappears after 1000ms. During the delay, when the dog is no longer visible on the screen as it is hidden in one of the dog houses (varying from 0s to 10s), a worm pops up in the center of the screen to distract the child from watching the dog houses. In the 0s delay the worm appearing in the screen is directly accompanied by the voice-over saying "*Waar is het hondje?*" (i.e., "*Where is the dog?*"; duration 1500ms). With longer delays the worm moves up and down together with a sound, before the voice-over instructs the child to find the dog. After 3500ms the dog re-appears in the correct dog house and the voice-over tells the child "*Daar is het hondje weer. Hij vindt het een leuk spelletje. Hij wil nog een keertje spelen*" (i.e., "*Here is the dog again. He likes the game. He wants to play again.*"; duration 6000ms) and then the next trial starts. After the last trial the voice-over tells the child "*Daar is het hondje weer. Hij is nu een beetje moe. Bedankt voor het spelen.*" (i.e., "*Here is the dog again. He is a bit tired now. Thanks for playing.*"). This task consisted of 18 trials. Position of hiding was randomly assigned (half of the time in the left and half of the time in the right dog house, and no more than three consecutive trials in the same position). After three consecutive trials the delay between hiding and the instruction to seek the dog increased from 0s to 10s with steps of 2s.

Functioning of the executive attention system was intended to be measured by: 1) the number of *correct searches* (i.e., the number of trials in which the child looked at the correct dog house directly in response to the voice-over asking where to find the dog), 2) computing the *mean delay* between hiding and the instruction to seek the dog for the trials in which the child looked at the correct dog house. To compute the mean delay, the trials with 0s delays were excluded, because these trials do not reflect a delay. More *correct searches* and a longer *mean delay* might be indicative of better functioning of the executive attention system.

Furthermore, one other variable was presumed to measure functioning of the alerting system: *total dwell time*. *Total dwell time* includes dwells at the dog houses from the time in the trial that the child is asked to search for the dog until the start of the next trial (total duration per trial 11,000ms). Longer *total dwell times* might reflect better sustained attention.

Data analysis

Matlab 7.11 (The MathWorks, Inc.) was used to analyze gaze data. Fixation detection was done by a self-written Matlab program (I.H.) that marked fixations by an adaptive velocity threshold method. We used an adaptive velocity threshold method to detect fixations because the amount of noise may vary a lot in eye-tracking data (especially with low frequency trackers such as the Tobii T60 and with non-grown-up participants). Many modern saccade and fixation detection methods are partly or fully adaptive to the noise in the data (Nyström & Holmqvist, 2010; Smeets & Hooge, 2003). Velocities were obtained by fitting a parabola through three subsequent data points. We used the derivative of this fitted parabola to estimate the value of the velocity of the second (centre) data point. This procedure was repeated for all data points (except the first and the last). In the present analysis, everything that is not a saccade is called a fixation (Holmqvist et al., 2011). To remove the saccades from the signal we calculated average and standard deviation from the absolute velocity signal. All data points with absolute velocities higher than the average velocity plus 3 times the standard deviation were removed. This procedure was repeated until the velocity threshold converged to a constant value or the number of repetitions reached 50. Then we removed fixations with durations shorter than 60 ms from the analysis. The value of 60ms was chosen because it is equal to three data samples. When a saccade was removed, the preceding and succeeding fixations were added together. Data of the children were included when they looked at the stimuli at least once during a task, as this provides sufficient information to compute the variables assessed by this task.

The quality of eye-tracking data is reflected by the amount of noise during fixations. By noise we refer to the variable position error that may depend on many factors ranging from eye physiology to calibration method (Nyström, Andersson, Holmqvist, & Van De Weijer, 2013). The root mean square (RMS) noise was used in this study. The RMS noise was determined by taking the square root of the sum of the squared angular distances (i.e., distances in degrees of visual angle between subsequent data samples) divided by the number of samples (Holmqvist et al., 2011; pp. 35).

To give a first impression of the reliability of the outcome measures, split-half reliability was investigated with the Spearman-Brown formula using Pearson correlations between the variables in the odd-numbered trials and the even-numbered trials.

Results

Cooperation of the children

All 16 participants provided data on all four tasks. Two children refused to sit in the car seat beforehand and were placed on their parents' lap, after which they participated with all tasks. Three children changed position (i.e., from car seat to parents lap) during the procedure, between the face and alerting task, n = 2, or during the alerting task, n = 1, because of crying, n =1, or refusal to sit in the car seat, n = 2, but they did participate with all tasks. They were not the only children who fussed or showed protest, but in the other cases it was to a lesser extent, so changing positions was not needed for them.

Viewing the video recordings showed that the children generally sat at ease, looked at the screen with interest most of the time, moved a bit with the sounds and sometimes looked at their parents.

Results of the tasks

In Table 4.1, means and standard deviations of the 13 variables intended to measure functioning of one of the three attention systems are presented. No outliers (i.e., >3 SD below or above mean) on these variables were found.

Table 4.1 Descriptive statistics of the outcome measures in all four tasks per attention system

	Mean	SD[a]	Range	25-75 % range	Possible range	Split-half reliability
Orienting system						
1. DIS mean dwell time (ms)	1453	276	1044 – 2245	1257 – 1594	0 – 140000	.74
2. DIS latency (ms)	505	118	356 – 827	438 – 560	0 – 5000	.33
3. DIS proportion correct	.97	.05	.83 – 1.00	.96 – 1.00	0 – 1.00	-.27
4. DIS transition rate[b]	.49	.14	.29 – .76	.37 - .57	0 – ∞	.82
5. FACE mean dwell time (ms)	1239	304	689 – 1891	1028 – 1423	0 – 132000	.73
6. FACE transition rate[b]	.65	.19	.39 – 1.13	.52 - .73	0 - ∞	.82
Alerting system						
7. DIS total dwell time (ms)	93555	23453	47652 – 122366	71841 – 115212	0 – 140000	.95
8. FACE total dwell time (ms)	72055	28299	14887 – 101147	44150 – 96427	0 – 132000	.91
9. AL total dwell time (ms)	50017	25083	7966 – 90977	29167 – 69249	0 – 128000	.91
10.AL difference in latency (ms)	136	293	-333 – 611	-132 – 400	-4000 - 4000	-.04
11. DR total dwell time(ms)	73469	34109	10916 – 140866	54050 – 95784	0 – 198000	.94
Executive attention system						
12. DR correct searches	9.19	3.51	4 – 15	7 – 12.50	0 – 18	.77
13. DR mean delay (s)	5.39	1.00	4 – 6.67	4.08 – 6.33	0 – 10	.46

Note. [a]Standard deviation between children; [b]Number of transitions per second; DIS = disengagement task, FACE = face task, AL = alerting task, DR = delayed response task

Disengagement task

In the disengagement task, the children looked at the stimuli (i.e., both central and peripheral) in 17.38, SD = 2.92, out of 20 trials (87%). The average amount of RMS noise was 0.24°, SD = 0.22, on the horizontal component of fixation and 0.32°, SD = 0.21, on the vertical component, which is respectively 25 and 19 times smaller than the size of the stimuli.

Individual variation was observed in all outcome measures, with less variation seen in the proportion of correct refixations. Most of the children (75%) had a proportion of correct refixations of 1.00, indicating that they refixated correctly in all trials.

Face task

In the face task, the children looked at the stimuli in 6.38, *SD* = 1.96, out of 8 trials (80 %). The average amount of RMS noise was 0.20°, *SD* = 0.18, on the horizontal component of fixation and 0.26°, *SD* = 0.13, on the vertical component, which is respectively 50 and 58 times smaller than the size of the stimuli. Individual variation was observed in all outcome measures.

Alerting task

In the alerting task, the children looked at the stimuli in 19.19, SD = 8.03, out of 32 trials (60%). The children looked somewhat more often in the signal trials, M = 10.13, SD = 4.44, than in the no-signal trials, M = 9.06, SD = 3.89, t(15) = 1.85, p = .08.

The mean difference in latency between no-signal and signal trials was 136ms, SD = 293, indicating marginally significant shorter latencies in signal than in no-signal trials, t(15) = -1.86, p = .08. In 68.7% of the children, the mean difference in latency had a positive value, showing that the child had shorter latencies in signal than in no-signal trials. The average amount of RMS noise was 0.34°, SD = 0.32, on the horizontal component of fixation, and 0.42°, SD = 0.37, on the vertical component, which is respectively 18 and 14 times smaller than the size of the stimuli. Individual variation was observed in all outcome measures.

Delayed response task

In the delayed response task children needed to be distracted from looking at the dog houses after disappearance of the dog, therefore it was checked whether the distraction (i.e., a worm popping up in the middle of the screen, accompanied by a tune) actually worked. Results showed that none of the children continuously looked at a dog house during the distraction period; they looked at the worm, at the dog houses (but not continuously) or away from both the dog houses and worm. It was concluded that the children indeed were distracted.

The children searched for the dog in 14.13, SD = 4.08, out of 18 trials (79%), and they searched correctly in 9.19, SD = 3.51, trials. This indicates that, on average, the children searched correctly in 65.6% of the trials in which they searched, which is more than the 50% that would be expected based on chance, $t(15) = 3.88$, $p = .001$.

The average amount of RMS noise was 0.22°, SD = 0.32, on the horizontal component of fixation and 0.23°, SD = 0.24, on the vertical component, which is respectively 45 and 42 times smaller than the size of the stimuli (i.e., the dog houses). Individual variation was observed in all outcome measures.

Split-half reliability

Split-half reliability for each outcome measure is presented in Table 4.1. A high reliability was found for *total dwell time* in all four tasks, and *transition rate* in both the disengagement and face task. A moderate to high reliability was found for *mean dwell time* in both the disengagement and face task, and *number of correct searches* in the delayed response task. For *latency* and *proportion of correct refixation*s in the disengagement task, *latency difference* in the alerting task, and *mean delay* in the delayed response task, the split-half reliability was weak.

Discussion

In this paper, the Utrecht Tasks for Attention in Toddlers using Eye Tracking (UTATE) is described in detail, and its potential to study attention capacities in 17- and 18-month-old toddlers is evaluated. Regarding the feasibility of the eye-tracking procedure for toddlers, it was found that the children cooperated quite well. Data were available from all participants on all four tasks. The quality of the data was good; the amount of RMS noise was much smaller than the size of the stimuli and was smaller than the precision reported by Tobii (2011). Individual differences were observed in most outcome measures. Consequently, it was concluded that the UTATE has the potential to elucidate important variation in looking behavior. In addition, a first indication of sufficient reliability was found for most of the variables.

Three of the four tasks (i.e., disengagement task, face task and delayed response task) were interesting enough for the children to participate in most of the trials. For the alerting task, the looking rate was somewhat lower, i.e., 60%. This task may require more effort of the children's attention capacities, because it came later in order, has many trials and therefore lasts long, and the same stimulus (the same bear appearing only in a different color) was used each time. Exactly for this reason, however, this task may provide valuable information regarding individual variation between the children in sustaining attention.

Individual variation in looking behavior was found in most outcome measures, with less variation seen in the proportion of correct refixations in the disengagement task. Most of the children (i.e., 75%) correctly refixated in all of the trials. Although this measure differentiated between the performances of infants until six months of age in a previous study (Butcher et al., 2000), this was not the case for the 17- and 18-month-old toddlers in our study. Perhaps, the capacity to refixate correctly is already fully developed at this age and therefore no longer differs as much between individual children. The children that were unable to refixate in all of the trials, however, may have difficulties in attention regulation strategies. Further research might focus on intra-individual differences within and between tasks to study individual patterns of attention capacities.

Good split-half reliability was found for nine out of 13 variables. Weak reliability was found for *latency* and *proportion of correct refixations* in the disengagement task, *latency difference* in the alerting task, and *mean delay* in the delayed response task. Low reliability of the *proportion of correct refixations* might be explained by the small variation in this variable as mentioned above. For *mean delay* in the delayed response task, low reliability might be due to differences in the delay per trial. As the delay increases with 2 seconds for every three consecutive trials, it was difficult to make an appropriate split, so other measures of reliability are needed to study reliability of this variable. Regarding *latency* in the disengagement task and *latency difference* in the alerting task further research is needed in a larger sample.

This study provided a first evaluation of the potential of the UTATE in a small number of children. We conclude that it is worthwhile to conduct further studies with the UTATE because it resulted in good quality data and it is feasible for use in studies on attention capacities in toddlers. The reliability and validity of the instrument need to be studied further in larger samples. This report also intended to describe the UTATE in great detail to allow replication and use of the UTATE by other researchers. Currently validation studies with a larger sample are being conducted to investigate whether the supposed underlying attention systems (i.e., orienting, alerting, and executive attention) are indeed measured with these tasks (De Jong, Verhoeven, Hooge, & Van Baar, 2013). In addition, it is studied how the results of the UTATE compare to other measures of attention, as well as to more general assessments of developmental level of toddlers. Finally, it will be studied whether the UTATE differentiates between children at high or low risk for developing attention and developmental difficulties. If the UTATE is able to do so, the battery could be used in studies on early attention development, on individual trajectories of attention development and in studies aimed at developing interventions to support high risk children.

Chapter 5

Factor Structure of Attention Capacities Measured With Eye-Tracking Tasks in 18-Month-Old Toddlers

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Abstract

Objective: Attention capacities are critical for adaptive functioning and development. Reliable assessment measures are needed for the study of attention capacities in early childhood. In the current study, we investigated the factor structure of the Utrecht Tasks of Attention in Toddlers using Eye Tracking (UTATE) test battery that assesses attention capacities in 18-month-old toddlers with eye-tracking techniques. **Method:** The factor structure of 13 measures of attention capacities, based on four eye-tracking tasks, was investigated in a sample of 95 healthy toddlers (18 months of age) using confirmatory factor analysis. **Results:** Results showed that a three-factor model best fitted the data. The latent constructs reflected an orienting, alerting, and executive attention system. **Conclusion:** This study showed support for a three-factor model of attention capacities in 18-month-old toddlers. Further study is needed to investigate whether the model can also be used with children at risk for attention problems.

Acknowledgement of author contributions

Marjanneke de Jong designed the study, performed the data collection, carried out the analyses, drafted the initial manuscript, revised the manuscript and approved the final manuscript as submitted.

Marjolein Verhoeven designed the study, reviewed and revised the manuscript and approved the final manuscript as submitted.

Ignace T.C. Hooge prepared the eye-tracking data for analyses, assisted in data analyses, reviewed and revised the manuscript and approved the final manuscript as submitted.

Anneloes L. van Baar conceptualized and designed the study, reviewed and revised the manuscript and approved the final manuscript as submitted.

Introduction

Attention capacities are needed already by young children for adaptive functioning and further cognitive as well as socio-emotional development. Problems in attention capacities are related to poor school performance (e.g., Breslau et al., 2009) and to lack of social competence (e.g., Andrade, Brodeur, Waschbusch, Stewart, & McGee, 2009). Attention problems are often not detected until school age but might already appear at a younger age (Ruff & Rothbart, 1996). Reliable assessments of attention capacities of young children (younger than 6 years of age) are needed to study early development in attention capacities.

In previous studies, attention is mostly conceptualized as a multi-dimensional construct. Posner and Petersen (1990) described three distinctive attention systems: orienting, alerting, and executive attention. Functioning of the orienting system reflects the capacity to orient to a target, that is, the ability to engage, disengage, and shift attention focus. The alerting system represents the ability to achieve and maintain a state of alertness. The third system, the executive attention system, is defined as goal-directed and planned attention (Mezzacappa, 2004; Posner & Petersen, 1990). These different attention functions can be seen as connected, but independent functions that develop at different moments and show different developmental courses, starting already in infancy (Colombo, 2001).

Few studies empirically investigated the structure of attention capacities in young children. In a study with 6- to 16-year-old children using the Test of Everyday Attention for Children [TEA-Ch], which is based on the attention systems distinguished by Posner and Petersen (1990), support was found for a three-factor model of attention, including selective (i.e., orienting), sustained (i.e., alerting) and executive attention (Manly et al., 2001). The same was found in a study with 5- to 15-year-old Chinese children using the TEA-Ch (Chan, Wang, Ye, Leung, & Mok, 2008). Two studies were found investigating attention structure at preschool age (Breckenridge, Braddick, & Atkinson, 2013; Steele, Karmiloff-Smith, Cornish, & Scerif, 2012). Steele et al. (2012) studied a group of 3- to 6-year-old children using computer tasks, where children had to press a button or touch the screen as response, and found support for a two-factor model of attention, including selective/sustained attention and executive attention. Breckenridge et al. (2013) used eight tasks (seven on a computer) with touching or verbal report as response types in 3- to 6-year-old children. They found a distinctive structure of attention for 3- to 4½-year-old versus 4½- to 6-year-old children. In 3- to 4½-year-old children, a two-factor model showed the best fit to the data including selective/executive attention and sustained attention. For 4½- to 6-year-old children, a three-factor model including selective, sustained and executive attention, best fitted the data (Breckenridge et al., 2013). Steele et al. (2012), suggested that attention might be less differentiated in young children. No studies were found investigating the structure of attention in children below 3 years of age.

Next to verbal responses and touching behavior, looking behavior might be used as an indicator of attention capacities in young children. Eye-tracking techniques can be used to accurately assess looking behavior. This technique has been successfully used to assess attention capacities in infants below 12 months of age (e.g., Butcher, Kalverboer, & Geuze, 2000; Hunnius, Geuze, & Van Geert, 2006). In toddlers, eye tracking has been used to study behaviors like anticipatory looks and goal-directed gaze shifts (e.g., Gredebäck, Stasiewicz, Falck-Ytter, Rosander, & Von Hofsten, 2009; Paulus, Hunnius, & Bekkering, 2011) and preferential looking behavior of toddlers with Autism Spectrum Disorder (e.g., Jones, Carr, & Klin, 2008). However, as yet, little is known about the feasibility and potential of eye-tracking technology to assess attention capacities in toddlers.

Based on the three attention systems described by Posner and Petersen (1990), a test battery of four eye-tracker tasks (the Utrecht Tasks of Attention in Toddlers using Eye Tracking [UTATE]) was designed and described in a pilot study (De Jong, Verhoeven, Hooge, & Van Baar, 2016). Testing the UTATE in 16 children showed that the test battery is feasible for use with toddlers and can result in data of good quality. In the current study, we will examine whether the supposedly underlying attention systems indeed are being measured with these tasks in a larger sample (n = 95) of 18-month-old toddlers.

Based on studies of attention in young children, 4 models were investigated in the current study: 1) a one-factor model, to study whether the attention capacities form a unitary construct, 2) a two-factor model as found in the study by Steele et al. (2012) including orienting/alerting and executive attention, 3) a two-factor model including orienting/executive attention and alerting based on findings of Breckenridge et al. (2013), and 4) a three-factor model including orienting, alerting and executive attention, based on Posner and Petersen's (1990) theory.

Method

Participants

Parents and children were recruited via the hospital where the children were born. Healthy term born children (gestational age 37-42 weeks) born between March 1, 2010 and April 1, 2011 were eligible for the study. Exclusion criteria were dysmaturity (birth weight below 10th percentile), multiple birth, admission to the Neonatal Intensive Care Unit, severe congenital malformations, antenatal alcohol or drug abuse by mother, and chronic antenatal use of psychiatric drugs by mother. Participants were 98 Dutch 18-month-old toddlers, M = 17.54 months, SD = .50, of whom 43 (43.9%) were boys.

The medical ethical committee of the Utrecht Medical Center approved this study as part of a larger study on attention capacities of young children. Informed consent was given by the parents. The children received a present after the visit and parents received refund of travel expenses.

Measures

Four eye-tracker tasks were used to measure the attention capacities of the toddlers, the UTATE: 1) disengagement task, 2) face task, 3) alerting task, and 4) delayed response task (De Jong et al., 2016). In the *disengagement task*, a visual stimulus was first presented at the center of the screen, and after 2s a second stimulus appeared at the left or the right side of the central stimulus. This task consisted of 20 trials. In the *face task*, first two identical pictures of child faces were shown, and after 8.5s, one of the pictures changed into a new picture and stayed on the screen together with the previously shown picture for 8s. The face task consisted of eight trials. In the *alerting task*, a visual stimulus was presented on the screen, in half of the trials preceded by a signaling sound. The alerting task consisted of 32 trials. In the *delayed response task*, a dog was hiding in one out of two doghouses and after a certain delay (i.e., varying from 0-10s), the child was asked to search for the dog. This task consisted of 18 trials in which the delay increased from 0 to 10s with steps of 2s after three consecutive trials. Timing and stimulus size are presented in Figure 4.2 (page 59). The tasks are described in more detail elsewhere (De Jong et al., 2016). Definitions of the variables observed in these four tasks are presented in Table 5.1 and described below per attention system.

Orienting system

The capacities to orient on a target concern the abilities to engage, disengage, and shift attention focus from a target (Posner & Petersen, 1990). Six variables were supposed to reflect functioning of the orienting system: *mean dwell time* and *transition rate* from both the disengagement and face task, and *proportion of correct refixations* and *latency* from the disengagement task. Mean dwell time in the disengagement task includes both dwells at the central and the peripheral stimulus.

Alerting system

The abilities to achieve and maintain a state of alertness form the alerting system (Posner & Petersen, 1990). Five variables were supposed to reflect functioning of the alerting system: *total dwell time* from all four tasks, and the *difference in latencies* in the alerting task.

Executive attention system

The executive attention system is defined as goal-directed, planned attention and the ability to inhibit behavior (Posner & Petersen, 1990). Two variables from the delayed response task were supposed to reflect functioning of the executive attention system: the number of *correct searches* and the *mean delay*.

Table 5.1 Definitions of the observed variables from the eye-tracker tasks

Outcome measure	Task	Definition
Orienting system		
Mean dwell time	DIS, FACE	Average length of the dwells. A dwell is the length of "one visit in an area of interest [AOI], from entry to exit" (Holmqvist et al., 2011).
Transition rate	DIS, FACE	The number of transitions (i.e., "movement from one AOI to another", (Holmqvist et al., 2011) divided by the total dwell time.
Proportion of correct refixations	DIS	A correct refixation indicates that the participant refixated from the central stimulus to the new stimulus after the new stimulus is presented. The proportion of correct refixations is the number of correct refixations divided by the total number of trials in which the child looked at the central stimulus when the new stimulus appeared.
Latency	DIS	The average time between appearance of the new stimulus and fixation on the new stimulus in trials in which the participant correctly refixated.
Alerting system		
Total dwell time	DIS, FACE, AL, DR	Sum of the length of all dwells. A dwell is the length of "one visit in an area of interest [AOI], from entry to exit" (Holmqvist et al., 2011).
Latency difference	AL	Difference between latencies in the trials in which a signal preceded the appearance of the stimulus (i.e., signal trials) and the trials in which the stimulus appeared without signal (i.e., no-signal trials).
Executive attention system		
Correct searches	DR	The number of trials in which the child looked at the correct dog house directly in response to the voice over asking where to find the dog.
Mean delay	DR	The mean delay between hiding and the instruction to seek the dog in the trials in which the child correctly searched for the dog.

Note. DIS = disengagement task, FACE = face task, AL = alerting task, DR = delayed response task.

Apparatus

The Tobii T60 Eye Tracker with an integrated 17-inch TFT screen with a resolution of 1280 by 1024 pixels was used (Tobii Technology, Stockholm, Sweden). The Tobii T60 measures corneal reflection at a frequency of 60 Hz with an accuracy of 0.5°, and it has a spatial resolution of 0.2°. Using a white background, the precision (i.e., amount of root mean square [RMS] noise) is 0.5° (Tobii, 2011). The head box, or freedom of head movements, is 44 x 22 x 30 cm. Head movements are compensated by the eye tracker, which results in a temporary accuracy error of 0.2°. When the eye tracker loses track of the child's eyes (e.g., fast head movements of more than 25 cm/s), it recovers in 300ms. E-prime 2.0 software (Psychology Software Tools, Pittsburgh, Pennsylvania) was used to present the stimuli on the screen.

Procedure

Children were seated in a car seat at a distance of approximately 65 cm from the eye tracker. In line with Hunnius and Bekkering (2010), a 9-point calibration was used, in which a movie clip of a bouncing ball accompanied by sound was presented at nine different points on the screen (i.e., left, middle, and right at the top, center, and bottom of the screen). Calibration was accepted when the child looked at seven or more of the calibration points. Otherwise, several points were recalibrated. After calibration, the four tasks were presented in the following fixed order: 1) disengagement task, 2) face task, 3) alerting task, and 4) delayed response task.

The face of the children was also recorded with a video camera behind the eye tracker to be able to check the behavior of the child during the procedure. The whole procedure took about 18 minutes to complete.

Data analysis

Matlab 7.11 (The MathWorks, Inc.) was used to analyze gaze data. Fixation detection was done by a self-written Matlab program (I.H.) that marked fixations by an adaptive velocity threshold method. We used an adaptive velocity threshold method to detect fixations because the amount of noise may vary a lot in eye-tracking data (especially with low frequency trackers such as the Tobii T60 and with non-grown-up participants). Many modern saccade and fixation detection methods are partly or fully adaptive to the noise in the data (Nyström & Holmqvist, 2010; Smeets & Hooge, 2003). Velocities were obtained by fitting a parabola through three subsequent data points. We used the derivative of this fitted parabola to estimate the value of the velocity of the second (center) data point. This procedure was repeated for all data points (except the first and the last). In the present analyses, everything that is not a saccade is called a fixation. To remove the saccades from the signal we calculated average and standard deviation from the absolute velocity signal. All data points having absolute velocities higher than the average velocity plus 3 times the standard deviation were removed. This procedure was repeated until the velocity threshold converged to a constant value or the number of repetitions reached 50. Then we removed fixations having durations shorter than 60 ms from the analysis. The value of 60ms was chosen because it is equal to three data samples. When a saccade was removed, the preceding and succeeding fixations were added together. Data of the children were included when they looked at the stimuli at least once during a task, and thereby providing data on the variables of this task.

To investigate the factor structure of the attention measures, confirmatory factor analysis with maximum likelihood was conducted using the Lavaan package (Rosseel, 2012) in the R system for statistical computing (R Core Team, 2012). Z-scores were used instead of raw scores because of large differences in scaling and variances between the variables. The observed variables were allowed to load on only one latent factor. Latent factors were allowed to correlate. As method effects of the different tasks could occur in our data, a correlated trait-correlated uniqueness model (CTCU; Marsh, 1989) was investigated. In this model, error covariances were freely estimated between observed variables from the same task, except for *correct searches* and *mean delay* from the delayed response task. These two variables are both indicators of the latent variable *executive attention*; therefore correlated error is already captured in the latent variable. This results in a model with 16 estimated error covariances.

To assess model fit, the chi-square test statistic (χ^2), the root mean square error of approximation (RMSEA), the standardized root mean squared residual (SRMR), the comparative fit index (CFI), the Tucker-Lewis index (TLI) and the Akaike Information Criterion (AIC) were used. The chi-square test measures equality between the population covariance matrix and the model-implied covariance matrix (Schermelleh-Engel, Moosbrugger, & Müller, 2003). RMSEA measures the approximate fit of the model in the population instead of exact fit (Schermelleh-Engel et al., 2003). SRMR is a measure of the difference between observed and model-implied covariances (Schermelleh-Engel et al., 2003). CFI is a comparison between the fit of the target model and a very restricted baseline model (Schermelleh-Engel et al., 2003). TLI measures the proportion of improvement in fit of the target model compared to the baseline model, corrected for degrees of freedom (Schermelleh-Engel et al., 2003). AIC is a descriptive measure that will be used to compare results of different models. The model with the lowest AIC value can be seen as the best fitting model (Schermelleh-Engel et al., 2003). A model was considered to show a good fit based on the following criteria: p value of chi-square >.05, RMSEA <.06, SRMR <.08, CFI >.95, TLI >.95 (Hu & Bentler, 1999).

Results

All participants (n = 98) produced data on at least one of the variables. Three participants produced no data on one or more of the variables, due to technical problems. These participants were excluded from further analyses. The other children produced data on all variables; therefore, the following analyses included data of 95 children. Descriptive statistics of the 13 variables are presented in Table 5.2. Next to the range, also the 25 to 75% range is presented in Table 5.2 to show the variation in scores without the more extreme scores as well.

Correlations between the observed variables are presented in Table 5.3. Large variation is seen in the correlations between the variables. Of the 78 correlations, 32 were found to be significant with 4 expected by chance. Of these correlations, 21 were moderate to strong (i.e., >.30), and these were found to be between variable pairs of the same task or between variable pairs of the same attention system.

Table 5.2 Descriptive statistics of the outcome variables

Variable	M (SD)	Range	25-75% range
Disengagement task			
Number of trials[a]	17.65 (2.70)	6 – 20	16 – 20
Number of valid trials[b]	14.25 (3.49)	4 – 20	12 – 17
Mean dwell time	1,444 (325)	952 – 2,520	1,241 – 1,602
Latency	610 (226)	347 – 1,517	463 – 693
Proportion correct refixations	0.97 (0.05)	0.76 – 1.00	1.00 – 1.00
Transition rate	0.46 (0.12)	0.22 - 0.79	0.39 – 0.52
Total dwell time	92,054 (21,377)	23,152 – 125,981	78,536 – 107,403
Face task			
Number of trials[a]	7.07 (1.24)	3 – 8	7 – 8
Mean dwell time	1,244 (266)	689 – 2,009	1,058 – 1,421
Transition rate	0.64 (0.15)	0.39 – 1.13	0.52 – 0.73
Total dwell time	79,132 (20,397)	14,887 – 113,896	68,368 – 95,401
Alerting task			
Number of trials[a]	21.55 (6.89)	5 – 32	17 – 27
Latency difference	127 (271)	-432 – 1,438	-7 – 278
Total dwell time	55,773 (22,223)	7,966 – 111,283	39,218 – 73,013
Delayed response task			
Number of trials[c]	14.82 (4.30)	0[d] – 18	14 – 18
Correct searches	9.45 (3.51)	0 – 18	8 – 12
Mean delay	5.35 (1.56)	0 – 9	4.75 – 6.25
Total dwell time	76,748 (29,477)	300 – 140,866	62,466 – 98,333

Note. [a]Number of trials in which the children looked at the stimuli; [b]Number of trials in which the children looked at the central stimulus when the peripheral stimulus was presented; [c]Number of trials in which the children looked at one of the dog houses after they were asked to search for the dog. [d]This value is 0 for one child, because this child looked at the stimuli for 300ms during another moment in a trial than the moment on which "number of trials" is based (see [c]).

Fit indices of the four tested models are shown in Table 5.4. The one- and two-factor models showed poor fit. The three-factor model showed good fit: chi-square = 62.46, ns, RMSEA = .06, SRMR = .08, CFI = .97, and TLI = .95. In addition, the AIC was lowest in the three-factor model, indicating that this model fitted the data best.

Factor loadings of the four models are presented in Table 5.5. The final (three-factor) model is presented in Figure 5.1. Factor loadings of the orienting system varied between .01 and .70. The orienting system is best reflected in *mean dwell times* and *transition rates* in the disengagement and face task. Two factor loadings were not significant and below .30: *latency* and

Table 5.3 Correlations between the outcome measures from the eye-tracker tasks

	1	2	3	4	5	6	7	8	9	10	11	12	13
Orienting system													
1. DIS mean dwell time	1												
2. DIS latency	.29**	1											
3. DIS proportion correct	-.23*	-.35**	1										
4. DIS transition rate	-.87**	-.39**	.24*	1									
5. FACE mean dwell time	.49**	.21*	-.07	-.42**	1								
6. FACE transition rate	-.37**	-.22*	.10	.40**	-.87**	1							
Alerting system													
7. DIS total dwell time	.61**	.07	.03	-.42**	.19	-.02	1						
8. FACE total dwell time	.36**	.11	-.04	-.24*	.59**	-.34**	.41**	1					
9. AL total dwell time	.26*	-.04	.16	-.15	.29**	-.11	.43**	.52**	1				
10. AL difference in latency	-.14	-.10	.06	.29**	.01	-.06	-.04	.08	.02	1			
11. DR total dwell time	.10	.06	-.01	-.04	.13	-.10	.17	.31**	.25*	-.15	1		
Executive attention system													
12. DR correct searches	.04	.01	-.00	.03	.07	.03	.16	.38**	.20	-.12	.70**	1	
13. DR mean delay	.17	.00	-.09	-.15	.14	-.15	.16	.27**	.16	-.10	.45**	.50**	1

Note. DIS = disengagement task, FACE = face task, AL = alerting task, DR = delayed response task. * = $p < .05$, ** = $p < .01$.

Table 5.4 Goodness-of-fit indices of the different models

Model	χ^2	df	RMSEA	SRMR	CFI	TLI	AIC
Model 1	101.04**	49	.11	.11	.91	.86	3,018.13
Model 2	81.43**	48	.09	.10	.94	.91	3,000.51
Model 3	98.66**	48	.11	.11	.91	.86	3,017.74
Model 4	62.64	46	.06	.08	.97	.95	2,985.73

Note. Model 1 = 1-factor model; Model 2 = 2-factor model including orienting/alerting and executive attention; Model 3 = 2-factor model including orienting/executive attention and alerting; Model 4 = 3-factor model including orienting, alerting and executive attention. RMSEA = root mean square error of approximation; SRMR = standardized root mean squared residual; CFI = comparative fit index; TLI = Tucker-Lewis index; AIC = Akaike Information Criterion. *$p<.05$; **$p<.01$.

Table 5.5 Standardized factor loadings of the observed variables of the four tested models

		Model 1	Model 2		Model 3		Model 4		
			O/A	E	O/E	A	O	A	E
1.	DIS mean dwell time	.38**	.38**	-	.56**	-	.58**	-	-
2.	DIS latency	.05	.04	-	.09	-	.15	-	-
3.	DIS prop. correct refixations	.03	.05	-	.03	-	.01	-	-
4.	DIS transition rate	-.20	-.19	-	-.34**	-	-.39**	-	-
5.	FACE mean dwell time	.40**	.41**	-	.58**	-	.70**	-	-
6.	FACE transition rate	-.13	-.11	-	-.29*	-	-.43**	-	-
7.	DIS total dwell time	.54**	.55**	-	-	.60**	-	.53**	-
8.	FACE total dwell time	.79**	.80**	-	-	.78**	-	.83**	-
9.	AL total dwell time	.64**	.64**	-	-	.68**	-	.64**	-
10.	AL latency difference	.06	.10	-	-	.07	-	.05	-
11.	DR total dwell time	.38**	.33**	-	-	.25**	-	.36**	-
12.	DR correct searches	.45**	-	.89**	.26*	-	-	-	.83**
13.	DR mean delay	.33**	-	.55**	.23	-	-	-	.58**

Note. Model 1 = 1-factor model, Model 2 = 2-factor model: orienting/alerting and executive attention, Model 3 = 2-factor model: orienting/executive attention and alerting, Model 4 = 3-factor model, O = orienting system, A = alerting system, E = executive attention system, DIS = disengagement task, FACE = face task, AL = alerting task, DR = delayed response task.
*=p<.05,** = p <.01.

proportion correct refixations in the disengagement task. Factor loadings of the alerting system varied between .05 and .83. One factor loading was not significant and below .30: *latency difference* in the alerting task. The alerting system is best reflected in *total dwell time* in all four tasks. Factor loadings of the executive attention system were significant and .83 for number of *correct searches* and .58 for *mean delay.* As some of the factor loadings were not significant, we also explored whether a model without these variables would fit the data. This model also showed good fit: chi-square = 36.66, $p = .047$, RMSEA = .07, SRMR = .07, CFI = .98, and TLI = .96.

Correlations between the latent variables were .72, $p < .001$, between orienting and alerting, .50, $p < .001$, between alerting and executive attention, and .26, $p = .032$, between orienting and executive attention. These correlations not only indicated some overlap in measurement of different attention systems but also showed that the three factors reflect different aspects of the children's functioning.

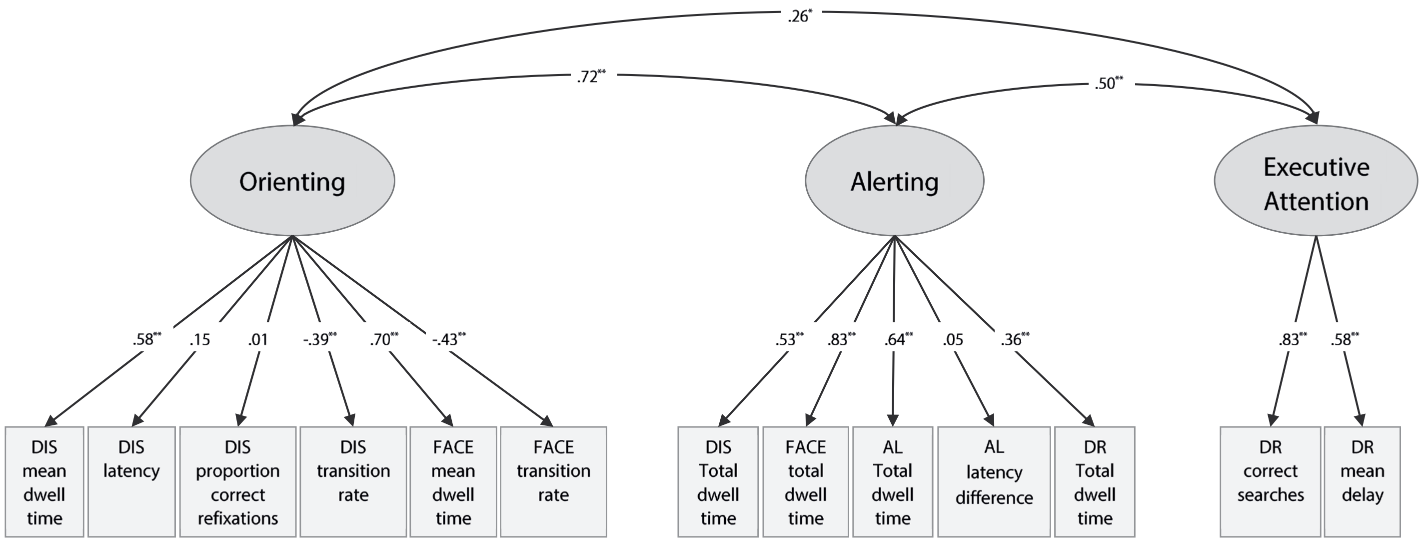

Figure 5.1. Three-factor model
Note. DIS = disengagement task, FACE = face task, AL = alerting task, DR = delayed response task.
*= p<.05, **= p <.01.

Discussion

The UTATE was found to measure functioning of three attention systems in 18-month-old toddlers, because the three-factor model best fitted the data. This result supported the theory of Posner and Petersen (1990) that distinguished three attention systems. The results are also in accordance with studies investigating the factor structure of attention in school-aged children (Breckenridge et al., 2013; Chan et al., 2008; Manly et al., 2001). However, our results on a sample of toddlers were in contrast to the findings in preschool-aged children, where a two-factor model showed the best fit (Breckenridge et al., 2013; Steele et al., 2012). Steele et al. (2012) suggested that attention might be less differentiated in younger children, which was not supported by our findings on even younger children. These contrasting findings might be due to differences in the methods used. While we used eye-tracking measures relying on eye movements and looking behavior, other studies used tasks where children had to press a button or touch the screen (Breckenridge et al., 2013; Steele et al., 2012) or had to verbally report (Breckenridge et al., 2013) as response. It might be that such responses provide a less differentiated representation of attention skills as they require additional maneuvers in which subtle differences between attention capacities might be lost.

Although the fit of the three-factor model was good, some of the factor loadings were low. *Latency* and *proportion of correct refixations* from the disengagement task did not significantly load on the orienting system. *Proportion of correct refixations* did not sufficiently differentiate between the children at 18 months of age, because on average, the children correctly refixated in 97% of the trials and 76% of the children correctly refixated in all trials. This lack of variation between the children might explain why the *proportion of correct refixations* did not load significantly on the orienting system. *Latency* did not load on the orienting system, which was surprising as it was related to *mean dwell time* and *transition rate* in the disengagement and face task (correlations between .21 and .39, see Table 5.3). Perhaps the way it was measured is important, as *mean dwell time* and *transition rate* were both based on more than one measurement per trial (i.e., a child could have more than one dwell and transition within a trial), whereas *latency* was not. *Latency* was based on only one measure per trial, as it reflected the time between appearance of the new stimulus and the first look at that new stimulus. Therefore, it may be that *latency* reflected something else than a generally reflexive orienting process at this age, for instance, a more self-generated shift in attention to a new stimulus. Further research is needed to investigate how *latency* is related to other measures that reflect age-related behavior, such as developmental level in cognitive skills.

With respect to the alerting system, *latency difference*, a variable from the alerting task, did not load significantly on the latent construct. The alerting system is supposed to be responsible for the ability to achieve and maintain a state of alertness (Posner & Petersen, 1990). Four out of the five variables of the alerting system were measures of sustained attention, while *latency difference* was mainly a measure of the ability to achieve a state of alertness. It might be that at toddler age, the ability to achieve a state of alertness differs from the ability to maintain it. This might explain the non-significant loading of *latency difference*. An extra analysis with the variables with non-significant factor loadings excluded also resulted in a model with good fit indices. Further study, for instance, concerning measurement invariance when comparing groups at risk of attention problems, could provide information about which model proves to be the most robust and useful in answering research questions on attention development.

A strong correlation was found between the orienting and alerting systems, a moderate effect was seen for the relationship between the alerting and executive attention systems, and a weak relationship was found for the orienting and executive attention systems. These relationships showed support for the findings and ideas of Colombo (2001) that attention systems may show different developmental courses, with orienting and alerting, that showed the strongest relationship in our sample of toddlers, developing at an earlier age than executive attention. All correlations were positive, indicating that a higher score on one attention system is related to a higher score on another attention system.

With respect to orienting, previous studies with young infants considered shorter mean dwell times, higher transition rates, higher proportions of correct refixations, and shorter latencies to be indicative of better functioning of the orienting system (Colombo, 2002; Rose, Feldman, & Jankowski, 2002). Our study with toddlers, however, showed opposite results: A higher score on orienting in our model (Figure 5.1) reflected longer mean dwell times and lower transition rates. Age differences between the samples in different studies could be important in explaining differences in results. The studies of Colombo (2002) and Rose et al. (2002) concerned infants below 1 year of age. It might be that in toddlers, longer mean dwell times and fewer transitions are indicative of better functioning of the orienting system and such behaviors thus have a different meaning than in infancy. In addition, short looking can be interpreted in several different ways, as it might reflect both efficient information processing, or in contrast, a short attention span (Atkinson & Braddick, 2012). Further research is currently conducted to investigate the functioning of the attention systems in relation to other measures of attention capacities, such as questionnaires filled out by parents and observations of child behavior during parent-child interactions.

Strength of this study was that the relatively objective eye-tracking measures were used to assess attention capacities. A limitation of the study was that the sample size is still rather small. Further research should investigate whether this model also fits data of larger samples. An important characteristic of this study is that a non-clinical sample was used. Further study is necessary to see whether the model also can be applied with children at risk for attention problems, such as preterm born children (e.g., Van Baar, Vermaas, Knots, De Kleine, & Soons, 2009).

In conclusion, this study showed support in a sample of 18-month-old toddlers for a three-factor model of attention capacities using orienting, alerting and executive attention as latent constructs, reflected in four eye-tracker tasks. The study of differences in attention capacities, as measured with the four eye-tracker tasks, for example, between groups of toddlers at risk for attention problems or not, and the study of the relationships of attention capacities with other developmental outcomes, can now be improved, as the 13 observed eye-tracking variables can reliably be reduced to three latent constructs.

Chapter 6

Attention Capacities of Preterm and Term Born Toddlers: A Multi-Method Approach

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Abstract

Objective: Many preterm children show difficulties in attention at (pre)school age. The development of attention capacities of preterm and term toddlers was compared using a longitudinal and multi-method approach at 12, 18 and 24 months. **Method**: Attention was measured for 123 preterm (32-36 weeks gestation) and 101 term born children, using eye tracking (18 months), observations during mother-child interaction (18 months), and mother-reports (12, 18, and 24 months). **Results:** Preterm toddlers had lower scores than term children on the eye-tracking measures of orienting and alerting. No group differences were found with observations, mother-reports, and the eye-tracking measure of executive attention. More preterm than term children had suboptimal scores on measures of the alerting system at 18 months, possibly indicating difficulties in attention development. **Conclusion:** Preterm children showed an increased risk for suboptimal functioning in alerting attention capacities, as early as at a toddler age.

Acknowledgement of author contributions

Marjanneke de Jong designed the study, performed the data collection, carried out the analyses, drafted the initial manuscript, revised the manuscript and approved the final manuscript as submitted.

Marjolein Verhoeven designed the study, reviewed and revised the manuscript and approved the final manuscript as submitted.

Anneloes L. van Baar conceptualized and designed the study, reviewed and revised the manuscript and approved the final manuscript as submitted.

Introduction

Around 9% of all children worldwide are born preterm after a gestational age of between 32 weeks and 36 weeks and 6 days (Blencowe et al., 2012). These children are at increased risk for a wide range of cognitive, school and behavior problems (De Jong, Verhoeven, & Van Baar, 2012), which include attention problems. When a child is born preterm, the brain is still immature. Therefore, brain development may have been affected in the neonatal period, which might result in attention problems or other difficulties in functioning (Kinney, 2006). Attention problems were reported in preterm children at preschool (Perricone, Morales, & Anzalone, 2013; Potijk, De Winter, Bos, Kerstjens, & Reijneveld, 2012) and school age (Talge et al., 2010; Van Baar, Vermaas, Knots, De Kleine, & Soons, 2009). Furthermore, 6 to 19 year old preterm children were found to have an increased risk for Attention Deficit Hyperactivity Disorder (Lindström, Lindblad, & Hjern, 2011).

The development of attention capacities of preterm children needs to be studied, since these capacities are a crucial part of everyday life, and attention problems might underlie other difficulties, such as cognitive problems (De Kieviet, Van Elburg, Lafeber, & Oosterlaan, 2012). Few studies as yet studied attention capacities in preterm children at toddler age. Studies at this age are important, because it is in this critical developmental phase that children gain increasingly more control over their attention capacities (Ruff & Rothbart, 1996). Furthermore, if differences between preterm and term born children are already noticeable at this age, early detection of difficulties in attention development might be facilitated. Such information could help designing interventions to improve these capacities and reduce problems in daily functioning.

Attention can be defined as a multi-dimensional construct including three attention systems: orienting, alerting, and executive attention (Posner & Petersen, 1990). Orienting represents the ability to engage, disengage, and shift attention. Alerting is the ability to achieve and maintain a state of alertness (i.e., sustained attention). Executive attention is a more self-generated form of attention, which is goal-directed and planned (Mezzacappa, 2004; Posner & Petersen, 1990). Research focusing on the three attention systems, as opposed to more general attention problems, could give more insight into the specific problems that preterm children might have, which would enable the development of intervention methods targeting these specific skills. Concerning very preterm children, born before 32 weeks' pregnancy, a few studies were done on the functioning of attention systems and these showed mixed results. There are indications that preterm children temporarily have better orienting skills (i.e., faster disengagement) during the first months of life than term born peers, but that this benefit disappeared after 3 to 4 months and the groups were found to perform equal (Butcher, Kalverboer, Geuze, & Stremmelaar, 2002; Hitzert et al., 2015; Hunnius, Geuze, Zweens, & Bos, 2008). At later age, both Snyder et al. (2007) and Pizzo et al. (2010) found that the preterm children performed slower than term children on all three attention systems at 4-6½ years of age. In contrast, De Kievit et al. (2012) found no group differences on the three attention systems at 7-8 years of age. Although it has been found that preterm children showed more attention problems (Perricone et al., 2013; Potijk et al., 2012), no studies were found as yet that investigated the functioning of the *separate attention systems* in detail in these children at toddler age.

Different methods may be used to measure attention, such as computerized tasks, observations and parent-reports. Previous studies with toddlers mainly used observations during play settings and/or questionnaires filled out by parents or caregivers in order to measure attention (Gaertner, Spinrad, & Eisenberg, 2008; Putnam, Gartstein, & Rothbart, 2006). A few studies investigated the relation between different methods, multiple informants and varying contexts, to measure attention (Davis, Burns, Snyder, & Robinson, 2007; Gaertner et al., 2008; Rothbart, Derryberry, & Hershey, 2000; Wass, 2014). When mothers reported better sustained attention capacities at 13½ months of age, more sustained attention was observed during a free play session in a lab setting (Rothbart et al., 2000). Gaertner et al. (2008) also found a (small) positive correlation between mother-reported and observed sustained attention at 30 months of age: children who had better sustained attention capacities according to their mother, were observed to play by themselves for a longer period of time. However, in the same study no relations were found between the assessments of sustained attention by different instruments, in different contexts or at different ages (Gaertner et al., 2008). Wass (2014) found no relation between peak look duration during computerized tasks, which can be considered a measure of the orienting system, and naturalistic/play tasks at 11 months of age. Davis et al. (2007) also found no relation between maternal report and attention measured with computerized tasks at 4-5 years of age.

It might be the case that different methods focus on different aspects of attention. It is not clear yet what instrument, or which combination of measurements, is the best method to obtain a good impression of the attention capacities of toddlers. Therefore, in the current study, attention capacities were measured repeatedly and by different types of instruments and informants. Recently, we have concluded that it is feasible to measure functioning of all three attention systems (i.e., orienting, alerting, and executive attention) in toddlers with a test battery of four computerized eye-tracking tasks; the Utrecht Tasks of Attention in Toddlers Using Eye Tracking (UTATE, De Jong, Verhoeven, Hooge, & Van Baar, 2013). Aside from the UTATE, video-taped observations during mother-toddler interaction in lab situations were used, as well as repeated mother-reports. The relationships between these different methods will be explored.

In the current study, attention capacities of preterm children born with a gestational age between 32 weeks and 36 weeks and 6 days, are compared to attention capacities of term born peers at toddler age using a multi-method approach with measurements at different time-points. Based on previous studies at (pre)school age (Perricone et al., 2013; Potijk et al., 2012; Talge et al., 2010; Van Baar et al., 2009), preterm children are expected to show suboptimal functioning, compared to their term born peers at toddler age, on the different indicators of attention capacities.

Method

Participants

Parents of preterm children born at a gestational age of 32 weeks and 36 weeks and 6 days in eight hospitals in and around Utrecht in the Netherlands were invited by letter by their pediatrician to participate in the study when their child was 10 months old. For the control group, parents of term born children with a gestational age of ≥37 weeks, born in four hospitals in and around Utrecht, were invited by letter by their midwives when their child was 10 months old to participate in the study. These children were all born between March 2010 and April 2011. For both groups, exclusion criteria were dysmaturity (i.e., birth weight below 10th percentile according to Dutch reference curves from Stichting Perinatale Registratie Nederland, 2014b), multiple births, admission to a tertiary Neonatal Intensive Care Unit, severe congenital malformations, antenatal alcohol or drug abuse by the mother, and chronic antenatal use of psychiatric drugs by the mother.

The medical ethical committee of the Utrecht Medical Center approved this study. Informed consent was given by the parents. The children received a small gift after the visit and the parents received refund of travel expenses.

Procedure

This study is part of an ongoing longitudinal project on the development of preterm children, the STAP Project (i.e., Study on Attention of Preterm children). When the children were 12, 18, and 24 months of age, corrected for prematurity, the mothers were asked to answer questionnaires concerning the development and behavior of their children and their parenting behavior. When the children were 18 months of corrected age, they visited our lab for an evaluation of attention capacities by means of an eye-tracking procedure and an observation of mother-child interaction. The visits were planned in such a way that these would not interfere with the children's sleeping schedules. The eye-tracking procedure was described in detail in De Jong et al. (2016). After the eye-tracking procedure, the mothers were asked to play with their child for 15 minutes: 5 minutes of free play and 10 minutes of structured play (i.e., reading a book and making a puzzle, both for 5 minutes). The interaction was videotaped and coded afterwards.

Instruments

Attention capacities were measured by eye-tracking techniques, observations, and questionnaires.

Eye-tracking measures

The Utrecht Tasks of Attention in Toddlers using Eye Tracking (UTATE) was used at 18 months of age to measure attention capacities, using four tasks: 1) a disengagement task, 2) a face task, 3) an alerting task, and 4) a delayed response task (De Jong et al., 2016). In the *disengagement task*, a visual stimulus was first presented at the center of the screen, and after 2s a second stimulus appeared at the left or the right side of the central stimulus, while the central stimulus stayed on the screen. This task consisted of 20 trials. In the *face task*, two identical pictures of children's faces were shown, and after 8.5s one of the pictures changed into a new picture and stayed on the screen together with the previously shown picture for 8s. The face task consisted of eight trials. In the *alerting task*, a visual stimulus was presented on the screen, preceded in half of the trials by a signaling sound. The alerting task consisted of 32 trials. In the *delayed response task*, a dog was hiding in one of two visible doghouses and after a certain interval (i.e., varying from 0-10s) the child was asked to search for the dog. This task consisted of 18 trials in which the interval increased from 0-10s with steps of 2s after three consecutive trials. The tasks are described in more detail elsewhere (De Jong et al., 2016). For the total group of children, the split-half reliability of the UTATE was found to be good ($r = .71 - .95$) for nine of thirteen variables. Moreover, evidence for construct validity was found as a Confirmatory Factor Analysis showed that the different aspects coded during the four tasks (see Table 5.1, page 74) could be reduced to three latent constructs: orienting, alerting and executive attention (De Jong et al., 2013).

The amount of root mean square (RMS) noise of the eye-tracking signals is a measure of data quality. Comparison of the RMS noise between the preterm and term born group showed no significant difference, indicating that the quality of the eye-tracking data was equal across the two groups, Wilk's $\Lambda = .93$, $F_{8,190} = 1.88$, $p = .07$.

A measurement invariance test on the factor structure that was confirmed in a sample of term born children (De Jong et al., 2013), following the procedure described by Van De Schoot et al. (2012), showed scalar invariance. This indicated that the same factor model applied to the preterm sample, and enabled a comparison of the mean scores on the three latent constructs across the two groups. Hence, scores on the latent constructs were used as measures of attention. For all constructs, higher scores were considered to be indicative of better attention skills.

Observational data

Mother-child interaction was observed in a lab setting at 18 months of age, in a room with a play mat on the floor, and a table and chair on the other side. First, three types of toys (i.e., a shape sorter, building blocks, and a pop up toy) were placed on the play mat, and the mothers were instructed to play with their child as they would do at home for 5 minutes (free play).Then the mothers were asked to read a book with their child for 5 minutes (task situation). Finally, the mothers were asked to make a puzzle with their child, again for 5 minutes (task situation).

The video-taped data were coded afterwards with the Coding Interactive Behavior observational system which is a global rating system (Feldman, 1998). In the current study, the child subscale *On-Task Persistence* was used as measure of functioning of the alerting system. On-task persistence is defined as persistence of a child for one activity, without quickly skipping from one activity to the next. On-Task Persistence was coded during both the unstructured free play (i.e., the first 5 minutes) and the structured task setting (i.e., 5 minutes reading a book and 5 minutes making a puzzle together) on a 5-point rating scale varying from low (1) "the child showed little persistence (i.e., lack of focus) and often moved from one activity to another activity" to high (5) "the child was consistently focused on one activity". One score was given for the total observation period of the free play setting (i.e., 5 minutes) and one score for the total observation period of the structured task setting (i.e., 10 minutes).

The scales were coded by nine trained and independent observers who were unaware of the birth status of the children. Interrater reliability, based on 21% of the videotapes that were double coded, was acceptable with an intraclass correlation of .76.

Questionnaires

The subscales *Attention Focusing* and *Attention Shifting* of the Early Childhood Behavior Questionnaire (ECBQ; Putnam et al., 2006) were used at 12, 18 and 24 months of (corrected) age. Attention focusing is a measure of functioning of the alerting system, and attention shifting measures the orienting system. These subscales both consist of 12 descriptions of behaviors. The mothers had to rate how often their child engaged in the behaviors during the last two weeks on a 7-point Likert scale varying from "never" (1) to "always" (7). Subscale scores consist of the average of the 12 items of that subscale. Cronbach's α of the attention focusing subscale varied between .86 and .88, and between .66 and .73 for the attention shifting subscale.

Neonatal and background characteristics

Neonatal characteristics concerning hypoglycemia (yes or no), phototherapy (yes or no), possible need for additional oxygen, and duration of hospital stay were based on the discharge letters in the hospital files. Background characteristics were provided by the parents on a short questionnaire.

Data analysis

Analyses of Covariance (ANCOVAs) were used to examine group differences on background characteristics. Multivariate Analyses of Covariance (MANCOVAs) were used to study group differences on eye-tracking measures, and Repeated Measures ANCOVAs for group differences on observations and mother-reports.

The distribution of the scores between the two groups will be compared using boxplots, to evaluate if equal numbers of children showed low scores and possibly suboptimal functioning or actual problems in attention development. Furthermore, all scores on the attention measures were also dichotomized using one SD below the mean of the term born group as cutoff point. Such scores were defined as 'suboptimal scores', indicating suboptimal attention capacities. Differences in percentages of suboptimal scores between the two groups were investigated with Logistic Regression Analyses and Chi-squared tests. The relationships between measures from different types of instruments and informants were investigated by Pearson's Correlations.

Results

Parents of 123 out of 333 eligible preterm children (37%) consented to participate in this longitudinal study and data on at least one of the outcome variables was available for all of them. The participating preterm children did not differ from nonparticipants in gestational age, birth weight, number of days in hospital, additional oxygen requirement, phototherapy requirement, gender, and percentage of first born children. A slightly higher incidence of hypoglycemia was observed in nonparticipants (11.2% vs 4.9%, $\chi^2 = 3.76$, $p = .05$). Parents of 103 out of 457 term born children (23%) consented to participate and data was available for 101 (98%) of them. The participating term born children did not differ from nonparticipants in gender, gestational age, birth weight, number of days in hospital, additional oxygen requirement, phototherapy requirement, hypoglycemia, and percentage of firstborns.

Sample characteristics are shown in Table 6.1. Mothers of preterm children were more often low educated than mothers of term born children ($\chi^2= 24.11$, $p < .001$). In addition, mothers of preterm children were slightly younger when their child was born (M = 31.1 years, SD = 4.5) than mothers of term born children (M = 32.6 years, SD = 4.2, $F_{1,222} = 6.96$, $p = .01$). Therefore, all analyses were adjusted for maternal education level and maternal age at birth. At 24 months of age (wave 3), preterm children were slightly younger according to their age corrected for prematurity (M = 23.3 months, SD = .5) than term born children (M = 23.7 months, SD = .9; $F_{1,207} = 11.38$, $p = .001$). As this age difference only occurred at wave 3, and adjusting for this age difference did not influence the results, we will only report the analyses in which no adjustment for the children's age was made.

Table 6.1 Neonatal and demographical characteristics of the participants

	Term born GA 37-41 weeks n = 101	Moderately and late preterm GA 32-36 weeks n = 123
Age in months wave 1		
Mean (SD)	11.5 (.7)	11.4 (.7)
Range	11-15	11-14
Age in months wave 2		
Mean (SD)	17.3 (.5)	17.3 (.5)
Range	17-18	17-19
Age in months wave 3		
Mean (SD)	23.7 (.9)	23.3 (.5)**
Range	23-30	23-25
Gestational age in weeks		
Mean (SD)	39.5 (1.0)	34.7 (1.3)***
32 weeks (%)		9.8%
33 weeks (%)		11.4%
34 weeks (%)		17.1%
35 weeks (%)		24.4%
36 weeks (%)		37.4%
37 weeks (%)	4.0%	
38 weeks (%)	10.9%	
39 weeks (%)	31.7%	
40 weeks (%)	40.6%	
41 weeks (%)	12.9%	
Birth weight in grams		
Mean (SD)	3572 (457)	2585 (517)***
Range	2795 – 5330	1420-3850
Gender (% boys)	45.5%	56.9%
First born (%)	51.5%	63.4%
Days in hospital		
Mean (SD)	.4 (1.0)	11.9 (9.8) ***
Range	0-6	1-42
Need for oxygen[a] (%)	0%	21.1%***
Photoherapy (%)	0%	35.0%***
Hypoglycemia (%)	0%	4.9%*
Ethnic origin (% Dutch)	96.0%	96.7%
Maternal education level		
Low[b]	3.0%	8.9%***
Medium[c]	11.9%	36.6%***
High[d]	85.1%	54.5%***
Maternal age at birth		
Mean (SD)	32.6 (4.2)	31.1 (4.5)**
Range	20-43	21-41

Note. [a]i.e. additional oxygen right after birth, nasal cannula, and/or continuous positive airway pressure (CPAP; n = 17); [b]no education, elementary school, special education or lower general secondary education; [c]high school or vocational education; [d]college, university or higher; * $p < .05$, ** $p < .01$, *** $p < .001$.

Differences between preterm and term born children on attention measures

The mean scores and percentages of children per group with suboptimal scores (i.e., >1 SD below mean of the term born group) for preterm and term born children on the 11 attention measures are presented in Table 6.2.

Table 6.2 Mean scores and percentage of children with suboptimal scores on attentional measures

	Term born GA 37-41 weeks			Moderately and late preterm GA 32-36 weeks				
	n	Mean (SD)	% suboptimal scores	n	Mean (SD)	% suboptimal scores	OR	95% CI OR
Orienting system								
Questionnaires								
Attention Shifting								
12 months	94	4.55 (.67)	14.3%	107	4.57 (.76)	17.6%	1.25	.58 – 2.72
18 months	94	4.62 (.58)	20.2%	107	4.62 (.62)	19.8%	1.22	.60 – 2.46
24 months	94	4.74 (.56)	15.6%	107	4.81 (.57)	14.4%	1.11	.50 – 2.47
Eye Tracking (18 months)								
Orienting	95	.00 (.53)	13.7%	101	-.23 (.41)*	19.8%	1.08	.47 – 2.46
Alerting system								
Questionnaires								
Attention Focusing								
12 months	94	3.75 (.81)	16.3%	107	3.73 (.88)	19.3%	1.07	.51 – 2.26
18 months	94	3.93 (.76)	14.1%	107	3.78 (1.00)	25.9%	1.86	.89 – 3.86
24 months	94	4.47 (.72)	16.8%	107	4.25 (.90)	29.7%	1.74	.86 – 3.54
Observations (18 months)								
On-task persistence								
Free play	98	3.33 (.73)	4.1%	116	3.20 (1.00)	19.0%	5.81**	1.87 – 18.00
Task	98	3.43 (1.00)	10.2%	116	3.13 (1.13)	25.9%	2.33*	1.03 – 5.23
Eye Tracking (18 months)								
Alerting	95	.00 (.49)	13.7%	101	-.33 (.61)**	38.6%	3.23**	1.54 – 6.75
Executive attention system								
Eye Tracking (18 months)								
Executive attention	95	.00 (.89)	13.7%	101	-.02 (.45)	4.0%	.18*	.05 - .67

Note. Adjusted for maternal education level and maternal age at birth. OR = Odds ratio, CI = confidence interval; * $p < .05$, ** $p < .01$.

Orienting system

A significant difference in mean scores between the groups was found for orienting, as measured with eye tracking ($F_{1,192} = 6.37$, $p = .01$, partial $\eta^2 = .03$), with preterm children scoring below their term born peers. Inspecting the boxplot (see Figure 6.1) shows a lower mean score for the preterm group while the distribution of the scores seems equal across the groups. Comparing the percentages of suboptimal scores between the groups indeed showed no difference between the preterm and term born group in number of children with suboptimal orienting abilities.

No group differences were found on mother-reported attention shifting at 12, 18 and 24 months of age for both mean scores ($F_{1,197} = .01$, $p = .91$, partial $\eta^2 = .00$), as well as the amount of suboptimal scores. This can also be seen in the boxplots (Figure 6.1), where both the mean scores as well as the distribution of the scores seem to be equal across the groups.

The amount of children having suboptimal scores on at least two of the four orienting attention measures is equal across both groups (13.8% in preterm versus 11.9% in term born group, $\chi^2 = 0.19$, $p = .67$).

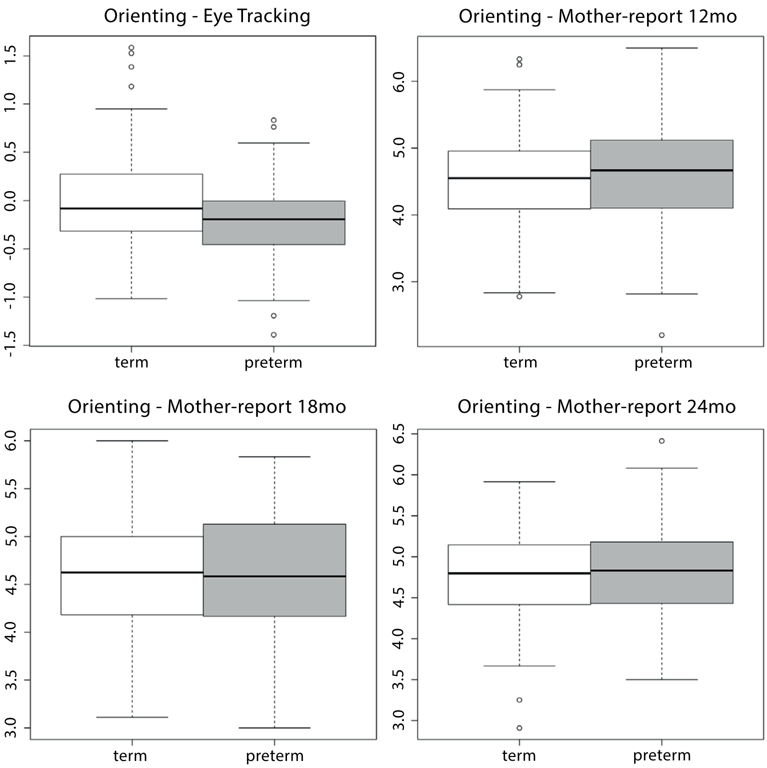

Figure 6.1. Boxplots of the orienting attention measures

Alerting system

Preterm children scored significantly below term born peers on the mean scores of alerting as measured with eye tracking ($F_{1,192} = 8.89$, $p = .003$, partial $\eta^2 = .04$). This is also visible in the boxplot (see Figure 6.2). This boxplot also shows a different distribution of the scores between the two groups, with more lower scores in the preterm group. Comparison of the percentage of suboptimal scores showed that more preterm children had suboptimal scores on functioning of the alerting system as measured with eye tracking (OR = 3.23, p = .002) in comparison to the term children.

Regarding observed on-task persistence in both the free play and the task setting at 18 months of age, no group differences were found in mean scores ($F_{1,210} = 1.23$, $p = .27$, partial $\eta^2 = .01$). Inspection of the boxplots (Figure 6.2) indicates a quite equal distribution of scores between the groups for the free play setting. In the task situation, however, there seems to be a larger number of preterm children with low scores. Comparison of the percentage of suboptimal scores indeed showed a larger number of preterm children with suboptimal scores in both the free play (OR = 5.81, p = .002) and the task setting (OR = 2.33, p = .04).

No group differences were found in mean scores on mother-reported attention focusing at 12, 18 and 24 months of age ($F_{1,197} = .46$, $p = .50$, partial $\eta^2 = .002$). Although the boxplots (Figure 6.2), seem to indicate somewhat more lower scores in the preterm group, comparison of the percentage of suboptimal scores showed no differences between the groups at 12, 18 and 24 months of age.

Of the preterm children, 42.3% had suboptimal scores on at least two of the six alerting attention measures; twice as many as in the term born group (21.0%, $\chi^2 = 11.34$, $p = .001$).

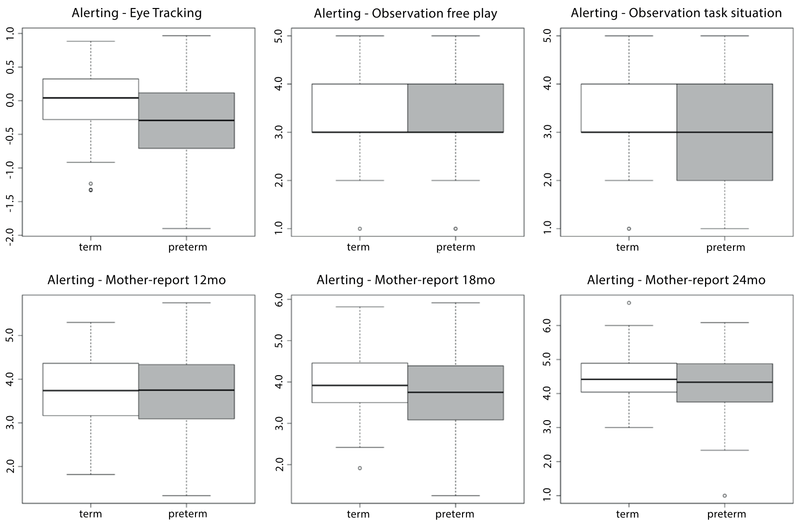

Figure 6.2. Boxplots of the alerting attention measures

Executive attention system

Preterm children did not differ from term born children regarding mean scores on executive attention as measured with eye tracking ($F_{1,192} = .27$, $p = .60$, partial $\eta^2 = .001$). The distributions of the scores seem to differ between the groups (see Figure 6.3), with a larger variation in scores in the term born group. The percentage of suboptimal scores on executive attention was found to be significantly smaller in the preterm group than in the term born group (OR = .18, p = .01).

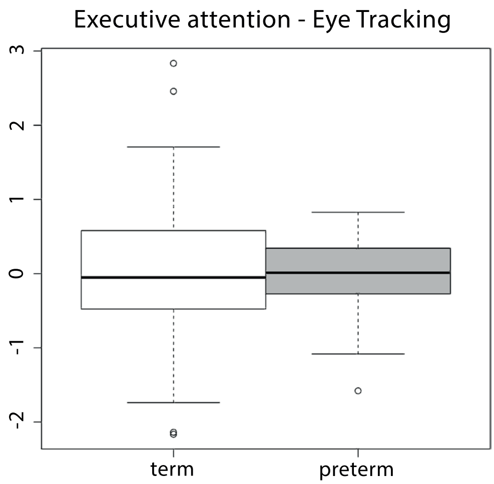

Figure 6.3. Boxplot of the executive attention measure

Relations between outcomes of different types of instruments and informants

Correlations between the different attention measures are presented in Table 6.3. Generally, no significant correlations were found between the outcomes of different instruments and informants, with a few exceptions between some measures of the alerting attention system, which did not show a great effect. Observed on-task persistence in a task setting at 18 months of age was positively related to both the eye-tracking measure of alerting at 18 months of age ($r = .21$, $p < .01$), and mother-report of attention focusing at 24 months of age ($r = .19$, $p < .01$).

Table 6.3 Correlations between the different attention measures

	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.
Orienting system											
Questionnaires											
Attention shifting (ECBQ)											
1. 12 months	1.00										
2. 18 months	.46**	1.00									
3. 24 months	.41**	.51**	1.00								
Eye tracking (18 months)											
4. orienting	.02	.11	.07	1.00							
Alerting system											
Questionnaires											
Attention focusing (ECBQ)											
5. 12 months	.16*	.19*	.09	.11	1.00						
6. 18 months	.15*	.39**	.32**	.18*	.48**	1.00					
7. 24 months	.05	.27**	.33**	.14	.34**	.61**	1.00				
Observations (18 months)											
On-task persistence											
8. free play setting	-.22**	-.20**	-.19**	.07	-.13	-.10	-.05	1.00			
9. task setting	-.11	-.02	-.03	.23**	-.07	.11	.19**	.36**	1.00		
Eye tracking (18 months)											
10. alerting	.02	.09	-.004	.72**	.07	.13	.11	.12	.21**	1.00	
Executive attention system											
Eye tracking (18 months)											
11. executive attention	.06	.03	-.02	.30**	.09	.06	.08	.04	.04	.52**	1.00

*Note.** = p <.05, ** = p <.01.

Discussion

The preterm children were found to differ from term born children in orienting and alerting attention abilities as early as at a toddler age. As a group, preterm toddlers scored lower than term born peers on orienting and alerting as measured with eye tracking. Additionally, a two to five times larger subgroup of preterm children showed suboptimal scores on the alerting attention system, as measured with eye tracking, as well as with observations of mother-child interaction (both the free play and the task setting). Furthermore, more than 40% of the preterm children had suboptimal scores on at least *two out of the six* alerting measures; twice as many as in the term born group. This suggests that an important subgroup of preterm children shows, as early as at a toddler age, suboptimal capacities in focusing their attention for a longer period of time.

Previous studies found that preterm children showed an increased risk for attention problems at preschool (Perricone et al., 2013; Potijk et al., 2012) and school age (Talge et al., 2010; Van Baar et al., 2009). The findings of the current study indicate that differences in attention capacities between preterm and term born children are already detectable at toddler age. The finding that our moderate to late preterm born toddlers scored lower on orienting and alerting abilities was in accordance with two of the three previous studies on very preterm, school-aged, children (De Kieviet et al., 2012; Pizzo et al., 2010; Snyder et al., 2007). An explanation for the differences in attention capacities of preterm and term born children might lie in differences in brain development. Preterm children are born with a still immature brain, not only regarding size (i.e., at 34 weeks the brain weighs only 65% of a brain at term), but also regarding structure (Kinney, 2006). Recently, it was found that at term age, the brain of preterm children was still smaller and had a different structure compared to that of term born infants (Walsh, Doyle, Anderson, Lee, & Cheong, 2014). This indicates that brain development outside the uterus differs from brain development inside the uterus, which might be related to later functioning and development. Brain areas involved in orienting and alerting capacities are the parietal lobes, frontal eye fields, and the thalamus (Fan, McCandliss, Fossella, Flombaum, & Posner, 2005). Further research to study whether those specific brain areas might differ between preterm and term born children and if this could explain the differences in attention capacities is worthwhile.

Preterm children as a group had lower scores than term born children on the orienting system as measured with eye tracking, whereas no differences appeared in the number and percentage of children with suboptimal scores on this measure. This might indicate a different distribution, and therewith a possibly different developmental trajectory of the orienting attention capacities for the two groups. This adds to previous findings that in infancy, preterm and term born children showed a different developmental trajectory regarding latency of gaze shifts, also a measure of the orienting system (Butcher et al., 2002; Hitzert et al., 2015; Hunnius et al., 2008). Longitudinal studies of the development of functioning of the orienting system are needed to investigate whether the two groups continue to differ in their development.

The results regarding executive attention showed no mean difference between the two groups; the percentage of suboptimal scores was even smaller in the preterm group compared to the term born group. This finding differed from two of the three studies on very preterm children, that showed that preterm children were outperformed by their term born peers (De Kieviet et al., 2012; Pizzo et al., 2010; Snyder et al., 2007). This difference in findings might be explained by the gestational age of the children. The previous studies concerned very preterm children who were born more immature and experienced more neonatal difficulties after birth than the preterm children in our study, putting these children at a higher risk for attention problems. It is possible that there are no problems in the development of executive attention in preterm children. The difference in findings might also be explained by differences in the age at which the children's attention skills were studied. Snyder et al (2007) and Pizzo et al (2010) examined the children when they were 4-6½ years of age, while in our study the children were only 18 months old. Executive attention only starts to develop at this young age (Ruff & Rothbart, 1996) and so the difference between preterm and term born children may not yet be visible. Finally, it might be that the measurements used did not capture the construct of executive attention sufficiently. No tasks were available as yet to measure executive attention directly (De Jong et al., 2016). We therefore used a task that was supposed to measure functioning of the dorsolateral prefrontal cortex (Goldman-Rakic, 1987), a brain area that is involved in executive functioning (Posner & Petersen, 1990). It is not clear if this task sufficiently measures executive attention. In addition, the score on this attention system was based on only two indicators, both from the last task in the test battery. Further research is needed to investigate whether this task is a sufficiently reliable and valid measure of executive attention.

No differences were found in mother-reports in any of the three ages, in mean levels or in percentages of suboptimal scores, despite the differences found in attention capacities using eye tracking and observational measures. It is possible that attention difficulties at these ages are not yet apparent to the parents. The differences in the methods used to evaluate the attention capacities may also be an important factor. The questionnaires concerned attention in everyday situations, as opposed to both the eye tracking and observational measures, which were about attention in a (social) lab context. While questionnaires were answered by mothers, the eye-tracking measures were technical measures, and the observations were coded by trained observers. Furthermore, the questions and response options in the questionnaires were of a general nature, while the eye-tracking measures were very specific and precise. The attention of a child during mother-child interaction is probably also influenced by the mother.

It might also be the case that preterm children primarily experience more difficulties with attention in task situations. Both the eye-tracking procedure and the observation were task situations: the child had to sit behind a computer screen, or play with his/her mother as instructed by the experimenter - even in the more unstructured situation labeled 'free play'. In contrast to the eye-tracking procedure and the observations, the questionnaires concerned 'voluntary' attention, in natural situations at home.

Overall, the different contexts used during the assessments may trigger specific or different aspects of attention capacities, which is also reflected in the generally low correlations between the measures. It should, however, be noted that the UTATE eye-tracking procedure used in this study is newly developed, and although the variables included as a measure of attention were based on existing literature, further research, e.g., regarding predictive validity, is still needed. Furthermore, future research should also be focused on the relationship between different instruments and informants, as well as on the predictive value of these measures for later functioning, in order to learn which measures are the most useful for early detection of attention difficulties.

A limitation of this study might concern the generalizability of the findings. The relatively low response rate might have resulted in a biased sample, which was found to include many good functioning children of highly educated parents. The number of low educated mothers was small in both the preterm and term born group. As there were more low educated mothers in the preterm group, the analyses were controlled for maternal educational level. However, low maternal education level is a risk factor for premature birth (Morgen, Bjork, Andersen, Mortensen, & Nybo Andersen, 2008; Petersen et al., 2009). Correcting for maternal education level might therefore be a form of overcorrection. Future research including a sample with more low educated mothers would allow investigation of the relationship between maternal education level and child outcome in both preterm and term born children. In addition, in this study only preterm children were included who did not need tertiary NICU admittance. Although this concerns the largest group of preterm children in the Netherlands (89.8%; Stichting Perinatale Registratie Nederland, 2013), the results might be different for the subgroup of children who needed admission to the NICU. For example, a recent study found that especially the children who were admitted to the NICU experienced problems in cognitive functioning (Baron, Erickson, Ahronovich, Baker, & Litman, 2011). Maternal level of education, as well as other background characteristics associated with preterm birth and development of the children, such as gender of the child and neonatal characteristics, should be studied in greater detail in a more diverse sample in future research in relation to attention problems.

Attention difficulties are often not diagnosed until children fall behind their peers in other domains of functioning, for example school functioning (Davis et al., 2007). In this study, preterm children were, as early as at a toddler age, found to show an increased risk for less optimal functioning in attention capacities. By focusing on the three attention systems instead of more general measures of attention, we found that preterm children specifically experienced difficulties in alerting attention capacities, and to a lesser extent in orienting capacities. These difficulties with alerting and orienting capacities might result in problems with learning other skills, as the ability to orient and sustain attention for a longer period of time, for example listening to instructions of a teacher, is needed to be able to learn new things. Therefore, further study and follow-up at older ages of attention capacities in preterm children is warranted. If the first signs of attention difficulties are already present and detectable at toddler age, even if these are only noticeable as suboptimal functioning, children could be supported sooner in their attention development using interventions. For example by a training to increase their focused attention using games, designed for toddlers (Wass, Porayska-Pomsta, & Johnson, 2011) or by instructing parents how to stimulate the attention capacities of their children.

Chapter 7

Cognitive Functioning in Toddlerhood: The Role of Gestational Age, Attention Capacities and Mother-Child Interaction

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Manuscript in revision for Child Development

Abstract

Why do preterm children show delayed development? Investigated was how an integrated model of biological risk, children's capacities, and maternal stimulation is related to cognitive functioning at toddler age. Participants were 189 children (gestational age 32-42 weeks). At 18 months of age, attention capacities were measured using eye tracking and maternal attention-directing behavior was observed. Cognitive functioning was measured at 24 months of age using the Bayley-III-NL. Cognitive functioning was directly predicted by the children's attention capacities and maternal attention-maintaining behavior. Gestational age affected cognitive functioning indirectly through the children's attention capacities, as well as through maternal behavior redirecting attention. In this way, a cascade of gestational age, children's attention capacities and maternal stimulation was important for early cognitive development.

Acknowledgement of author contributions

Marjanneke de Jong designed the study, coordinated the data collection, carried out the analyses, drafted the initial manuscript, revised the manuscript and approved the final manuscript as submitted.
Marjolein Verhoeven designed the study, reviewed and revised the manuscript and approved the final manuscript as submitted.
Arnoldina P.G.F. Maingay-Visser assisted in data collection, reviewed the manuscript and approved the final manuscript as submitted.
Louise Spanjerberg assisted in data collection, reviewed the manuscript and approved the final manuscript as submitted.
Anneloes L. van Baar conceptualized and designed the study, reviewed and revised the manuscript and approved the final manuscript as submitted.

Introduction

Preterm children are at risk for developmental delay in all domains of functioning, including cognition (e.g., Poulsen et al., 2013). Compared to term born children, preterm children showed lower results regarding cognitive functioning (e.g., Poulsen et al., 2013), with more children scoring below the levels expected for their age (Talge et al., 2010; Wolke & Meyer, 1999). Furthermore, compared to the general population, a larger subgroup of preterm children was found to need special education (Johnson et al., 2009; Van Baar, Vermaas, Knots, De Kleine, & Soons, 2009). It is not clear why preterm children experience problems in cognitive functioning, and why some have more difficulties than others. It has been suggested that the children's attention capacities play a central role in the association between gestational age and cognitive development (e.g., Lawson & Ruff, 2004). In this study, we examined how cognitive development at 24 months of age is related to gestational age, attention capacities of the children, and maternal behavior directed at their children's attention during interaction.

Although children born before 37 weeks' gestation are designated as preterm, many studies focused on development of very preterm children, born before 32 weeks' gestation. However, most preterm children are born moderately to late preterm (Blencowe et al., 2012). There is increasing evidence that these children are also at risk for developmental problems, as they are still immature at birth (e.g., De Jong, Verhoeven, & Van Baar, 2012; Potijk, De Winter, Bos, Kerstjens, & Reijneveld, 2012; Van Baar et al., 2009). As gradual effects of gestational age on child outcome have been found (Eryigit-Madzwamuse & Wolke, 2015; Jaekel, Baumann, & Wolke, 2013), we studied gestational age as a continuous variable, varying between 32 and 42 weeks. This range of gestation represents 96% of all births in the Netherlands (Stichting Perinatale Registratie Nederland, 2014a).

The finding that preterm born children are at risk for problems in cognitive functioning is often explained as a direct consequence of biological risk reflected in low gestational age. Lower gestational age indicates less mature brain development at birth (Kinney, 2006). In addition, preterm born children are exposed to different sensory experiences (e.g., brighter light, louder sounds and sometimes painful procedures) than unborn children of the same gestation within the womb. For these unborn children, growth and development is directly affected by the neurobiological functioning and life style of their mothers. The early experiences of preterm born children might specifically affect their brain maturation (i.e., structure and function) and therewith their further cognitive functioning and development (Als et al., 2004). Jaekel and colleagues (2013) showed that with lower gestational age - and more immature brains - cognitive scores were also lower at 8½ years of age. However, not all preterm children develop cognitive problems, and cognitive functioning is not solely affected by gestational age and the consequences of preterm birth. It is probable that a combination of biological risk, child characteristics and environmental factors is important.

Regarding child characteristics, attention capacities have been hypothesized as a mediator of the relationship between gestational age and cognitive functioning (Reuner, Weinschenk, Pauen, & Pietz, 2015; Rose, Feldman, Jankowski, & Van Rossem, 2008). This idea is based on findings that attention capacities were predictive for cognitive functioning (e.g., Bornstein & Sigman, 1986; Lawson & Ruff, 2004) and that preterm children more often showed attention problems than term born children (Aarnoudse-Moens, Weisglas-Kuperus, Van Goudoever, & Oosterlaan, 2009; Anderson et al., 2011; De Kieviet, Van Elburg, Lafeber, & Oosterlaan, 2012). Two studies specifically investigated this hypothesis (Reuner et al., 2015; Rose et al., 2008). Rose et al. (2008) found that orienting attention capacities measured at 12 months of age mediated the relation between birth status (i.e., preterm vs term) and cognitive functioning at 2 and 3 years of age. This study, however, mainly included very preterm children. As these very preterm children are born more immature and they experience more neonatal difficulties, these findings may not be generalizable to the large group of moderately to late preterm born children. Reuner et al. (2015) studied a sample with gestational ages varying from 23 to 41 weeks, including moderately preterm children. They found that focused attention (i.e., part of the alerting attention system) measured at 7 months of age mediated the relation between gestational age and cognitive functioning. This mediating role was only found for cognitive functioning measured concurrently at 7 months of age, and not for cognitive functioning at 24 months of age. Investigation of attention capacities at toddler age is needed, however, as it has been suggested as an important period in attention development in which important variation can be detected (Ruff & Rothbart, 1996).

According to the bio-ecological model of Bronfenbrenner (1979), development is influenced by biological and child characteristics, but also by the interaction of an individual with its (social) environment. This environment entails a broad range of direct and indirect influences. Parents form an important part of the environment of young children, and parenting behavior has repeatedly found to be related to cognitive functioning of the child (e.g., Landry, Smith, & Swank, 2006; Lemelin, Tarabulsy, & Provost, 2006). One way in which parents can promote development of their children is by a process called *scaffolding* (Wood, Bruner, & Ross, 1976), which was related to Vygotsky's theory of *zone of proximal development* (Vygotsky, 1978). Scaffolding means that a parent supports the child in achieving a goal or performing a task he or she is otherwise unable to accomplish. This facilitates learning, because the parent stimulates and helps the child to gradually perform somewhat more difficult tasks. One way in which parents support their child's development (i.e., scaffolding), is by directing their children's attention. With these *attention-directing behaviors*, parents support the child's attention capacities. With maintaining behaviors parents support their child in staying focused on an object or activity for a longer period of time than the child would do by itself (Bono & Stifter, 2003). Redirecting attention behavior supports the child in focusing on another object or activity than the one he or she was engaged in (Bono & Stifter, 2003).

When mothers showed more behavior directed at maintaining their child's attention, previous studies found that their children showed better cognitive functioning in infancy and at toddler age (Landry, Smith, Swank, & Miller-Loncar, 2000; Smith et al., 1996). The frequency of maternal behavior maintaining their children's attention was also positively related to executive functioning at preschool age, which was related to cognitive functioning (Conway & Stifter, 2012). These studies indicate that maternal behavior maintaining attention is beneficial for the cognitive development of their child. For maternal behavior aimed at redirecting the child's attention, results are mixed. Three studies found that children whose mothers showed high frequencies of redirecting behavior showed worse cognitive functioning in infancy (Pridham, Becker, & Brown, 2000) and preschool age (Conway & Stifter, 2012; Landry et al., 2000). However, the opposite was found at toddler age: more redirecting behavior of the mothers was then related to better cognitive functioning of their children (Landry et al., 2000). The authors suggested that at an early age children need more redirection, while this is less needed when children grow older and are more fully participating in social interactions. This suggestion, however, does not explain why Pridham and colleagues (2000) found a negative relation already in infancy. Further research on this relationship is needed.

It is possible that maternal attention-directing behavior directly influences cognitive functioning of their children, but as these maternal behaviors connect specifically to attention capacities of the children, it is likely that this relationship is mediated by the children's attention capacities. The mediating role of the children's attention capacities in the relationship between maternal attention-directing behavior and the children's cognitive outcome has, however, not been studied before. A link between maternal attention-directing behavior and children's attention capacities should then exist as well and this has been found before. When mothers showed more attention maintaining behavior, their children were better able to focus their attention for a longer period of time during infancy and at toddler age, which is in line with the suggested supporting role of maintaining behavior (Bono & Stifter, 2003; Findji, 1998; Findji, 1993; Landry & Chapieski, 1988; Pridham et al., 2000). In line with the suggestion that redirecting behavior, on the other hand, would interrupt the child's attention (Pridham et al., 2000), two studies found that children of mothers showing *more* redirecting behavior, showed less attention capacities at infant and toddler age (Bono & Stifter, 2003; Landry & Chapieski, 1989). As attention capacities were found to predict cognitive functioning (e.g., Bornstein & Sigman, 1986; Lawson & Ruff, 2004), the current study not only investigates if observed maternal attention-directing behavior is directly related to cognitive functioning at 24 months of age, but also if the attention capacities of toddlers at 18 months of age mediate that relationship.

In sum, we will investigate a model concerning the combined longitudinal relationships of biological factors (i.e., gestational age), child characteristics (i.e., attention capacities), and maternal stimulation (i.e., maternal attention-direction behavior) on cognitive functioning at toddler age, see Figure 7.1. Based on previous research we expect a positive indirect effect of gestational age on cognitive functioning through attention capacities, such that gestational age is positively related to attention capacities, which in turn are positively related to cognitive functioning (gestational age → attention capacities → cognitive functioning). Next to that, we expect an indirect relation of maternal attention-directing behavior on cognitive functioning through attention capacities (maternal behavior → attention capacities → cognitive functioning). We expect that maternal maintaining behavior is positively related to the attention capacities of the children, while maternal redirecting behavior is expected to be negatively related to attention capacities. Furthermore, as there are indications that mothers of preterm children differ in parenting behavior from mothers of term born children (e.g., Miles & Holditch-Davis, 1995; Muller-Nix et al., 2004), we also explore if gestational age is predictive of maternal behavior, and whether this results in a second indirect effect of gestational age on child outcome through maternal behavior (gestational age → maternal behavior → attention capacities → cognitive functioning). Based on the model of Posner and Petersen (1990) attention is defined as a multi-dimensional construct including three attention systems: orienting, alerting, and executive attention. Focusing on

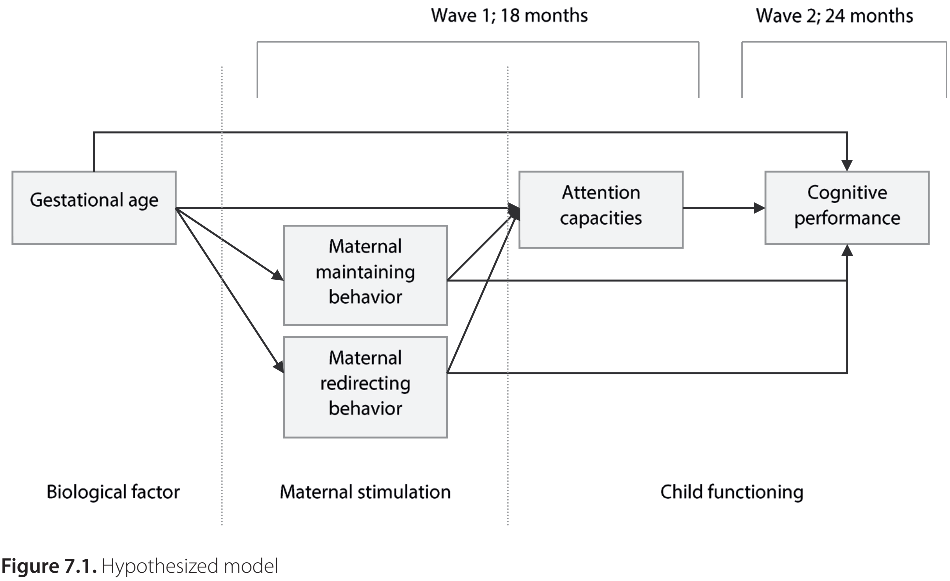

Figure 7.1. Hypothesized model

the separate attention systems will give more insight in the specific attentional capacities that might be involved.

Method

Participants

The full sample consisted of 226 participants. Complete data were available for 189 children of which 96 are born moderately preterm (gestational age M = 34.65 weeks, SD = 1.37) and 93 are born at term (gestational age M = 39.46 weeks, SD = 1.00). Children with complete data did not differ from the other participants in gestational age, gender, birth weight, number of days in hospital after birth, ethnic origin, maternal education level, and maternal marital status. Sample characteristics are presented in Table 7.1. Around half, 50.8%, of the children were boys, 56.6% were firstborn, and 96.3% had the Dutch nationality. The children were on average 17.55 months (SD = .50) at Wave 1, and 23.64 months (SD = .59) at Wave 2. Almost all mothers lived together with a partner (i.e., 98.4%) and the majority of the mothers were educated at high school or university level (70.9%).

Procedure

This study is part of an ongoing longitudinal project on the development of moderately preterm children, the STAP Project (i.e., Study on Attention of Preterm children), and was approved by the medical ethical committee of the Utrecht Medical Center. The children were born between March 2010 and April 2011, at a gestational age between 32 and 42 weeks in nine hospitals in and around Utrecht in the Netherlands. Exclusion criteria were dysmaturity (i.e., birth weight below 10^{th} percentile according to Dutch reference curves from Stichting Perinatale Registratie Nederland, 2014b), multiple birth, admission to a tertiary Neonatal Intensive Care Unit, severe congenital malformations, antenatal alcohol or drug abuse by the mother, and chronic antenatal use of psychiatric drugs by the mother. Their parents were invited by letter of their pediatricians or midwives to participate in the study when their child was 10 months old. When they agreed to participate, parents gave informed consent.

When the children were 18 months of age (corrected for prematurity; Wave 1), they visited our lab for an evaluation of attention capacities by means of an eye-tracking procedure as well as for an observation of mother-child interaction. The eye-tracking procedure was described in detail in De Jong et al. (2016). After the eye-tracking procedure, mothers were asked to play with their child for 15 minutes: 5 minutes of free play and 10 minutes of structured play (i.e., reading a book and making a puzzle, both for 5 minutes). The interaction was videotaped and coded afterwards. Coders were blinded for gestational age of the

Table 7.1 Background characteristics of the participants

	Total sample GA 32-41 weeks n = 189
Age in months wave 2	
Mean (SD)	17.55 (.50)
Range	17-18
Age in months wave 3	
Mean (SD)	23.64 (.59)
Range	23-27
Gestational age in weeks	
Mean (SD)	37.02 (2.69)
32 weeks (%)	5.8%
33 weeks (%)	5.3%
34 weeks (%)	8.5%
35 weeks (%)	12.7%
36 weeks (%)	18.5%
37 weeks (%)	2.1%
38 weeks (%)	5.3%
39 weeks (%)	15.9%
40 weeks (%)	19.6%
41 weeks (%)	6.3%
Gender (% boys)	50.8%
First born (%)	56.6%
Days in hospital	
Mean (SD)	6.34 (9.37)
Range	0-42
Ethnic origin (% Dutch)	96.3%
Maternal education level	
Low[a]	5.8%
Medium[b]	23.3%
High[c]	70.9%
Marital status (% Married/ Living together)	98.4%

Note. [a]no education, elementary school, special education or lower general secondary education; [b]high school or vocational education;[c]college, university or higher.

children. At 24 months of (corrected) age (Wave 2), the children and their mothers visited us for a developmental assessment. Examiners were again blinded for gestational age of the children. After both visits, the children received a small gift and the parents received refund of travel expenses.

Instruments

Attention capacities

The Utrecht Tasks of Attention in Toddlers using Eye Tracking (UTATE) was used at 18 months of (corrected) age to measure the attention capacities including four tasks: 1) disengagement task, 2) face task, 3) alerting task, and 4) delayed response task (De Jong et al., 2016). In the *disengagement task*, a visual stimulus was first presented at the center of the screen, and after 2s a second stimulus appeared at the left or the right side of the central stimulus, while the central stimulus stayed on the screen. This task consisted of 20 trials. In the *face task*, two identical pictures of child faces were shown, and after 8.5s one of the pictures changed into a new picture and stayed on the screen together with the previously shown picture for 8s. The face task consisted of eight trials. In the *alerting task*, a visual stimulus was presented on the screen, in half of the trials preceded by a signaling sound. The alerting task consisted of 32 trials. In the *delayed response task*, a dog was hiding in one out of two doghouses and after a certain delay (i.e., varying from 0-10s) the child was asked to search for the dog. This task consisted of 18 trials in which the delay increased from 0-10s with steps of 2s after three consecutive trials. The tasks are described in more detail elsewhere (De Jong et al., 2016). The split-half reliability was good ($r = .71 - .95$) for nine of thirteen variables.

Different aspects of looking behavior were coded during these four tasks, which could be reduced to three latent constructs: the orienting, alerting and executive attention systems (De Jong, Verhoeven, Hooge, & Van Baar, 2013). Scores on these latent constructs were used as measures of attention. For all constructs, higher scores were considered to be indicative of better attention skills.

Maternal attention-directing behavior

Mother-child interaction was observed in a lab setting at 18 months of (corrected) age, in a room with a play mat on the floor, and a table and chair on the other side. First, three types of toys (i.e., a shape sorter, building blocks, and a pop up toy) were placed on the play mat, and mothers were instructed to play with their child as they would do at home for 5 minutes (free play). Second, mothers were asked to read a book with their child for 5 minutes (task situation). Finally, mothers were asked to make a puzzle with their child, again for 5 minutes (task situation).

The video-taped interactions were coded afterwards with the Parental Attention Directing observation system (PAD; De Jong, Verhoeven, & Van Baar, 2016) based on Landry et al. (2006). In this system, the frequency of maternal attention-directing behavior is coded separately for maintaining and redirecting behavior. Maintaining behaviors are attempts of mothers to keep the child focused on the object or activity he or she is already engaged in, such as praise or encouragement. Redirecting behavior are attempts to redirect the child's attention to another object or activity, such as calling the child's name or showing and naming a new play object.

The data were coded by eight trained observers. For interrater reliability approximately half (53%) of the videotapes were double coded. The interrater reliability was good with an intraclass correlation of .88.

Cognitive functioning

At 24 months of (corrected) age, a trained examiner performed the Dutch version of the Bayley-III (Bayley, 2006) - the Bayley-III-NL (Van Baar, Steenis, Verhoeven, & Hessen, 2014) - to assess the child's developmental level.

The Bayley-III-NL consists of five subtests: Cognition, Fine Motor, Gross Motor, Receptive Communication and Expressive Communication. In the current study only the score on the Cognition subtest was used. The index score based on Dutch norms was used, which has a mean of 100 and a SD of 15 (Van Baar et al., 2014). The reliability and validity of the Bayley-III-NL is good (Van Baar et al., 2014).

Data analyses

Pearson's correlations were used first, to examine the univariate relationships between the variables in the proposed model (see Figure 7.1). To test the indirect effects, structural equation modeling was conducted using the Lavaan package (Rosseel, 2012) in the R system for statistical computing (R Core Team, 2012). Indirect effects were tested using the product of the coefficients of the predictor and mediation variable. The model was tested separately for each of the three attention systems. Furthermore, the models were also tested adjusted for maternal education level as this could be a possible confounder. Because gestational age was not equally distributed in the data, all models were bootstrapped and the 95% bootstrapped confidence intervals were used as indicator of significance of the coefficients in the model (Finney & DiStefano, 2006). To assess model fit, the chi-square test statistic (χ^2), the root mean square error of approximation (RMSEA), the standardized root mean squared residual (SRMR), the comparative fit index (CFI) and the Tucker-Lewis index (TLI) were used. A model was considered to show a good fit when: p-value of χ^2 >.05, RMSEA <.06, SRMR <.08, CFI >.95, and TLI >.90 (Hu & Bentler, 1999). Participants were included in the analyses when they had complete data on all variables in the model.

Results

Descriptive statistics

The means and standard deviations, as well as the intercorrelations of the variables in the model are presented in Table 7.2. With a mean cognitive index score of 102.17 (SD = 11.10) on the Bayley-III-NL, the children in this sample showed normal cognitive development. Concerning maternal attention-directing behavior was found that mothers showed more maintaining than redirecting behavior ($t(188) = 28.47$, $p < .001$). The frequencies of maintaining and redirecting behavior were not related ($r = .02$, $p = .74$). The means of the three attention measures reflect the standardized scores on the latent constructs and the correlations between the three attention measures were moderate to strong ($r = .30$ to $.73$).

Table 7.2 Means, standard deviations of and correlations between model variables

	1.	2.	3.	4.	5.	6.	7.	8.
1. Gestational age	1							
2. Maternal maintaining behavior	.04	1						
3. Maternal redirecting behavior	-.22**	.02	1					
4. Orienting	.24**	.10	-.19**	1				
5. Alerting	.24**	.12	-.27**	.73**	1			
6. Executive attention	.02	.01	-.14	.30**	.52**	1		
7. Cognitive functioning	.13	.21**	-.11	.21**	.20**	.08	1	
8. Maternal education level	.25**	.07	-.18*	.21**	.28**	.15*	.22**	1
Mean	37.02	185.86	48.56	-.11	-.16	-.01	102.17	-
SD	2.69	59.65	30.43	.48	.58	.71	11.10	-

Note. * $p < .05$, ** $p < .01$

Correlations between model variables

Gestational age was not related to cognitive functioning, but it was positively related to orienting and alerting attention abilities. No relation was found with executive attention. Furthermore, gestational age was negatively related to maternal redirecting behavior, whereas no relationship was found with maternal maintaining behavior. Orienting and alerting abilities, but not executive attention, were positively related to cognitive functioning. Maternal maintaining behavior was positively related to cognitive functioning, but was unrelated to attention capacities. The opposite was found for maternal redirecting behavior, which was unrelated to cognitive functioning, but negatively related to orienting and alerting abilities (see Table 7.2). Based on these correlations, we tested the model presented in Figure 7.2

for both orienting and alerting abilities separately. As executive attention was unrelated to gestational age and cognitive functioning, no further analyses were conducted for this attention system.

Orienting abilities

The fit measures showed that the unadjusted model had good fit (χ^2 = 4.23, n.s., RMSEA = .02, SRMR = .04, CFI = .99, and TLI = .99). All parameters were statistically significant, see Table 7.3. Lower gestational age was predictive of less orienting abilities and more maternal redirecting behavior. More maternal redirecting behavior was predictive of less orienting abilities. Less orienting abilities were predictive of lower cognitive scores. More maternal maintaining behavior was predictive of better cognitive functioning. The four indirect effects that were tested were all significant: 1) the effect of gestational age on cognitive functioning through orienting abilities, 2) the effect of gestational age on orienting abilities through maternal redirecting behavior, 3) the effect of gestational age on cognitive functioning through both orienting abilities and maternal redirecting behavior, and 4) the effect of maternal redirecting behavior on cognitive functioning through orienting abilities. In this model, 7.3% of the variance in cognitive scores was explained by gestational age, orienting capacities, and maternal maintaining and redirecting behavior.

Adjustment for maternal education level yielded the same results. The model fit was less than the fit of the unadjusted model, but still acceptable (χ^2 = 10.56, n.s., RMSEA = .04, SRMR = .04, CFI = .94, and TLI = .89).

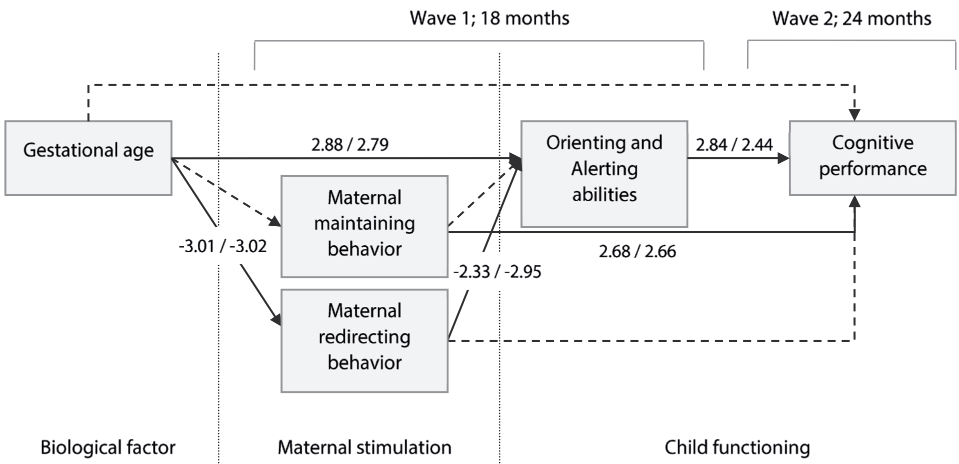

Figure 7.2. Tested model for orienting and alerting attention abilities.
Note. For a more parsimonious model, paths indicated by dashed lines were not included in the model, as those univariate correlations were small and not significant; Z-scores are presented for orienting on the *left* and alerting on the *right*.

Table 7.3 Parameter estimates of the final models

	Estimate	Z value	95% CI low	95% CI high
Orienting				
GA → orienting	.04	2.88	.01	.06
GA → redirecting	-2.52	-3.01	-4.23	-.91
Redirecting → orienting	-.002	-2.33	-.004	-.001
Maintaining → cognitive functioning	.04	2.68	.01	.06
Orienting → cognitive functioning	4.39	2.84	1.46	7.53
Indirect effect				
GA → orienting → cognitive functioning	.17	2.15	.04	.33
GA → redirecting → orienting	.006	2.00	.001	.01
GA → redirecting → orienting → cognitive functioning	.03	1.54	.003	.07
Redirecting → orienting → cognitive functioning	-.01	-1.70	-.03	-.001
Alerting				
GA → alerting	.04	2.79	.01	.07
GA → redirecting	-2.52	-3.02	-4.19	-.91
Redirecting → alerting	-.004	-2.95	-.008	-.002
Maintaining → cognitive functioning	.04	2.66	.01	.06
Alerting → cognitive functioning	3.30	2.44	.63	5.97
Indirect effect				
GA → alerting → cognitive functioning	.14	1.83	.02	.30
GA → redirecting → alerting	.01	2.39	.003	.02
GA → redirecting → alerting → cognitive functioning	.04	1.58	.004	.09
Redirecting → alerting → cognitive functioning	-.01	-1.77	-.03	-.002

Note. 95% bootstrapped confidence intervals indicate significance of the coefficients in the model when these contain no zero.

Alerting abilities

For alerting abilities, the unadjusted model showed good fit as well (χ^2 = 5.43, n.s., RMSEA = .04, SRMR = .04, CFI = 0.97, and TLI = 0.92). All parameters were significant, see Table 7.3. Lower gestational age was predictive of less alerting abilities and more maternal redirecting behavior. More maternal redirecting behavior was predictive of less alerting abilities. Less alerting abilities were predictive of lower cognitive scores. More maternal maintaining behavior was predictive of better cognitive functioning. Again, all four indirect effects were significant. In this model, 6.6% of the variance in cognitive scores was explained by gestational age, alerting capacities, and maternal maintaining and redirecting behavior.

After adjusting for maternal education level the results remained the same, however, the adjusted model did not show a good fit (χ^2 = 15.63, p = .05, RMSEA = .07, SRMR = .06, CFI = .85, and TLI = .72).

Discussion

Findings from this study showed that an integrated model of biological risk, child characteristics, and maternal stimulation is related to cognitive functioning at two years of age. Gestational age had no direct effect, but an indirect effect on cognitive functioning was found through orienting and alerting attention capacities of the children and maternal redirecting behavior: lower gestational age resulted in less orienting and alerting attention skills of the children, and in more redirecting behavior of the mothers, which in turn was related to lower cognitive scores of the children. Also, maternal behavior redirecting attention was only *indirectly* related to cognitive functioning, through orienting and alerting capacities of the children. Maternal behavior maintaining attention, on the other hand, was only *directly* related to cognitive functioning: more maintaining behavior predicted better cognitive scores. These findings remained the same after adjusting for maternal education level, although the fit of the models was less than of the unadjusted models.

Although previous studies mainly included very preterm children and measured attention in infancy (Reuner et al., 2015; Rose et al., 2008), an indirect effect of gestational age on cognitive functioning through attention abilities was also expected for our sample of children at toddler age, with gestational ages varying from moderately preterm to term birth. This finding shows that being born just a few weeks early still is negatively related to later developmental outcomes such as attention capacities and cognitive functioning. This concurs with the finding from previous studies comparing moderately preterm and term born children on several developmental outcomes (e.g., De Jong et al., 2012; Van Baar et al., 2009).

With respect to alerting attention capacities, Reuner et al. (2015) found an indirect effect of gestational age on cognitive functioning through alerting attention capacities only when attention and cognitive functioning were measured at the same age (i.e., 7 months), but not for cognitive functioning measured at 24 months of age. The authors suggested that this might have been due to the fact that alerting attention capacities are just starting to develop, and that alerting attention capacities measured after the first birthday might be more predictive of later cognitive functioning (Reuner et al., 2015). The current study indeed showed a predictive relation of alerting attention capacities measured at 18 months of age on cognitive functioning measured six months later.

In contrast to the finding that alerting in infancy was not predictive of later cognitive functioning, Rose et al. (2008) focused on *orienting* capacities in their study, and they found a predictive relation of orienting capacities on later cognitive functioning already when orienting was measured at 12 months of age. It might be that the predictive value of orienting and alerting capacities differ. Further longitudinal studies of attention capacities in relation to later cognitive functioning could investigate at which age attention capacities become predictive of later development, and whether this differs for orienting and alerting attention capacities.

Regarding maternal attention-directing behavior, we expected an indirect effect on cognitive functioning through attention capacities of the children. For maternal redirecting behavior, results indeed showed that less redirecting behavior was related to better attention skills, which lead to better cognitive functioning six months later. The finding that maternal redirecting behavior was negatively related to attention capacities of the children is in line with previous studies (Bono & Stifter, 2003; Landry & Chapieski, 1989), but this study adds to the previous literature by showing that through attention capacities, maternal redirecting behavior indirectly affects cognitive functioning. This finding indicates that interventions aimed at improving maternal attention redirecting behavior might be successful in enhancing children's cognitive development.

Maternal attention - maintaining behavior, on the other hand, was directly and positively related to cognitive functioning. This direct relation between maternal attention-maintaining behavior and cognitive functioning has been found in previous studies (Conway & Stifter, 2012; Landry et al., 2000; Smith et al., 1996). Maternal behavior maintaining attention might be directly related to cognitive functioning as this results in a situation where the child actually is stimulated to learn how to handle an object or how to complete a task, which may facilitate cognitive functioning. However, previous studies also found a positive relation between maternal maintaining behavior and attention capacities of their child (Bono & Stifter, 2003; Findji, 1998; Findji, 1993; Landry & Chapieski, 1988; Pridham et al., 2000), which was not found in our study. Why maternal maintaining behavior was related to cognitive functioning, but not to attention capacities in our study might be explained as follows. Four of the five studies on the relation with attention capacities measured maternal behavior when the children were between 5 and 8 months of age (Findji, 1998; Findji, 1993; Landry & Chapieski, 1988; Pridham et al., 2000), while in our study maternal behavior was measured at 18 months of age. It might be that maternal behavior during infancy has different effects than maternal behavior at toddler age. Bono and Stifter (2003) measured maternal behavior at 10 and 18 months of age, and also did not find a relation between maternal maintaining behavior and concurrent child functioning. They suggested that it might be that a certain, and constant amount of maternal maintaining behavior over time is enough for the development of the attention capacities of the child, and that more of this behavior has no additional beneficial effects (Bono & Stifter, 2003). This might be true, but, further research is needed to investigate this suggestion, and to study if the influence of maternal maintaining behavior on the child's attention capacities is different at different ages.

The relation between gestational age and maternal behavior was explored without specific expectations. Gestational age was found to be negatively related to redirecting behavior, but no relation was found with maintaining behavior. As redirecting behavior can be seen as a type of controlling behavior this may support the findings that mothers of preterm children are more controlling than mothers of term born children (Muller-Nix et al., 2004). The finding that the relation with gestational age differs for redirecting and maintaining behavior might also be due to a reciprocal relationship between maternal behavior and child functioning. In our model, we proposed that maternal behavior would be predictive of the children's attention skills and cognitive performance. However, it is likely that the relation between maternal behavior and child functioning reflects a transactional process (Sameroff, 2010). In this view, maternal behavior and child functioning form a dynamic and reciprocal cycle. In the current study, maternal behavior and attention capacities of the children were measured at the same age. Therefore, the association between maternal redirecting behaviors and the children's attention skills might also be reversed: i.e., when children show little attention abilities, mothers have to use more redirecting behavior when trying to explain something to the child. As lower gestational age was associated with less orienting and alerting attention capacities, this might have evoked more redirecting behavior of the mothers. Given that maternal attention maintaining behavior was unrelated to orienting and alerting, this might explain why this maternal behavior was not related gestational age. Further longitudinal research is needed to investigate the exact direction of these effects.

For executive attention, no relations were found with gestational age and cognitive functioning. This might be due to the age of the children and the measurement used. Executive attention starts to develop at the end of the first year (Ruff & Rothbart, 1996), and it could be that the children in our study were too young to measure executive attention sufficiently. Furthermore, research is needed to investigate whether the measure used actually captured the variation in executive attention skills at this age.

Although we investigated a combination of possible factors of influence, only a relatively small amount of variance in cognitive functioning was explained by those factors (i.e., around 7%). This means that a lot of variance in cognitive functioning must be explained by other factors, which could be of genetic origin (e.g., Plomin & Spinath, 2004). Other factors of importance might be different basic cognitive functions like information processing speed or working memory (Rose et al., 2008), child characteristics such as neonatal risk (i.e., complications during the neonatal period that might affect later development; Baron, Erickson, Ahronovich, Baker, & Litman, 2011) or temperament (Lemelin et al., 2006), or paternal behavior next to maternal behavior (Verhoeven, Junger, Van Aken, Deković, & Van Aken, 2010), and other parental interaction behaviors such as sensitivity. Further research is needed to investigate which other factors are predictive of cognitive functioning of the child.

Strength of the current study is that an integrated model of biological, child and maternal stimulation factors was investigated in a longitudinal and multi-method design. Most previous studies focused only on one of these factors, or only on direct relations between factors. Focusing on a combination of factors and on indirect effects provided more insight in which factors influenced the relation between biological risk (i.e., gestational age) and later developmental outcome. Gestational age is difficult to influence, but factors that increase or decrease the impact of low gestational age, like maternal behavior or child characteristics, can be a target for designing intervention or prevention programs.

A limitation of this study is that generalizability of the results is limited as relatively healthy preterm and term born children, and only children born between 32 and 41 weeks of pregnancy, were studied. It was found that moderately preterm children who were admitted to the NICU had more cognitive difficulties than moderately preterm peers who were not (Baron et al., 2011). Furthermore, there are indications that children born after 42 weeks of pregnancy also have an increased risk for developmental difficulties (El Marroun et al., 2012). Next to neonatal characteristics, the small number of lower educated mothers also limits generalizability. Another limitation is the rather small sample size in comparison to the complexity of the tested models, which might have increased the change of Type II errors. It is important that future studies confirm the results of the present study.

In conclusion, an integrated model showed that gestational age had an indirect effect on cognitive functioning at two years of age, as this relation was mediated by orienting and alerting attention abilities of the child and maternal attention directing behavior measured at 18 months of age. These findings reflect a cascade of biological risk, the children's attention capacities, maternal stimulation resulting in cognitive functioning.

Chapter 8

General Discussion

An infrequently studied group of children at risk for developmental problems was investigated in this dissertation: children born between 32 and 36^{+6} weeks of gestation, referred to as moderately preterm. They were compared to term born children regarding their behavior and development, and specifically their attention capacities. These studies were deemed necessary at toddler age, because at (pre)school age moderately preterm children had been found to be at risk for cognitive, school, and attention problems (Perricone, Morales, & Anzalone, 2013; Potijk, De Winter, Bos, Kerstjens, & Reijneveld, 2012; Talge et al., 2010; Van Baar, Vermaas, Knots, De Kleine, & Soons, 2009). The aims of this dissertation were threefold. The first aim was to investigate the kind and the extent of the differences in behavior and development between moderately preterm and term born children (Chapter 2 and 3). The second aim was to study differences in attention capacities between moderately preterm and term born children at toddler age. In relation to this aim, a test battery to measure attention capacities in toddlers was designed and described in Chapters 4 and 5. Differences in attention capacities between moderately preterm and term born children were examined in Chapter 6. The third aim was inspired by the unified theory of development of Sameroff (2010), that emphasizes that it is important to study the combined influence of biological factors and child characteristics, as well as of the environment in which the child grows up. For this aim, an integrated model was investigated with gestational age as a biological factor, attention capacities as a characteristic of the children, and maternal stimulation during interaction as an environmental factor in relation to cognitive development at two years of age (Chapter 7). In the current chapter, the main findings of the studies in this dissertation will be summarized and discussed. Next to that, the strengths and limitations of the studies, directions for future research, and clinical implications will be described.

Main findings and discussion

Differences in behavior and development between preterm and term born children

In Chapter 2, a systematic review of the existing literature on the associations between moderately preterm birth and long-term outcomes was presented. This review included 28 studies that investigated school outcome, cognitive functioning, behavior problems, and/or psychiatric disorders in moderately preterm children and adults. It was found that moderately preterm children showed lower IQ scores, experienced more school problems, more behavior problems, and more attention problems, and that they were diagnosed with ADHD more often than their term born peers. This indicates that moderately preterm birth places children at risk for later difficulties in behavioral and developmental outcomes.

The literature review also showed that studies at toddler age were scarce. Moderately preterm children under the age of three were only examined in five studies regarding their cognitive functioning. Moreover, only one study investigated their behavior problems. These studies gave a first indication that moderately preterm children differ from term born children in cognitive and behavioral functioning already before the age of three. Early recognition is important in order to prevent that problems (and their impact) aggravate when children grow older. Therefore, a study on behavior and development of 24-month-old moderately preterm toddlers in comparison to term born toddlers was reported in Chapter 3. From this study, it was concluded that after age correction, the moderately preterm group showed more internalizing behavior problems and (slightly) lower scores on receptive communications skills than the term born group.

Developmental outcomes and age correction

When comparing developmental outcomes of preterm children with that of term born peers, there is always the issue whether to correct age for prematurity, or only use the chronological age since birth. The Dutch Youth Healthcare organization (i.e., Jeugdgezondheidszorg) recommends the use of age correction for all preterm children under 24 months of age when examining physical growth, cognitive, motor, and language development (Van Der Pal-De Bruin, Heerdink, Kamphuis, & Pols, 2014). In both Chapter 2 and 3 it was shown that whether or not to correct age for prematurity resulted in different findings and conclusions. In the review study (Chapter 2), this conclusion was mainly based on comparison of studies that either did, or did not, correct age for prematurity. However, the small age span of the norm tables of the Bayley-III (i.e., 2 to 4 weeks) enables to compute scores for both corrected and uncorrected age based on one assessment moment. In one study in the review (Chapter 2), scores based on both corrected and uncorrected age were used to examine how age correction affected the results (Romeo et al., 2010). It was found that moderately preterm children at 12 and 18 months of age were delayed in cognitive functioning, but only when age was not corrected for prematurity. This is in accordance with our finding (Chapter 3) that the differences between moderately preterm and term born toddlers in cognitive, motor, and expressive language skills were no longer statistically significant after age correction.

Sometimes, it is not possible to study the impact of age correction for prematurity unless the measure is done twice at both the corrected and uncorrected age, for instance concerning our measures of behavior problems and attention capacities, because no age specific norms were available, or only norms for one large age group (1½ - 5 years for the CBCL).

Until now it remains unclear which of the scores (i.e., corrected or uncorrected for prematurity) is most predictive of later functioning of the children. The few studies that investigated this showed inconsistent results, with two studies showing no difference in predictive value of corrected and uncorrected scores (Siegel, 1983; Sugita, Iai, Inoue, & Ohta, 1990), and one showing that corrected scores were most predictive of later functioning (Rickards, Kitchen, Doyle, & Kelly, 1989). Knowledge regarding this predictive value is important, not only for research purposes, but especially for clinical practice. It might be that using corrected scores results in overestimation of the actual developmental level of the child, leading to under referral to intervention and support. At the same time, using uncorrected scores could lead to an underestimation of the actual developmental level, resulting in over referral, and unnecessary concerns by parents. For the time being, it seems best to examine children at the corrected age, as this allows an equal amount of time for development in moderately preterm and term born children. However, for clinical practice, it might be best, when the measurement used allows computation of scores based on both corrected and uncorrected age, to take both scores into account when assessing developmental outcome of an individual child.

Behavior problems

At 24 months of (corrected) age, more behavior problems were found in our study on moderately preterm children compared to their term born peers. These problems specifically concerned internalizing, not externalizing, behavior problems (Chapter 3). Internalizing behavior includes withdrawn, anxious, and depressed behaviors (Achenbach, 1991). This finding is in accordance with two previous studies, included in the review (Chapter 2), which found higher scores on internalizing behavior and no difference or only a slightly higher score on externalizing behavior in moderately preterm children compared to term born peers at school age (Talge et al., 2010; Van Baar et al., 2009). Also for very and extremely preterm children it is found that they experience more internalizing, but not externalizing, behavior problems (e.g., Aarnoudse-Moens, Weisglas-Kuperus, Van Goudoever, & Oosterlaan, 2009; Anderson, Doyle, & Victorian Infant Collaborative Study Group, 2003). Likewise, very preterm adults were more likely to show a withdrawn personality (Eryigit-Madzwamuse, Strauss, Baumann, Bartmann, & Wolke, 2015).

It was suggested that the withdrawn personality, and therewith more internalizing behavior, might be a result of alterations in brain development following preterm birth (Eryigit-Madzwamuse et al., 2015). At the same time, the relation between gestational age and internalizing behavior might be – partially – mediated by parenting. It could be that parents of preterm children are more protective, controlling, and over involved, which influences their children's behavior and personality development. In term born children it has indeed repeatedly been found that parenting behavior, such as overprotection, is related to internalizing symptoms, such as anxiety, of their children (e.g., McLeod, Wood, & Weisz, 2007; Van Der Bruggen, Stams, & Bögels, 2008). It was also found that mothers of preterm children were more overprotective than mothers of term born children (e.g., Pyhälä et al., 2011).

In the sample of the STAP Project, the relation between positive parenting behavior and internalizing behavior of the children was investigated. It was found that the relation between gestational age and internalizing behavior at age 3 was less strong when mothers showed high levels of warmth, stimulation, and positive discipline at 12, 18 and 24 months of age (Van Wijngaarden, De Jong, Verhoeven, Deković & Van Baar, 2016). This is a first indication that while moderately preterm birth places children at risk for internalizing behavior problems, positive parenting behavior might be a protective factor that reduces the risk.

Moderately versus late preterm

In the literature review (Chapter 2), it was suggested that developmental outcome could be different when a distinction is made between moderately (i.e., gestational age 32-33 weeks) and late (i.e., gestational age 34-36 weeks) preterm birth. Within the review, two studies analyzed differences between moderately and late preterm born children and found that moderately preterm children had more school problems than late preterm children (Chyi, Lee, Hintz, Gould, & Sutcliffe, 2008; Van Baar et al., 2009). In our own sample, however, no indications of differences between moderately preterm and late preterm children were found comparing the mean scores on developmental and behavioral outcome (i.e., difference of 0.07 – 0.84 on the scaled scores of the Bayley-III-NL and of 0.26 – 1.14 on the T-scores of the CBCL) .

Attention capacities of preterm children

In Chapter 2, it was concluded that moderately preterm children experience attention problems and ADHD symptoms at school age more often than their term born peers (Lindström, Lindblad, & Hjern, 2011; Linnet et al., 2006; Talge et al., 2010; Van Baar et al., 2009). As the first years of life are very important in the development of attention (Ruff & Rothbart, 1996), research focusing on attention capacities of toddlers was recommended. Before it became possible to compare attention capacities of moderately preterm and term born toddlers, an instrument and a test battery to measure functioning of the orienting, alerting, and executive attention systems was needed. Therefore, the Utrecht Tasks for Attention in Toddlers using Eye Tracking, the UTATE, was developed. The development and initial validation of this test battery were reported in Chapter 4 and 5.

UTATE

In Chapter 4, the UTATE was described in detail and tested in a small sample of 16 term born toddlers at 18 months of age. This pilot study led us to conclude that the UTATE was feasible for use with 18-month-old toddlers, that it resulted in data of good quality, and showed individual differences for most of the outcome measures. The split-half reliability in this pilot sample indicated that the reliability of most of the variables was sufficient. Later, reliability of the UTATE was determined for the total sample of moderately preterm and term born children. The split-half reliability results also showed good reliability for most of the variables (Chapter 6 and 7).

Validity and factor structure

A first step in evaluating the validity of the UTATE was the study described in Chapter 5, investigating the factor structure of the variables assessed by the four different tasks in the group of term born children. Confirmatory factor analyses were performed to examine whether the three different attention systems, orienting, alerting and executive attention, underlying the UTATE were indeed represented in the data. Based on theory and previous studies, four models were tested. Results showed that a three factor model, reflecting orienting, alerting, and executive attention, best fitted the data. The 13 variables of the UTATE could reliably be reduced to these three latent constructs, supporting the construct validity of the UTATE. Furthermore, a measurement invariance test investigating whether the model from Chapter 5 was also applicable to moderately preterm children, a group at risk for attention difficulties, showed scalar invariance, indicating that the UTATE measured the same constructs in moderately preterm as well as term born children. This provided another indication of validity of the UTATE.

In a study with the term born children of the STAP project, initial evidence was found for convergent, discriminant, and concurrent validity (Maat, De Jong, Verhoeven, & Van Baar, 2016). Proof of convergent validity was found because the UTATE was related to other measures of attention assessed with questionnaires and observations. As attention capacities are not supposed to be related to motor skills, the finding that the UTATE was not related to gross motor skills of the children was seen as proof of discriminant validity. Concurrent validity was found as the UTATE was more strongly related to other measures of attention that were assessed at the same age as the UTATE, than to measures assessed at younger or older ages (Maat et al., 2016).

Furthermore, the finding that the UTATE was able to distinguish between a group of children at risk for attention problems (i.e., moderately preterm children) and a group of typical developing children (i.e., term born children; Chapter 6) also supports the validity of the UTATE. Finally, in Chapter 7 an indication of predictive validity was shown as the UTATE was related to cognitive functioning six months later. Taken together, these findings support the conclusion that the UTATE is a promising measure to assess attention capacities in toddlers.

Executive attention

Although it was concluded in Chapter 4 and 5 that using the UTATE as measurement of the three attention systems, orienting, alerting and executive attention, seemed appropriate, there also were concerns about the possibility to measure executive attention in 18-month-old toddlers. In Chapter 7, it was found that the measure of executive attention was not related to cognitive functioning, while previous studies with (pre)school aged children showed that executive attention is related to school competence (e.g., Blair & Razza, 2007; Checa & Rueda, 2011). Furthermore, while differences between moderately preterm and term born children were found for orienting and alerting capacities, no differences were found for executive attention (Chapter 6). It might, of course, simply be that moderately preterm children do not have difficulties with executive attention. For somewhat older children, however, it has previously been found that moderately preterm children experience more difficulties than their term born peers with executive functioning, including executive attention (Baron, Kerns, Müller, Ahronovich, & Litman, 2012; Cserjesi et al., 2012). The age of the children, 18 months at the time of assessment, may have been specifically important. At this age, executive attention might only be starting to develop (Rueda & Posner, 2013; Ruff & Rothbart, 1996). This could make it difficult to measure executive attention in this age group, which is also reflected in the fact that no tasks were available to directly measure executive attention in toddlers when this research project was started. Although the delayed response task we used is intended to measure functioning of the brain area that is involved in executive attention (i.e., dorsolateral prefrontal cortex; Kane & Engle, 2002), it might be that at this young age executive attention could not yet be measured in full.

Preterm versus term born children

In Chapter 6 the attention capacities of moderately preterm and term born children were compared at 12, 18 and 24 months of (corrected) age using questionnaires answered by mothers (12, 18 and 24 months of age), the UTATE (18 months of age), and observations during mother-child interaction (18 months of age). Results showed that moderately preterm children differed from term born children in orienting and alerting attention abilities. No group differences were found for executive attention.

For alerting, preterm toddlers as a group performed worse than their term born peers on the eye-tracking measure. In addition, a larger subgroup of preterm children showed suboptimal functioning on alerting, as measured with observations and eye-tracking. For orienting, it was also found that preterm children as a group performed worse than term born children on the eye-tracking measure. However, the number of children showing suboptimal levels of orienting skills did not differ between moderately preterm and term born children. These findings indicate that moderately preterm children especially seem to have difficulties regarding sustaining their attention for a longer period of time (i.e., alerting), as early as at toddler age.

Differences in measurement methods

Results of our study showed that the correlations between the different measures of attention were generally low. Several explanations were discussed: 1) differences in informants: while questionnaires were answered by mothers, observations were coded by independent observers, and the eye-tracking measures were computed with an algorithm; 2) differences in setting: questionnaires concern a more general assessment of attention in everyday situations across a period of two weeks, in contrast to both observations and eye tracking, which measured attention in a lab-context at one moment; and 3) differences in scaling: the eye-tracking measure is very precise, while the rating scales of the questionnaires and observations were more general. It is likely that due to these differences, all measures capture different aspects of attention. Although this might explain the low correlations between the different measures, it still does not give an answer to the question which method is best to get a good impression of the attention capacities of the children. It is possible that one specific measure is most predictive of child functioning, but it might also be that a combination of all measures captures the child's capacities best. Based on the findings in Chapter 6 and 7, the more fine-grained eye-tracking measure seemed able to capture differences between preterm and term born children and predicted cognitive functioning six months later. Therefore, this method might be the best to detect attention difficulties at this young age.

Brain development

One explanation for the differences in attention capacities between preterm and term born children might be that brain development is altered by preterm birth. In Chapter 1, the brain areas that are involved in functioning of the different attention systems were mentioned (see Figure 1.1, page 14). Based on the results of Chapter 6 that moderately preterm children especially seem to experience difficulties regarding alerting attention capacities, it might be that especially the development and functioning of the specific brain areas involved in alerting capacities (i.e., frontal and parietal lobes and the thalamus; Fan, McCandliss, Fossella, Flombaum, & Posner, 2005) differ between preterm and term born children.

In very preterm children, a review study showed evidence for reduced volume in the frontal and parietal lobes and reduced thalamic volume (Volpe, 2009). As it is suggested that development of the thalamus probably occurs between 15 and 34 weeks of gestation (Volpe, 2009), it could be questioned whether the thalamic volume is also decreased in moderately preterm children, who are mostly born after the period during which the thalamus develops. Nevertheless, moderately preterm children are born with a less mature brain than term born children, which might implicate reduced volume of the frontal and parietal lobes, which are also involved in alerting attention capacities (Fan et al., 2005).

A few studies measured brain volume and structure in moderately preterm children at term equivalent age, and these found that moderately preterm children then had smaller and less mature brains than term born children, hence a delay in brain development may have occurred (Kelly et al., 2015; Munakata et al., 2013; Walsh, Doyle, Anderson, Lee, & Cheong, 2014). Only one study investigated volume of specific brain regions, instead of focusing on the whole brain (Rogers et al., 2014). In this study, based on a MRI performed at around 10 years of age, it was found that moderately preterm children had smaller right temporal and right parietal lobes than term born children (Rogers et al., 2014). It is not clear whether the size of the thalamus was also investigated separately. The finding that the right parietal lobe was still smaller in moderately preterm children, however, might explain why they differed from term born children on orienting and alerting attention capacities.

The role of biological, child, and environmental factors in development of preterm and term born children

In Chapters 2, 3, and 6 development was studied by comparing preterm children with term born children. These studies are important to gain knowledge about the risk of preterm birth. However, it is also important to focus on other factors, next to gestational age, that might influence development. The transactional relation between parent and child is also likely to influence the child's development, in line with the contextual and regulation models as described in the unified theory of development of Sameroff (2010). In order to integrate the findings of Chapters 3 and 6, together with a focus on the relationship between parent and child, we investigated the role of gestational age, attention capacities of the child, and maternal attention-directing behavior during interaction on cognitive development in Chapter 7.

Results of this study showed that gestational age had no direct effect on cognitive functioning, but an indirect effect was found: lower gestational age was related to more maternal behavior redirecting their children's attention, which predicted less orienting and alerting attention skills of the children. In turn, this was related to lower cognitive scores of the children at the age of two. At the same time, more maternal behavior focused at maintaining their children's attention was found to directly predict better cognitive functioning. This study, therefore, showed that a cascade of biological risk, maternal stimulation, and attention capacities of the children was associated with their cognitive outcome at two years of age.

Biological risk: gestational age as continuous variable

There is a long research tradition in which, just as in Chapter 3 and 6, gestational age is studied as a dichotomous variable: a child is born preterm or not. Although these studies give important insights in the risk of preterm birth, there are indications that it is also meaningful to study gestational age as a continuous variable. First of all, several studies show that children born at 37 or 38 weeks of gestation (i.e., term born according to the official definition of the World Health Organization) also have more neonatal morbidity (Sengupta et al., 2013), lower cognitive scores (Rose et al., 2013), more school problems (Chan & Quigley, 2014; Noble, Fifer, Rauh, Nomura, & Andrews, 2012), and more behavior problems (Robinson et al., 2013) than children born between 39 and 41 weeks of gestation. This is not surprising, as the brain keeps developing and might benefit from a few extra weeks within the womb. Next to the effect of being born a few weeks early, being born too late (i.e., after 42 weeks of gestation) also seems to increase the risk for developmental and behavior problems (El Marroun et al., 2012; Lindström, Fernell, & Westgren, 2005). This might be due to non-optimal functioning of the 'old' placenta, less corticotrophin-releasing hormone secretion, or a higher risk for perinatal complications, such as deprivation of oxygen during birth (El Marroun et al., 2012). These findings point to the importance of studying gestational age as a continuous variable, as every week might matter and may result in improved development until a gestation of 41 completed weeks. Using gestational age as a dichotomous variable masks such within-group differences.

Child factors: orienting versus alerting attention capacities

In Chapter 7, the results concerning the relations between gestational age, attention capacities of the child, maternal behavior and cognitive functioning were identical for orienting and alerting attention capacities of the children. Due to this finding and the high correlation between the constructs (i.e., $r = .73$) it might be questioned whether these two measures really reflected separate capacities. There are, however, several reasons why orienting and alerting still can, or even must, be treated as separate constructs. First of all, the constructs are theoretically different. While orienting represents the ability to engage, disengage, and shift attentional focus, alerting is the capacity to achieve and maintain a state of alertness (Posner & Petersen, 1990). In other words, orienting is the capacity to select where to attend to, and alerting is the capacity to stay focused on an object or activity for a longer period of time. This theoretical distinction was confirmed statistically in Chapter 5: it was shown that the three factor model, with orienting and alerting as separate constructs, fitted the data better than a two-factor model with orienting and alerting as a single construct. Next to that, in Chapter 6 the findings regarding group differences between preterm and term born children were not identical for orienting and alerting attention. Although preterm children as a group had lower scores than term born children on both orienting and alerting, only for alerting a significantly larger subgroup of preterm children showed suboptimal scores. These findings support the notion that orienting and alerting are separate constructs.

Environmental factor: maternal stimulation during interaction

Although some previous studies focused on parenting behavior of parents with very preterm children (e.g., Miles & Holditch-Davis, 1995; Muller-Nix et al., 2004), this study was one of the first focusing on the relation between gestational age and parenting behavior of mothers with moderately preterm children. Results showed that when the child was born with a lower gestational age, mothers showed more attempts to redirect the attention of their child during interaction. It is possible that gestational age influences behavior of the mother, as preterm birth might, for example, result in more concerns about the child's development which could lead to compensatory parenting behavior (Miles & Holditch-Davis, 1997). As already mentioned in Chapter 7, it might also be that gestational age has affected the attention capacities of the children, which then evoke a certain type of maternal behavior. In other words, the effect of gestational age on maternal behavior might be indirect, through its effect on the attention capacities of the children. However, as no direct relationship between maternal redirecting behavior and cognitive functioning was present, this order of effects seemed less likely.

Small amount of explained variance

The factors we chose to study in relation to cognitive outcome in Chapter 7 explained only around 7% of the variance in cognitive outcome. Nevertheless, our study was one of the first combining biological, child, and environmental factors within one model. However, the relatively small amount of explained variance implies that much of the variance will be explained by other factors.

According to the unified theory of development of Sameroff (2010), child development is likely to be an outcome of factors within the child (including genetic factors), environmental factors, and the interaction between those factors. Several other factors, potentially important for cognitive development, were mentioned shortly in Chapter 7. Biological factors might be neonatal morbidity such as infections, hyperbilirubinemia, hypoglycemia, and breathing difficulties, as these have been related to cognitive functioning in very preterm children (e.g., Perlman, 2001). As moderately preterm children have an increased risk for neonatal morbidity compared to term born children (Raju, 2012), these factors might also be important in moderately preterm children. In our own sample, the number of children with neonatal morbidity was too small to investigate their relationship with the children's developmental outcome.

Child factors that might be related to cognitive development could consist of basic cognitive functions, other than attention. Rose et al. (2008) included, next to attention capacities, also recognition memory, processing speed, recall memory, and representational competence in their model to predict cognitive outcome. They found that these four capacities, together with attention, mediated the relation between gestational age and cognitive functioning in a sample of mainly very preterm children. Better basic functions (attention and processing speed) were found to predict better complex functions (recognition memory, recall memory, and representational competence), which in turn predicted cognitive outcome (Rose et al., 2008).

In addition, temperament might be of importance. Child temperament has been related to cognitive functioning, in that positive aspects of temperament (i.e., extraversion, surgency, and behavioral control) were found to be positively related to cognitive functioning, while negative aspects (e.g., frustration, sadness, and high activity level) were negatively related to cognitive functioning (e.g., Lemelin, Tarabulsy, & Provost, 2006; Salley & Dixon, 2007). Previous studies showed that preterm children more often had a more difficult temperament (e.g., less soothable, more withdrawn) than term born children (e.g., Hughes, Shults, Mcgrath, & Medoff-Cooper, 2002), although there are also studies showing no differences (e.g., Larroque, Guédeney, Marchand, Burguet, & EPIPAGE Study Group, 2005). As no studies, as yet, focused on temperament in moderately preterm children, further research on temperament of moderately preterm children and the role of temperament in the relation between gestational age and cognitive functioning seems worthwhile.

Regarding environmental factors, we focused at maternal interaction behavior and we included two specific types of behavior in our models. Results showed that maternal attention-directing behavior is related to attention capacities and cognitive functioning of their children. Although these are meaningful and interesting findings, other types of parenting behavior might also be important, such as sensitivity or intrusiveness, which are found to be related to cognitive functioning (e.g., Tamis-LeMonda, Shannon, Cabrera, & Lamb, 2004). Furthermore, a next step might be to include behavior of the fathers, as paternal behavior is also related to child outcome (e.g., Verhoeven, Junger, Van Aken, Deković, & Van Aken, 2010).

Several factors are mentioned that might be related to cognitive functioning of the children. However, it is not possible to include all factors at once, and therefore our model, including biological, child, and maternal stimulation factors was an important first step.

Strengths and limitations

A first strength of the studies described in this dissertation is the focus on moderately preterm children, born between 32 and 36^{+6} weeks' gestation. The majority of preterm children is born moderately preterm, and although the number of studies focusing on moderately preterm children has increased over the last ten years, studies regarding behavior and development of these children are still limited. A second strength of the empirical studies is the focus on toddler age. Most previous studies focused on preschool and school age. However, when difficulties in behavior and development are already visible in toddlerhood, children at risk can be supported earlier and the chances to prevent or reduce later problems increase. A third strength is the use of standardized and validated instruments (i.e., UTATE, CBCL and Bayley-III-NL) and a multi-method design to measure behavior and development of the children, which increases the reliability of the findings of our studies. A fourth strength is the use of a longitudinal design. The longitudinal design makes it possible to follow the developmental course and to study predictors of developmental or behavioral outcomes. A final strength is the inclusion of measures of maternal behavior during interaction. Although it is well known that parents are important in the development of children, only a few studies have been published that focused on parental behavior of mothers with moderately preterm children.

A limitation of the studies in this dissertation concerns the generalizability of the findings. There are several reasons why generalizability might be limited. First, there was little variation in maternal education level and most mothers in the sample were highly educated. Studies with samples that are more diverse regarding maternal education level might show different results. Nevertheless, in Chapter 7 it was shown that although maternal education level was related to cognitive functioning of the children, controlling for maternal education level did not change the results. Another factor that might limit the generalizability concerns the selection criteria used for the preterm children. We only included relatively healthy preterm children that did not need NICU admittance. This can, however, also be seen as a strength, because the (small) subgroup with NICU admittance probably has to cope with greater neonatal morbidity and therefore has a greater risk for developmental problems. Inclusion of this subgroup could as such also have disturbed the results. Findings of our studies show that even *healthy* moderately preterm children are at increased risk for behavioral and developmental difficulties.

Future directions

The studies in this dissertation resulted in more knowledge about behavior and development of moderately preterm born children at toddler age. Further research on several topics is needed and some of the main topics will be presented. First, although the UTATE seems a promising instrument to measure attention capacities of toddlers, there were concerns regarding measuring executive attention. Future research is needed to investigate if our measurement indeed captured executive attention, for example by studying if executive attention measured with the UTATE is related to measures of executive attention at later ages. If not, further research should focus on alternative ways to measure executive attention in toddlers.

Second, in Chapter 7, results showed that the effect of gestational age on cognitive functioning was indirect through maternal behavior and attention capacities of the children. However, as already mentioned, only a small percentage of variance in cognitive functioning was explained by those factors and future research is needed in which other factors are involved.

Finally, it is important to follow the development of the children of the STAP project when they grow older. Studying the children at later ages will show if and how functioning during toddlerhood is predictive of later functioning. Are children who experience difficulties at school age already different in their development at toddler age?

Clinical implications

The findings of the literature review and empirical studies indicate that moderately preterm children are at increased risk for developmental and behavioral difficulties in comparison to their term born peers. The empirical studies furthermore showed that differences between the groups regarding behavior, development and attention capacities were already visible at toddler age. If future research shows that these early differences are predictive of later functioning, intervention or prevention might already be started at this young age.

We have seen that not all moderately preterm children show suboptimal functioning at toddler age. Therefore, the children who might need support in their development need to be identified first. For this purpose, it seems worthwhile to follow moderately preterm children regularly after discharge from the hospital. As it concerns about 10.000 children each year, a screening procedure might be used in order to reduce costs. Example is a three-step screening procedure presented by Steenis (2015), in which first a screening questionnaire answered by parents can be used, followed by a professional screening instrument, such as the Bayley Screener (Bayley, 2006), when a child is at risk for a delay in development according to the parental report. If this professional screening gives the same result as the parental report, the more extensive Bayley-III-NL can be administered to detect children that might need support.

As we found evidence that attention difficulties underlie later cognitive functioning, interventions at a young age might specifically target attention capacities of the children. This can be done by training attention capacities of the toddlers. Wass, Porayska-Pomsta, and Johnson (2011) developed a training for infants and toddlers consisting of several computerized games. An example is the "butterfly game" in which a butterfly is presented on the screen. When the child focuses on the butterfly the butterfly is going to fly across the screen (as a reward), but at the same time distracters appear. If a child changes its focus to a distracter, the butterfly stops flying and the distracter disappears. This task is used to train a child to focus attention for a longer period of time. It was found that this training resulted in better sustained attention and cognitive control in 11-month-old children (Wass et al., 2011).

In addition, as Chapter 7 showed that maternal attention-directing behavior was also related to attention capacities and cognitive functioning of the children, mothers (and fathers) might (also) be a target of intervention. Because the relation between mother and children is supposed to be transactional (i.e., mothers and children influence each other; Sameroff, 2010), a combination of training both parents and children might be most effective.

General conclusion

Based on the studies in this dissertation, it can be concluded that moderately preterm children are at increased risk for difficulties in sustaining attention for a longer period of time, for internalizing behavior problems, and for less well developed receptive language skills as early as at toddler age. Furthermore, it was found that cognitive functioning at two years of age was indirectly predicted by gestational age through both orienting and alerting attention capacities and maternal behavior aimed at redirecting the child's attention. The effect sizes found might seem to be small. However, such small differences might be early indicators of more serious difficulties at later age. Therefore, follow up of the sample in this project is needed to investigate the developmental course of these children. In this way we will learn more about the risk of being born just a few weeks early: step-by-step.

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Summary

Every year, more than 10.000 children in the Netherlands are born moderately preterm after 32 to 36^{+6} weeks of gestation, which is 6.1% of all births. These children are at risk for difficulties on the short and long term. At school age, moderately preterm children were found to show attention problems in particular. Such attention problems might underlie the difficulties they experience regarding school and cognitive functioning. Although there was increasing interest in the development of moderately preterm children during the last decade, still little is known about the early development and functioning of these children at toddler age. Therefore, the aims of this dissertation were to study:

1. Differences in behavior and development of moderately preterm and term born children
2. Differences in attention capacities of moderately preterm and term born children
3. The role of biological factors, child characteristics, and maternal stimulation in the development of moderately preterm and term born children

These aims were addressed in this dissertation in one review and five empirical studies. For the empirical studies, data was used from the STAP project: a longitudinal research project on the attention capacities of preterm children. In this project, a group of 123 moderately preterm and 103 term born children was studied longitudinally at 12, 18, and 24 months of age.

Behavior and development of moderately preterm children

An overview of outcome studies on behavior and development of moderately preterm children is presented in Chapter 2. Based on 28 studies, it was found that moderately preterm children showed lower IQ scores, experienced more school problems, more behavior problems and more attention problems than term born children. Furthermore, moderately preterm children were more often diagnosed with ADHD than term born peers.

These previous studies mainly focused on school-aged moderately preterm children. It was concluded that more information was needed about the developmental course of moderately preterm children and the age of onset of their problems. As the first years of life are a very important period in development, in Chapter 3 behavior and development at toddler age was investigated. At 24 months of corrected age, moderately preterm children were found to show more internalizing behavior problems and less receptive language skills. Differences regarding cognitive, motor, and expressive language functioning were only found when age was not corrected for prematurity. This shows that correcting age for prematurity affected the outcomes for the moderately preterm children.

Attention capacities of moderately preterm children

In order to perform a detailed study of attention capacities of toddlers, a new instrument had to be designed. The Utrecht Tasks for Attention in Toddlers using Eye Tracking, the UTATE, was described in Chapter 4. The UTATE consists of four tasks measuring functioning of the orienting, alerting, and executive attention systems with an eye tracker. In a pilot study, it was shown that the UTATE was feasible for use with 18-month-old toddlers. Furthermore, the UTATE resulted in data of good quality, that showed individual differences for most of the outcome measures. The split-half reliability was good for most of the variables. Next, a confirmatory factor analysis showed that the thirteen variables could be reduced to three latent constructs, reflecting orienting, alerting, and executive attention. Furthermore, a measurement invariance test showed that the same model was applicable to moderately preterm children, which allowed comparison of this group with the term born group regarding the mean scores on the latent constructs.

Differences between moderately preterm and term born children on the UTATE and other measures of attention were investigated in Chapter 6. Results showed that moderately preterm children performed worse on orienting and alerting skills as measured with the UTATE compared to term born peers at 18 months of age. Furthermore, a larger subgroup of preterm children showed suboptimal functioning on alerting as measured with observations and eye tracking. More than 40% of the preterm children had suboptimal scores on at least two out of the six alerting measures. This indicates that moderately preterm children especially seem to have difficulties with sustaining their attention for a longer period of time (i.e., alerting), already at toddler age. No differences were found for executive attention, or for attention as measured by questionnaires answered by mothers.

The role of biological factors, child characteristics, and maternal stimulation in the development of moderately preterm and term born children

In Chapter 7, an integrated model of gestational age, attention capacities and maternal stimulation when the children were 18 months of age was investigated in relation to cognitive functioning of the children at 24 months of age. An indirect relation between gestational age and cognitive functioning was found through maternal behavior and attention skills of the children: lower gestational age was related to more maternal behavior redirecting the children's attention, which was related to less orienting and alerting attention skills, that in turn predicted lower cognitive scores of the children at two years of age.

In addition, more maternal attempts to maintain the attention of their children were related to better cognitive scores at the age of two.

In conclusion, these studies showed that moderately preterm children are at increased risk for difficulties in sustaining attention for a longer period of time, for internalizing behavior problems, and for less developed receptive language skills as early as at toddler age. In addition, it was found that a cascade of biological risk, maternal stimulation, and attention capacities of the children was associated with cognitive outcome of the children at two years of age. The studies in this dissertation showed that moderately preterm children need attention!

Samenvatting

(Summary in Dutch)

Elk jaar worden er in Nederland meer dan 10.000 kinderen matig te vroeg geboren na een zwangerschapsduur van 32 tot 36 weken en 6 dagen. Dit is 6.1% van alle geboortes. Deze kinderen hebben een verhoogd risico op verschillende problemen, zowel op de korte als de lange termijn. Op schoolleeftijd laten matig te vroeg geboren kinderen vooral aandachtsproblemen zien. Deze aandachtsproblemen zouden onderliggend kunnen zijn aan moeilijkheden die ze ervaren met cognitief en sociaal functioneren, het leren en het gedrag thuis en op school. Ondanks groeiende interesse in de ontwikkeling van matig te vroeg geboren kinderen gedurende het laatste decennium, is er nog steeds weinig bekend over de ontwikkeling en het functioneren van deze kinderen op de peuterleeftijd. Het doel van deze dissertatie was dan ook om meer inzicht te verkrijgen in:

1. Verschillen in gedrag en ontwikkeling tussen matig te vroeg en op tijd geboren kinderen
2. Verschillen in aandachtvaardigheden tussen matig te vroeg en op tijd geboren kinderen
3. De rol van biologische factoren, kenmerken van het kind en maternale stimulatie in de ontwikkeling van matig te vroeg en op tijd geboren kinderen

De verworven wetenschappelijke inzichten zijn in deze dissertatie beschreven in een literatuurreview en vijf empirische studies. Voor de empirische studies is gebruik gemaakt van data van het STAP project: een longitudinale Studie naar de Aandachtvaardigheden van Premature kinderen. In dit project is een groep van 123 matig te vroeg en 103 op tijd geboren kinderen onderzocht op de leeftijd van 12, 18 en 24 maanden.

Gedrag en ontwikkeling van matig te vroeg geboren kinderen

Om een overzicht te krijgen van de huidige stand van de kennis met betrekking tot gedrag en ontwikkeling van matig te vroeg geboren kinderen is in Hoofdstuk 2 een overzicht gepresenteerd van de uitkomsten van eerdere onderzoeken. Op basis van 28 studies is geconcludeerd dat matig te vroeg geboren kinderen over het algemeen lagere IQ scores laten zien en meer schoolproblemen, gedragsproblemen en aandachtsproblemen ervaren dan op tijd geboren kinderen. Daarnaast zijn matig te vroeg geboren kinderen vaker gediagnosticeerd met ADHD dan op tijd geboren leeftijdsgenoten.

Deze voorgaande studies waren met name gericht op matig te vroeg geboren kinderen in de schoolleeftijd. Geconcludeerd werd dat meer informatie nodig was over het ontwikkelingstraject van matig te vroeg geboren kinderen en de leeftijd waarop hun problemen zich voor het eerst openbaren. Aangezien de eerste levensjaren een belangrijke en vormende periode zijn, is in Hoofdstuk 3 het gedrag en de ontwikkeling op peuterleeftijd onderzocht. Op de gecorrigeerde leeftijd van 24 maanden lieten matig te vroeg geboren kinderen meer internaliserende gedragsproblemen en minder taalbegrip zien dan op tijd geboren leeftijdsgenoten. Verschillen met betrekking tot cognitie, motoriek en taalproductie werden alleen gevonden wanneer de leeftijd niet gecorrigeerd werd voor prematuriteit. Dit laat zien dat het corrigeren van de leeftijd voor prematuriteit invloed heeft op de uitkomsten voor matig te vroeg geboren kinderen.

Aandachtvaardigheden van matig te vroeg geboren kinderen

Om gedetailleerd onderzoek te kunnen doen naar de aandachtvaardigheden van peuters was een nieuw instrument nodig. Daarom is door ons de *Utrecht Tasks for Attention in Toddlers using Eye Tracking*, de UTATE, ontwikkeld en dit instrument staat beschreven in Hoofdstuk 4. De UTATE bestaat uit vier taken om het functioneren van het *orienting* (vermogen om te focussen, focus los te laten en focus te wisselen), *alerting* (vermogen om alert te worden en te blijven), en executieve aandacht (doelgerichte aandacht) systeem te meten met behulp van een eye tracker. Uit een pilot studie bleek dat de UTATE goed uitvoerbaar is bij peuters van 18 maanden oud. Daarnaast leverde de UTATE data van goede kwaliteit en kwamen op de meeste uitkomstmaten individuele verschillen naar voren. De *split-half* betrouwbaarheid was voor de meeste variabelen goed. Bovendien liet een confirmatieve factor analyse zien dat voor op tijd geboren kinderen de 13 afzonderlijke variabelen gereduceerd konden worden tot drie latente constructen die *orienting*, *alerting* en executieve aandacht reflecteerden. Met een meetinvariantie-test werd aangetoond dat ditzelfde model ook toepasbaar was op de matig te vroeg geboren kinderen, wat betekent dat de gemiddelde scores op de latente constructen van deze groep kinderen vergeleken konden worden met de scores van op tijd geboren kinderen.

Verschillen in aandachtvaardigheden tussen matig te vroeg en op tijd geboren kinderen gemeten met de UTATE en andere metingen van aandacht zijn onderzocht in Hoofdstuk 6. Resultaten lieten zien dat matig te vroeg geboren kinderen minder goed presteerden op *orienting* en *alerting* vaardigheden gemeten met de UTATE vergeleken met op tijd geboren leeftijdsgenoten op de leeftijd van 18 maanden. Ook was er binnen de te vroeg geboren groep een grotere subgroep van kinderen die suboptimaal functioneerden op *alerting* vaardigheden gemeten met observaties en eye tracking. Daarnaast had meer dan 40% van de te vroeg geboren kinderen suboptimale scores op tenminste twee van de zes *alerting* maten. Dit impliceert dat matig te vroeg geboren kinderen al op peuterleeftijd meer moeilijkheden lijken te hebben met voornamelijk het volhouden van aandacht voor een langere tijd. Er zijn geen verschillen gevonden voor executieve aandacht of voor aandacht gemeten via vragenlijsten die ingevuld zijn door moeders.

De rol van biologische factoren, kindkenmerken en maternale stimulatie in de ontwikkeling van matig te vroeg en op tijd geboren kinderen

Om te onderzoeken welke factoren gerelateerd zijn aan cognitieve ontwikkeling is in Hoofdstuk 7 een geïntegreerd model onderzocht, waarbij gekeken is hoe zwangerschapsduur, aandachtvaardigheden van het kind en stimulatie van aandacht door de moeder, gemeten op de leeftijd van 18 maanden bepalend zijn voor het cognitief functioneren van de kinderen op de leeftijd van 24 maanden. Een indirecte relatie tussen zwangerschapsduur en cognitief functioneren werd duidelijk en bleek te lopen via maternaal gedrag en aandachtvaardigheden van de kinderen: kortere zwangerschapsduur was gerelateerd aan meer frequent gedrag van moeder gericht op het sturen van de aandacht van het kind, wat gerelateerd was aan mindere *orienting* en *alerting* vaardigheden. Deze aandachtvaardigheden bleken vervolgens lagere cognitieve scores van de kinderen op tweejarige leeftijd te voorspellen. Daarnaast werd gevonden dat meer gedrag van moeder dat gericht was op het vasthouden van de aandacht van het kind samenhing met betere cognitieve scores op tweejarige leeftijd.

Concluderend kan gesteld worden dat matig te vroeg geboren kinderen al op peuterleeftijd een verhoogd risico laten zien op moeilijkheden met het volhouden van aandacht voor een langere periode, voor internaliserende gedragsproblemen en voor minder ontwikkeld taalbegrip. Daarnaast werd gevonden dat een cascade van biologisch risico, maternale stimulatie en aandachtvaardigheden van het kind gerelateerd waren aan cognitieve uitkomsten op tweejarige leeftijd. De studies in deze dissertatie laten zien dat matig te vroeg geboren kinderen aandacht nodig hebben!

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About the author

Marjanneke de Jong was born on May 21st 1987 in 's-Hertogenbosch. After completing pre-university education (VWO) at the Scholengemeenschap Cambium in Zaltbommel in 2005, she studied Pedagogical and Educational Sciences (Bachelor) at the Radboud University Nijmegen. Subsequently, she attended the Research Master's program in Behavioral Science at the same university and graduated cum laude in 2010. In September 2010, she started her PhD project at the research group of Clinical Child and Family Studies at Utrecht University and wrote her dissertation on behavior and development of moderately preterm toddlers under supervision of prof. dr. Anneloes van Baar and dr. Marjolein Verhoeven. During her PhD, she also gained teaching experience by supervising student's Bachelor and Master theses. After her PhD, Marjanneke continues working as a lecturer at the research group of Clinical Child and Family Studies at Utrecht University and aspires to continue scientific research on behavior and development of (moderately) preterm born children.

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