Functioning of very preterm born children at preschool age: Follow-up of an early intervention programme
Verkerk, Gijs

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Functioning of very preterm born children at preschool age
Follow-up of an early intervention programme

Gijs Verkerk
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Follow-up of an early intervention programme

ACADEMISCH PROEFSCHRIFT

ter verkrijging van de graad van doctor
aan de Universiteit van Amsterdam
op gezag van de Rector Magnificus
prof. dr. D.C. van den Boom
ten overstaan van een door het college voor promoties
ingestelde commissie, in het openbaar te verdedigen in de Agnietenkapel
op vrijdag 10 januari 2014, te 14:00 uur

door

Gijsbertus Josephus Quirinus Verkerk
geboren te Leeuwarden
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               prof. dr. A.L. van Baar

Faculteit der Geneeskunde
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Chapter 1

General introduction
This thesis aims to contribute to improvements in the care of children born preterm with a gestation of less than 32 weeks and/or a birth weight below 1500 grams (VLBW). This thesis compares aspects of development of a cohort of VLBW children with their term born peers at 44 months of corrected age (CA). The VLBW children of this cohort participated in a randomised controlled trial which examined the effect of an early neurobehavioural intervention: The Infant Behavioral Assessment and Intervention Program (IBAIP). This thesis also describes the effects of the IBAIP at 44 months CA.

**Very Low Birth Weight Infants**

Due to advances in perinatal and neonatal care, increasing numbers of VLBW children are born alive. The mortality rates of those children born extremely preterm, defined as born with a gestational age (GA) of less than 28 weeks, are decreasing. Each year approximately 2500 VLBW infants are born alive in the Netherlands. In the future, assuming that the shift in viability towards a younger gestational age (≤ 24 weeks) will continue, the number of VLBW infants who survive, receive neonatal intensive care and are discharged from hospital, will almost certainly increase.

**Development of VLBW infants**

VLBW infants are at risk of severe impairment(s) such as cerebral palsy (CP), visual and/or hearing impairment and cognitive difficulties. However, the rate of severe impairment in VLBW infants is declining, and the care of VLBW infants is now more focused on decreasing the impact of moderate impairments (minor neurological dysfunction) and/or combinations of mild impairments. These moderate impairments occur more frequently than severe impairments and a combination of mild impairments can impact on an infant's capacity to use compensatory strategies.

VLBW infants may be delayed in their motor or cognitive development, for example: in their ability to change positions and move, in their learning capacity, and their ability to interact with their environment. VLBW infants may continue to experience difficulties throughout childhood. With regard to motor development, visual motor integration and visual perception, VLBW children are shown to be at a disadvantage. In addition, VLBW children are also at a disadvantage with regard to mental functioning, for example: impaired language development, cognition, executive functioning and attention. Behaviour problems and psychiatric disorders are also found more often in VLBW children. At the time of school entry it is not clear whether these disadvantages negatively affect the ability of VLBW children to achieve their learning potential. However, VLBW children tend to have lower levels of academic attainment than their term born peers.
The risk of impaired development continues until adult age. Despite that the majority of VLBW adolescents have similar levels of health and well being as their term born peers at 20 years of age 35-37, several studies have reported other problems at adult age. For example, VLBW adults tend to be less physically active during leisure time 35 and are three times more at risk of unemployment or non-participation in education at 19 years of age compared to their term born peers 38. Furthermore, the longitudinal study: Project on Preterm and Small for gestational age infants (POPS), in the Netherlands, showed that young adults who were born very preterm had impairments in multiple domains 38. Compared to term born peers, VLBW adults have less physical resilience 37,39, perform less well on motor 40, cognition 41,42, attention 43,44, executive functioning 42 and have more psychiatric disorders 45-47. Thus, the disadvantages for VLBW infants compared to term born peers continue into adulthood.

**Factors influencing development**

During the last trimester of gestation, the size of the brain increases four fold 48 and in this trimester axonal development and the development of myelin producing oligodendrocytes progresses rapidly 49. In VLBW infants these fast developmental changes happen outside of the womb's protection. Therefore, VLBW infants are at risk of impaired brain development 50-56 and consequently problems in psychomotor development 50,57-59.

Several risk factors play a role in the origin of developmental difficulties in VLBW infants: shorter gestation 26,60,61, lower birth weight 62-64, necrotising enterocolitis 65, sepsis 66, intraventricular hemorrhage (IVH) 67,68, periventricular leukomalacia 49, bronchopulmonary dysplasia (BPD) 69, a low parental socio-economic status 70,71 and male gender 70,72.

A preterm birth can impact significantly on family functioning 73,74. Mothers of VLBW infants tend to experience more stress 75,76, have a lower health related quality of life 77 and suffer more often from depression and anxiety 78. Parenting a VLBW infant can be more demanding than parenting a term born infant because VLBW infants are at risk of multiple regulatory problems concerning feeding, excessive crying and/or sleeping 79. In addition, VLBW infants can show behaviours which are difficult to read for parents 80, which is attributed to neurological immaturity in VLBW infants 80. Unclear behavioural signs and regulatory difficulties of the infant and high levels of stress and depression of the mother negatively influence the parent-infant interaction. Developmental outcomes for VLBW infants are likely to be determined by complex relationships and interactions between these biological and environmental factors 81.
Optimal nurturing conditions may support the development and self-regulation of VLBW infants. Responsive parenting is considered to be a crucial factor for helping to ensure optimal parent-infant interaction and attachment. Responsive parenting involves a level of interaction in which parents consistently exhibit high levels of warmth and acceptance towards their children and regard them as unique individuals. At the same time the parents also exhibit cognitively responsive behaviours towards their children via, for example, rich language input and maintaining the child’s attention. These responsive behaviours are contingently linked to the child’s signals. Research has shown that responsive parenting has a positive effect on the cognitive and social development of the child. Supporting a parent’s capacity to respond appropriately to their child may therefore be a key area for targeted intervention.

Interventions for VLBW infants

In the past decennia, several early intervention programmes have been developed which aim to optimise the neuro-behavioural development of VLBW infants. The best known, and most often used intervention is the Newborn Individualized Care and Assessment Program (NIDCAP) which is used in the neonatal intensive care unit (NICU). The NIDCAP aims to minimise the mismatch between the premature infant’s brain expectations and the experience of stress and pain in the NICU. NIDCAP promotes an appropriate physical environment in the NICU for infant and family; adapts the timing and organisation of medical and nursing interventions to the individual needs of each infant and family, and supports the parents’ capacity to nurture, cherish and take pride in supporting their infant’s development. Several systematic reviews have shown that NIDCAP is effective for enhancing the development of VLBW infants, although a recent systematic review concluded that there is insufficient evidence to show that NIDCAP improves long-term neurodevelopmental and short-term medical outcomes. In addition, a small RCT recently found better brain functioning and brain structure in those VLBW infants who received NIDCAP. However, long term follow-up studies of RCTs are still missing. These studies are required, for example, to determine the long term benefits for VLBW children and to justify the cost of the interventions.

Infant Behavioral Assessment and Intervention Program (IBAIP)

Besides the NIDCAP which is used in hospitals, several early developmental intervention programmes aim to enhance infant development after discharge from hospital. Post-discharge early intervention programmes for preterm (<37 weeks) infants have a positive influence on cognitive and motor outcomes during infancy, with cognitive benefits persisting up to 5 years of age. Specifically, interventions that focus on both parent-infant interaction and infant...
development have been found to be effective 96. However, for determining the long term effect of post-discharge early intervention programmes, RCTs with long term follow up are required 97,98.

One of the post-discharge early intervention programmes is the IBAIP: Infant Behavioral Assessment and Intervention Program 99. The IBAIP and the NIDCAP are both based on the Synactive Model of Newborn Behavioral Organization and Development 80,99. This model recognises that the infant's autonomic, motor, state and attention/interaction systems are continuously interacting with each other and the environment. The infant actively shapes his or her own environment by selecting information, reacting to this, and initiating and eliciting action in others. This neuro-behavioural process is visible in approach behaviour, self-regulatory behaviour and stress behaviour of the infant.

In the IBAIP, the neuro-behavioural competence of the infant is assessed with the Infant Behavioral Assessment (IBA) 100. The IBA is an observational tool that evaluates the infant's neuro-behavioural organisation during interactions of the infant with his or her environment. The IBA contains satisfactory psychometric properties in VLBW infants 101. The IBA discriminates between 113 well-defined behaviours in the autonomic, motor, state, and attention/interaction subsystem of neuro-behavioural functioning. Within the IBA the infant's behaviour is interpreted in relation to his or her capacity to approach information, exhibit stressful behaviour, and self-regulate during interaction. Self-regulatory behaviours are utilised by the infant in order to concentrate, cope and/or console him or herself 101. When self-regulatory behaviours are accompanied by a higher amount of approach behaviours the infant's self-regulatory competence may be considered to be more optimal. When regulatory behaviours are accompanied by a higher amount of stress behaviours, self-regulatory competence may be considered to be less optimal.

The IBAIP interventionist uses the IBA to sensitisate parents to the way in which their infant processes environmental information, because sensitive and responsive parent-infant interaction is beneficial for the development of the VLBW infant 85,102,103. The IBAIP interventionist helps parents adjust the environment to their infant's neuro-behavioural needs and to offer co-regulatory support during their infant's interactions. As this co-regulatory support focuses on midline orientation (e.g. bringing hands together and hands to mouth), which enhances postural control (e.g. head and body righting in different positions), it also addresses specific motor problems in VLBW infants 104. The IBAIP interventionist gives parents detailed information about their infant's development, in order to strengthen the parents' capacity to guide their infant's subsequent developmental steps and to support realistic expectations of their child's functioning 105. The programme aims to strengthen the parent's mindful attention towards their infant's behavioural expressions and development, which may enhance their emotional availability, intrinsic motivation, feelings of joy and confidence in themselves and their child 105.
Effectiveness of the IBAIP

In January 2004 a multi-centre RCT was undertaken to investigate the effectiveness of the IBAIP. VLBW infants were included until April 2006. In this study, the intervention infants (N=90) and their parents received 1 IBAIP session shortly before discharge, followed by 6 to 8 interventions at home, until the infant was 6 months of corrected age (CA). The control infants (N=86) received standard care and, when required, non-IBAIP trained paediatric physical therapy. Regular outpatient visits to the paediatrician were standard in both the intervention and control groups.

Results of the IBAIP

The children from the intervention group demonstrated significantly better motor, mental, and behavioural outcomes compared to the control group at 6 months CA. In addition, the mothers who had received IBAIP responded more sensitively when interacting with their infants, compared to the mothers in the control group.

At 24 months CA, the intervention group demonstrated better motor outcomes compared to the control group, but the mental and behavioural outcomes did not differ significantly from the control group. However, the intervention had a positive impact on mental development in high risk subgroups of infants with bronchopulmonary dysplasia and those with combined biological and social risk factors.

Follow-up study of the IBAIP at 44 months

In order to evaluate whether the positive effects of the IBAIP were sustainable, this cohort was reassessed at 44 months CA. This is an important time of transition for children in the Netherlands, in that they start school at 48 months of uncorrected age. This transition to school is a stressful experience for many children and there is an absence of research in this area pertaining to VLBW children. School-readiness includes several areas: physical, cognitive and social as well as a positive attitude towards learning. Participating in a large peer group in school demands a number of skills, e.g. appropriate levels of motor coordination, being able to perform routine daily activities and being able to adjust to the behavioural and social norms of the school. To summarise, it is not clear whether the levels of physical, cognitive and social skills in VLBW children are sufficient for coping with the demands of school life.

A comprehensive assessment was therefore collated which could be completed at home. Assessments were performed at home to avoid the extra stress of being assessed in hospital and to make participation in this study easier for parents and children. Mindful of the limited capacity of 4 year old children to carry out assignments on request, the assessment of each child...
took less than one hour. In addition, the parents completed questionnaires which related to
every-day behavioural situations of their child and were interviewed about their child’s level of
independence in daily activities. The investigator (GV) also systematically observed the behaviour
of the children during testing. The comprehensive assessment evaluated: word comprehension;
visual motor-integration including visual perception and motor coordination; cognitive skills, for
example, copying, problem solving and constructing; executive functioning including attention;
sensory processing, and levels of independence in daily activities. In addition, behaviour problems
were assessed.

In order to compare the performance of the VLBW children of the RCT with term born
children, the Amsterdam Public Health Service sent 200 letters to parents of children who would
reach 44 months within a few months. The comparison group of term born children and their
parents were matched with the VLBW group for gender, having a low educated mother and
having a mother born abroad.

**Objectives and outline of this thesis**

This thesis has 2 objectives.

The primary objective of this thesis is to evaluate the effect of the IBAIP at preschool age of 44
months CA. The VLBW children were extensively assessed in the domains of executive functioning,
behaviour, cognition, motor coordination, sensory processing and daily activities. Regarding this
primary objective the main question is: which aspects of development are positively influenced by
the IBAIP at preschool age?

The secondary objective is to compare outcomes of the VLBW children of the RCT with term
born peers. Regarding this objective the main question is: in which aspects of development do
VLBW children at preschool age differ from term born peers?
The primary objective is addressed in chapters 2 and 3 and the second objective is addressed in
chapters 2,3,4,5 and 6.

**Chapter 2** describes the effect of the IBAIP on sensory processing and daily activities at
preschool age. The performance of the VLBW children who received the intervention is compared
with the VLBW children of the control group. Comparisons with term born peers are also made.

**Chapter 3** presents the results of the IBAIP on executive functioning, motor coordination,
behaviour and cognition at preschool age. In addition, comparisons with term born peers are
made.
Attention problems hinder overall cognitive productivity\textsuperscript{110} and interfere with academic development\textsuperscript{111} thus it is important to identify these problems. Chapter 4 sets out the performance of VLBW preschoolers compared to term born peers on measurements of attention from 3 different sources: children’s performance on attention tasks, questionnaires completed by parents and behavioural observations by the investigator. In addition, the association between lower attention at preschool age and educational provision at 5½ years is evaluated.

It is useful to known whether VLBW children experience limitations in those daily activities which are important for participating in family life and with their peers when approaching school entry age. Chapter 5 evaluates whether VLBW children have limitations in daily activities when they start school and whether assessments at 24 months can predict these limitations in daily activities.

VLBW children are found to have combined difficulties in several developmental domains which appear to impede their academic performance at school age\textsuperscript{14,16,17,112}. Therefore, in Chapter 6 the VLBW children are compared to their term born peers with regard to multiple mild difficulties in several aspects of development. In addition, the association between developmental difficulties at 44 months CA and educational provision at 5½ years CA in VLBW children is explored.

Chapter 7 presents a general discussion and conclusions. Suggestions for improving the care of VLBW children and further research are given.
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Chapter 2

The Infant Behavioral Assessment and Intervention Program in Very Low Birth Weight Infants improves independency in mobility in daily activities at preschool age

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Bregje Houtzager
Joke Kok
Frans Nollet

The study presented in this chapter is a follow-up at preschool age of the multi-centre RCT of IBAIP versus usual care in VLBW infants. The RCT was performed in Amsterdam, The Netherlands (IBAIP RCT registered on controlled-trial.com number ISRCTN65503576).
ABSTRACT

Objective: To evaluate the effects of the Infant Behavioral Assessment and Intervention Program (IBAIP) in very low birth weight infants on sensory processing and daily activities at preschool age.

Study Design: Follow up of children included in a randomized controlled trial. Eighty-six infants were enrolled in post-discharge IBAIP until 6 months corrected age, and 90 infants received standard care. At 3½ years of age the Sensory Profile-Dutch version (SP-NL) and Pediatric Evaluation of Disability Inventory-Dutch version (PEDI-NL) were administered. For comparison, parents of 41 term born children also completed the SP-NL.

Results: Seventy-six children (88%) in the IBAIP group and 75 children (83%) in the control group were examined at 44 months corrected age. After adjustment for pre-randomization differences in perinatal characteristics, the IBAIP group outperformed the control group significantly on SP-NL domains of oral sensory processing and sensory processing related to endurance/tone and PEDI-NL domains of mobility. The control group only scored significantly lower than the term group on SP-NL domain endurance/tone. The VLBW groups performed significantly below PEDI-NL's norm.

Conclusion: In line with the positive developmental effects of the IBAIP until 24 months corrected age, independency in mobility in daily activities was improved at 3½ years.
INTRODUCTION

Children born preterm have significantly more neurodevelopmental problems than their age-related peers 1-4. These problems can persist into adulthood and impede participation in life situations 5-6. Various early intervention programs were developed in order to prevent these problems. Early intervention programs assist parents in supporting the resilience of their very preterm infants, aiming to prevent developmental difficulties at a later age. These programs demonstrated a small but significant impact on cognitive development at preschool age, but not on motor outcomes 7-9.

Our group carried out a randomized controlled trial (RCT) on the effect of the Infant Behavioral Assessment and Intervention Program© (IBAIP) 10 in very low birth weight (VLBW) infants and showed improved mental, motor and behavioural development at 6 months corrected age (CA) and improved motor development at 24 months CA 11,12. The results also suggested that the most vulnerable children benefitted most from the IBAIP.

IBAIP aims to enhance sensory processing and neurobehavioral stability during daily activities 10. The infant’s active participation in daily activities without stress is regarded as basic for adequate functional development during childhood 10,13-15. The purpose of this follow-up study is to determine whether the positive effects of the IBAIP in VLBW children sustain by improving sensory processing and daily activities at 3½ years CA. We also aimed to determine whether VLBW children differed from term born children and whether subgroups of VLBW children selectively benefitted from the intervention.

METHODS

A follow-up study was designed for children included in the multi-centre RCT of IBAIP in VLBW infants 11. The RCT was carried out in 7 hospitals in Amsterdam, The Netherlands. The Medical Ethics Committee of the Academic Medical Centre, Amsterdam approved this follow-up study. Recruitment of infants with a gestational age (GA) < 32 weeks, birth weight < 1500 grams, or both took place between January 2004 and April 2006. Infants were randomized in the intervention or control group with a computer-generated randomization scheme, stratified for GA (<30 and ≥ 30 weeks) and recruitment site, with twins assigned to the same group. A total of 176 infants participated; 86 infants received IBAIP and 90 infants received standard care. This trial was registered with the controlled-trials.com, number ISRCTN65503576.
Intervention infants received one IBAIP intervention shortly before discharge, from the hospital, and 6 to 8 interventions were provided at home, until they reached the CA of 6 months. The intervention implied that parents were guided by an IBAIP-trained paediatric physical therapist to observe their infant's attempts to process and explore information and to regulate themselves during an interaction with the parent, toy or both. The observations aimed to sensitize parents to their infant's strengths and needs to interact. Accordingly, parents were encouraged to offer co-regulation, to adjust the environment to the infant's needs, and/or to enjoy their infant's growing development and independency.

Both infants in the intervention and control group visited the outpatient clinics for regular consultations by paediatricians. When necessary, the infant's paediatrician was free to refer an infant to a paediatric physical therapist not trained in the IBAIP. In addition, both groups received 3 home visits, at term, 3 and 6 months, to assess the infant's neurobehavioral and developmental outcomes for the study.

When the children were 3½ years of age, parents were asked to participate with their children in a follow-up study. The percentage of mothers born abroad in this cohort is higher (39%) than average for the Dutch population. Parents were asked to complete a questionnaire concerning sensory processing in daily activities (Sensory Profile-Dutch version (SP-NL)) and were interviewed about the functional performance of their children and the caregiver's assistance in daily living (Pediatric Evaluation of Disability Inventory-Dutch version (PEDI-NL)). For the SP-NL, there are no Dutch norms. Therefore, a group of 42 term born children was matched with the VLBW group on the basis of country of birth of the mother, level of education of the mother, and sex. Inclusion criteria for the term group were: born after at least 37 weeks of gestation, birth weight at least 2500 grams and no referral to psychologist, paediatrician, or other physician because of developmental or health problems.

**Assessment instruments**

The SP-NL is a questionnaire that assesses the responses of children to naturally occurring sensory experiences in their every day environments. Responses to each of the 125 items of the SP-NL are rated on a 5-point Likert scale, in which 1 = always: when presented with the opportunity, the child responds in the manner described 100% of the time, and 5= never: when presented with the opportunity, the child never responds in this fashion, or 0% of the time. The 125 items can be categorised in 14 domain scores and 9 factor scales, only the 14 domain scores are used in this study. Higher scores represent better performance. The SP-NL is a reliable and valid measure.
The PEDI-NL measures independency in daily living of children from 6 months to 7½ years of age on the basis of a structured interview with a parent or caretaker. The PEDI-NL consists of 228 items. It assesses both the functional performance and the caregiver's assistance in the domains of self care, mobility and social function. Dutch norms for these domains exist, with a mean and standard deviation (SD) of 50 (10), respectively. Higher scores represent better performance. The psychometric properties of PEDI-NL are good.

**Assessment procedure**

A few months before the 176 VLBW children reached the corrected age of 44 months, their parents were asked to participate in this follow-up study. The Amsterdam's Public Health Service sent 200 letters to parents of term-born children, who would reach the age of 44 months in a few months, asking them to participate in the term comparison group. All consecutive term-born children were included until the term comparison group matched the VLBW group. The SP-NL questionnaire was sent to the parents who were willing to participate. During a home visit, one or both parents signed a form of written consent for participating in the follow-up study and were interviewed using the PEDI-NL. The examiner collected the SP-NL, and in case of missing values, parents were asked finally to complete the omitted items. The examiner (G.V.) was blinded for group assignment.

**Statistics**

Data were analyzed using Statistical Package for the Social Sciences 16.0 (SPSS Inc, Chicago, Illinois). Differences in sociodemographic and perinatal characteristics were analyzed with Student t tests or \( \chi^2 \) tests. Analysis of variance was used to analyze group differences on SP-NL and PEDI-NL, both uncorrected and corrected for baseline differences. Missing values of the SP-NL were handled according to the SP-NL manual. To compare the adjusted means of the VLBW groups with the PEDI-NL norm and SP-NL means (SD) of the term group, SD was calculated from the standard error. To get insight into a possible cultural bias on the PEDI-NL, we repeated this analysis in the subgroup of VLBW children born to native Dutch mothers. For the analyses of the differences in the groups on PEDI-NL and SP-NL, we set the level of significance at 0.01 instead of 0.05 to correct for multiple testing.

The effect of IBAIP appears to be large in the most vulnerable preterm infants. At 24 months CA, we found significant interaction effects between the IBAIP and bronchopulmonary dysplasia (BPD), defined as oxygen therapy > 36 weeks post menstrual age, and multiple risk children, but no interaction between IBAIP and GA <28 weeks, abnormal results on cranial ultrasound scanning (US), or low maternal education. We wanted to explore the effect of these factors again...
in this study, and were also interested in the influence of sex. However, the group of children with the multiple risk factor was too small and was not further evaluated. To explore the interactions, multiple regression analyses on the PEDI-NL and SP-NL domains were performed, by adding the interaction terms in separate analyses. Differences in characteristics at baseline were included in these multiple regression analyses.

RESULTS

From the original cohort of 176 VLBW infants, data were collected from 151 children (86%) at mean CA (SD) of 44 (0.5) months; 76 children of the IBAIP (88%) and 75 children of the control group (83%) participated. The participants did not differ significantly from the 25 non-participants for perinatal characteristics, socio-demographic factors, and mental developmental index and psychomotor developmental index at 24 months of Bayley Scales of Infant Development-II. However, children who did not participate were significantly less often first born ($p = 0.005$) and significantly more often had a father who was born outside the Netherlands ($p = 0.002$).

Despite random assignment, there were some significant differences in pre-randomization perinatal characteristics between the IBAIP group and control group (Table 1). More children in the IBAIP group were born at < 28 weeks gestation than in the control group. In addition, more children in the IBAIP group were oxygen dependent for a period of > 28 days, had septic periods before discharge, received surfactant, and received indomethacin. Comparisons between the IBAIP and control groups were adjusted for these perinatal differences.
### Table 1: Sociodemographic and perinatal characteristics

<table>
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<th>Control group (N=75)</th>
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<td>Paternal Age mean (SD), y</td>
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<td>36 (6.6)</td>
<td>.915</td>
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<td>49 (65)</td>
<td>.216</td>
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<td>44 (59)</td>
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<td>Father born in the Netherlands (%)</td>
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<td>Gender: male (%)</td>
<td>43 (57)</td>
<td>32 (43)</td>
<td>.104</td>
</tr>
<tr>
<td>Singleton (%)</td>
<td>54 (71)</td>
<td>59 (79)</td>
<td>.349</td>
</tr>
<tr>
<td>Family status of 2 parents (%)</td>
<td>62 (82)</td>
<td>68 (91)</td>
<td>.157</td>
</tr>
<tr>
<td>Perinatal factors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gestation (weeks), mean (SD)</td>
<td>29.6 (2.2)</td>
<td>30.0 (2.1)</td>
<td>.261</td>
</tr>
<tr>
<td>Gestation&lt;28 weeks, (%)</td>
<td>20 (26)</td>
<td>8 (11)</td>
<td>.020</td>
</tr>
<tr>
<td>Birth weight (g), mean (SD)</td>
<td>1228 (345)</td>
<td>1311 (322)</td>
<td>.193</td>
</tr>
<tr>
<td>Antenatal steroid use (%)</td>
<td>55 (72)</td>
<td>55 (73)</td>
<td>1.00</td>
</tr>
<tr>
<td>Indomethacin use (%)</td>
<td>17 (22)</td>
<td>7 (9)</td>
<td>.044</td>
</tr>
<tr>
<td>APGAR score at five minutes, mean (SD)</td>
<td>8.5 (1.6)</td>
<td>8.5 (1.4)</td>
<td>.937</td>
</tr>
<tr>
<td>Surfactant (%)</td>
<td>31 (41)</td>
<td>17 (23)</td>
<td>.023</td>
</tr>
<tr>
<td>Artificial ventilation (%)</td>
<td>37 (49)</td>
<td>26 (35)</td>
<td>.099</td>
</tr>
<tr>
<td>Oxygen therapy ≥ on 28 days (%)</td>
<td>32 (42)</td>
<td>15 (20)</td>
<td>.005</td>
</tr>
<tr>
<td>Oxygen therapy at 36 wk pma (%)</td>
<td>22 (29)</td>
<td>8 (11)</td>
<td>.007</td>
</tr>
<tr>
<td>Postnatal steroid use (%)</td>
<td>5 (7)</td>
<td>2 (3)</td>
<td>.442</td>
</tr>
<tr>
<td>Cranial ultrasound abnormal (%)</td>
<td>27 (36)</td>
<td>19 (25)</td>
<td>.174</td>
</tr>
<tr>
<td>IVH grade I + II / III + IV *</td>
<td>13 / 5</td>
<td>8 / 3</td>
<td>1.00</td>
</tr>
<tr>
<td>Ventricular dilatation (%)</td>
<td>1 (1)</td>
<td>3 (4)</td>
<td>.367</td>
</tr>
<tr>
<td>Necrotizing enterocolitis (%)</td>
<td>4 (5)</td>
<td>1 (1)</td>
<td>.367</td>
</tr>
<tr>
<td>Septic periods before discharge (%)</td>
<td>46 (60)</td>
<td>30 (40)</td>
<td>.015</td>
</tr>
</tbody>
</table>

#### At Discharge

<table>
<thead>
<tr>
<th></th>
<th>IBAIP group</th>
<th>Control group (N=75)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days post menstrual age, mean (SD)</td>
<td>266 (17)</td>
<td>263 (17)</td>
<td>.241</td>
</tr>
<tr>
<td>Length of hospitalization days, mean (SD)</td>
<td>59 (30)</td>
<td>51 (25)</td>
<td>.080</td>
</tr>
<tr>
<td>Weight (g), mean (SD)</td>
<td>2430 (455)</td>
<td>2370 (418)</td>
<td>.402</td>
</tr>
<tr>
<td>Oxygen supply at discharge (%)</td>
<td>5 (7)</td>
<td>3 (4)</td>
<td>.719</td>
</tr>
</tbody>
</table>

Independent sample t-tests and χ² tests.

* Cerebral haemorrhage (IVH) was defined according to Papile 29
At 44 months CA, 8 children (5%) received a diagnosis of cerebral palsy (CP) by a paediatrician or child neurologist, 5 in the control group and 3 in the IBAIP group ($p = .494$). From the 57 parents of term born children who were willing to participate, 42 were selected. The matched term comparison group consisted of 21 boys (51%), 16 children (39%) with mothers who were not born in the Netherlands, 14 children (36%) with mothers who had ≤ 4 years education after primary school, and mean (SD) age of 44 (0.4) months. One of the 42 children in the term comparison group was excluded because he was referred to a physician for developmental delay. The Figure shows a flowchart of the children included in this study and the collected data of the study groups at 44 months CA.

**Figure**: Flowchart

Overview data collection of 151 VLBW children and 41 term born children at 44 months of corrected age since randomization during neonatal period.

**SP-NL, sensory processing in every day environments**

There were no differences between the IBAIP group and the control group on the SP-NL at a significance level of .01. Adjusted for baseline differences, the IBAIP group performed significantly better than the control group on 2 of the 14 SP-NL domains (Table 2), oral sensory processing and sensory processing related to endurance/tone. The scores of both VLBW groups were comparable with the term comparison group, except that the control group scored significantly lower on the domain of sensory processing related to endurance/tone domain (Table 2).
### Table 2: Sensory Profile-NL (SP-NL)

<table>
<thead>
<tr>
<th>Intervention effect</th>
<th>IBAIP (n=75)</th>
<th>Control (n=74)</th>
<th>Term (n=40)</th>
<th>Adj. Mean (SD)</th>
<th>p</th>
<th>p1</th>
<th>p2</th>
<th>BPD</th>
<th>GA</th>
<th>US</th>
</tr>
</thead>
<tbody>
<tr>
<td>Auditory processing</td>
<td>33.4 (4.9)</td>
<td>32.9 (4.9)</td>
<td>33.3 (3.7)</td>
<td>.544</td>
<td>.910</td>
<td>.653</td>
<td>.572</td>
<td>.096</td>
<td>.187</td>
<td></td>
</tr>
<tr>
<td>Visual processing</td>
<td>39.3 (5.3)</td>
<td>38.9 (5.3)</td>
<td>39.4 (4.5)</td>
<td>.587</td>
<td>.919</td>
<td>.614</td>
<td>.312</td>
<td>.122</td>
<td>.192</td>
<td></td>
</tr>
<tr>
<td>Vestibular processing</td>
<td>49.8 (5.1)</td>
<td>49.0 (5.1)</td>
<td>49.2 (3.7)</td>
<td>.323</td>
<td>.513</td>
<td>.827</td>
<td>.284</td>
<td>.014</td>
<td>.636</td>
<td></td>
</tr>
<tr>
<td>Touch processing</td>
<td>82.1 (7.7)</td>
<td>79.8 (7.7)</td>
<td>81.1 (5.7)</td>
<td>.074</td>
<td>.472</td>
<td>.351</td>
<td>.026</td>
<td>.011</td>
<td>.032</td>
<td></td>
</tr>
<tr>
<td>Multi sensory processing</td>
<td>30.2 (3.8)</td>
<td>29.9 (3.8)</td>
<td>30.6 (2.9)</td>
<td>.662</td>
<td>.562</td>
<td>.312</td>
<td>.336</td>
<td>.840</td>
<td>.770</td>
<td></td>
</tr>
<tr>
<td>Oral sensory processing</td>
<td>55.5 (7.0)</td>
<td>52.0 (7.0)</td>
<td>52.5 (6.9)</td>
<td>.003</td>
<td>.030</td>
<td>.715</td>
<td>.135</td>
<td>.076</td>
<td>.044</td>
<td></td>
</tr>
<tr>
<td>Sensory processing related to endurance and tone</td>
<td>43.4 (4.7)</td>
<td>40.8 (4.6)</td>
<td>43.7 (1.7)</td>
<td>.001</td>
<td>.698</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
<td>235</td>
<td>0.03 (4.2)</td>
<td></td>
</tr>
<tr>
<td>Modulation related to body position/movement</td>
<td>44.1 (5.9)</td>
<td>42.1 (5.8)</td>
<td>43.2 (5.5)</td>
<td>.048</td>
<td>.427</td>
<td>.327</td>
<td>&lt;.001</td>
<td>0.066</td>
<td>0.01 (6.7)</td>
<td></td>
</tr>
<tr>
<td>Modulation of movement affecting activity level</td>
<td>27.8 (4.8)</td>
<td>27.7 (4.8)</td>
<td>26.4 (4.6)</td>
<td>.825</td>
<td>.134</td>
<td>.164</td>
<td>.053</td>
<td>.050</td>
<td>.098</td>
<td></td>
</tr>
<tr>
<td>Modulation of sensory input affecting emotional responses</td>
<td>18.3 (2.4)</td>
<td>17.7 (2.4)</td>
<td>18.3 (2.5)</td>
<td>.184</td>
<td>1.00</td>
<td>.212</td>
<td>.092</td>
<td>.230</td>
<td>.084</td>
<td></td>
</tr>
<tr>
<td>Modulation of visual input on emotions and activity level</td>
<td>16.9 (2.6)</td>
<td>16.6 (2.6)</td>
<td>16.3 (2.2)</td>
<td>.413</td>
<td>.217</td>
<td>.537</td>
<td>.023</td>
<td>.001 (3.6)</td>
<td>.447</td>
<td></td>
</tr>
<tr>
<td>Emotional/social responses</td>
<td>74.8 (8.9)</td>
<td>73.1 (9.0)</td>
<td>76.6 (5.5)</td>
<td>.256</td>
<td>.247</td>
<td>.027</td>
<td>.053</td>
<td>.132</td>
<td>.106</td>
<td></td>
</tr>
<tr>
<td>Behavioral outcomes of sensory processing</td>
<td>19.8 (3.5)</td>
<td>19.4 (3.6)</td>
<td>20.0 (2.7)</td>
<td>.585</td>
<td>.754</td>
<td>.358</td>
<td>.079</td>
<td>.056</td>
<td>.239</td>
<td></td>
</tr>
<tr>
<td>Items indicating threshold for response</td>
<td>13.6 (2.2)</td>
<td>13.2 (2.2)</td>
<td>13.9 (1.0)</td>
<td>.279</td>
<td>.416</td>
<td>.059</td>
<td>.010 (2.6)</td>
<td>.859</td>
<td>.068</td>
<td></td>
</tr>
</tbody>
</table>

**Intervention effect:** Adjusted Means and SD corrected for pre-randomization differences: use of surfactant, indometacin, oxygen ≥ 28 days, sepsis before discharge, <28 weeks of gestation.

Higher scores represent better performance.

p IBAIP (n=75) compared with Control (n=74) with analysis of variance. p1 IBAIP (n=75) adjusted mean (SD) compared with term comparison group (n=40) with independent sample t test. p2 Control (n=74) adjusted mean (SD) compared with term comparison group (n=40) with independent sample t test.

In case of a significant interaction term with p < .01 the mean difference is presented between the intervention and control children with the specific risk factor (i.e. having BPD, GA < 28 weeks, abnormal cranial US results). No significant interaction effects were found between intervention and sex and education level of the mother.
**PEDI-NL, self care, mobility and social function**

On the PEDI-NL there were no differences between the IBAIP group and the control group at a significance level of .01. Adjusted for baseline differences, the IBAIP group significantly outperformed the control group on the PEDI-NL mobility skills and mobility assistance (Table 3). The adjusted mean differences were 4 points on the mobility skills domain and 7 points on mobility assistance domain. Comparing the scores of the VLBW groups with the Dutch norm of 50 revealed a developmental delay in both VLBW groups in 3 of the 6 domains namely self care assistance, mobility skills and social function assistance (Table 3). For mobility skills and social function assistance these differences surpassed the minimal clinically important difference of 11 points for both VLBW groups. In addition, the control group but not the IBAIP group scored significantly below the Dutch norm on 2 other domains; self care skills and mobility assistance. When comparing a subgroup of VLBW children born to native Dutch mothers with the Dutch norm, a developmental delay (p <.001) was found in the same domains as the total VLBW groups; self care assistance, mobility skills and social function assistance. Furthermore, also in this subgroup the delay for mobility skills and social function assistance surpassed the minimal clinically important difference.

Positive significant interaction effects (p ≤.01) based on multiple regression analyses were found between intervention and BPD for 3 domains of SP-NL, between intervention and GA<28 weeks for one domain of SP-NL and between abnormal US for 2 domains of SP-NL (Table 2). No significant interaction effects were found between intervention and sex or intervention and education level of the mother for SP-NL. Positive significant interaction effects were found between intervention and BPD for 2 domains of PEDI-NL and intervention and boys for 2 domains of PEDI-NL (Table 3). No significant interaction effects were found between intervention and US, intervention and GA <28 weeks, or intervention and education level of the mother for PEDI-NL. To summarize, IBAIP seemed more effective in subgroups of infants with BPD, boys, infants born at gestational age <28 weeks and infants with abnormal US.
Table 3: Pediatric Evaluation of Disability Inventory

<table>
<thead>
<tr>
<th></th>
<th>Intervention effect</th>
<th>Intervention effects of intervention:</th>
<th>BPD</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IBAIP</td>
<td>Control</td>
<td>Norm</td>
<td>p</td>
</tr>
<tr>
<td>Self care skills</td>
<td>49.2 (9.1)</td>
<td>45.7 (9.1)</td>
<td>50 (10)</td>
<td>.023</td>
</tr>
<tr>
<td>Self care assistance</td>
<td>44.4 (8.0)</td>
<td>42.0 (8.0)</td>
<td>50 (10)</td>
<td>.063</td>
</tr>
<tr>
<td>Mobility skills</td>
<td>39.0 (7.8)</td>
<td>34.9 (7.8)</td>
<td>50 (10)</td>
<td>.002</td>
</tr>
<tr>
<td>Mobility assistance</td>
<td>52.4 (11.1)</td>
<td>45.8 (11.1)</td>
<td>50 (10)</td>
<td>.001</td>
</tr>
<tr>
<td>Social function skills</td>
<td>49.2 (7.5)</td>
<td>47.8 (7.5)</td>
<td>50 (10)</td>
<td>.261</td>
</tr>
<tr>
<td>Social function assistance</td>
<td>39.3 (6.7)</td>
<td>36.6 (6.7)</td>
<td>50 (10)</td>
<td>.016</td>
</tr>
</tbody>
</table>

Intervention effect: Adjusted means and (SD) corrected for pre-randomization differences: use of surfactant, indometacin, oxygen ≥ 28 days, sepsis before discharge, <28 weeks of gestation.

Higher scores represent better performance.

p IBAIP group (n=76) compared with control group (n=74) with analysis of variance.

p’ IBAIP group (n=76) adjusted mean (SD) compared with PEDI-NL norm with independent sample t-test.

p’’ Control group (n=74) adjusted mean (SD) compared with PEDI-NL norm with independent sample t-test.

In case of a significant interaction term with p <.01 the mean difference is presented between the intervention and control children with the specific risk factor (i.e. having BPD and boys). No significant interaction effects were found between intervention and GA < 28 weeks, abnormal cranial US results and education level of the mother.
DISCUSSION

We have assessed sensory processing and independency in daily activities at 44 months CA to determine whether positive outcomes in children who received IBAIP were sustained. In line with the improved developmental outcomes of the IBAIP at 24 months CA\textsuperscript{12} better functional outcomes at 44 months CA were found specifically covering the motor domain. Furthermore, the 2 sensory processing domains improved by the IBAIP relate to body awareness, postural control and stamina. Although non-significant, all other outcomes were in the same direction favouring the IBAIP group.

In agreement with the findings at 24 months CA\textsuperscript{12}, the outcomes at 44 months suggest that IBAIP may be particularly effective in the most vulnerable children born preterm. At preschool age, boys, infants with BPD, infants born with a GA < 28 weeks, and infants with abnormal US results appeared to profit most from the intervention. The outcomes of this study support that the effect of the IBAIP sustains until 44 months CA, and improved motor development at 24 months seems to lead to better performance of daily activities especially independency in mobility.

In contrast to other studies,\textsuperscript{7-9,23-27}, this post-discharge intervention study reported functional motor improvements in very preterm born infants at the preschool age of 44 months. IBAIP helped the parents support their infant’s self-regulating motor actions (for instance; hands to the midline, hand to mouth, holding on, sucking, and support for feet) and to adjust the sensory input to their infant’s needs\textsuperscript{10,11}. We hypothesize that this may have improved the quality of the sensory motor experiences and the body awareness of infants that received IBAIP, which may have resulted in better performance of daily activities at preschool age\textsuperscript{13,14}. The intervention may have been particularly effective in the most vulnerable infants as their parents are most likely to need specific sensitivity and nurturing qualities to achieve the postural control and optimal sensory processing that these infants often lack. In these vulnerable infants neurobehavioral support may have been particularly important to enable the infant’s successful participation with their environment. However, the subgroups of BPD, abnormal US results, and GA<28 weeks are too small to draw firm conclusions. Further research on the effect of IBAIP on these groups is recommended.

Specific aspects of our study design, apart from the intervention program, may have influenced the outcome. The implementation by IBAIP trained paediatric physical therapists and the use of functional measurements may have played a role in the detection of the positive outcomes in the motor domain at preschool age. The PEDI was developed for children with physical limitations and is commonly used in rehabilitation settings. The outcomes of this study show that the PEDI may also be useful to monitor functional development in preterm infants with time.
The term born comparison children performed comparably with the VLBW groups on nearly all domains of the SP-NL, except that the control group scored significantly lower on the sensory processing related to endurance/tone domain. The small number of term born comparison children may have limited the statistical power to detect a significant difference in groups. However, no trends in any specific direction could be detected either. It seems that our VLBW children performed comparable to term born children on the SP-NL. We can not verify this against normative data because of the absence of Dutch norms for the SP-NL.

Both VLBW groups had a developmental delay in the PEDI-NL domains mobility skills, self-care assistance and social function assistance. Separate analyses of VLBW children born to native Dutch mothers indicated that the developmental delay could not be attributed to a cultural bias. Apparently, mobility as measured with the PEDI-NL is less developed in VLBW children compared with their peers. This is in line with a meta-analysis that concluded that motor difficulties in VLBW children persist until adolescence. The PEDI-NL assesses both the child's functional abilities (skills) and the level of assistance from the caregiver. Although the self-care and social function skills of the VLBW children were comparable with the norm, they were more assisted on these domains than their peers. VLBW children may have problems performing these skills in daily situations, or their parents tend to give more assistance then necessary.

Strengths of our follow up study are a high response rate of 86% and the use of a matched comparison group. This is notable for a cohort in which 39% percent of the mothers were not born in the Netherlands.

Because parents were aware of their group allocation, this might have influenced their responses on the SP-NL and PEDI-NL and contributed to the positive outcomes. However, we think this could not explain all the positive outcomes because this follow-up was performed > 3 years after the end of the intervention.

Although children who received IBAIP still differ considerably from term born children at preschool age, their gains in daily activities may support their participation in age appropriate activities and their next developmental steps. Moreover, these gains may contribute to a higher quality of life at preschool age. Further studies evaluating the effect of IBAIP at 3½ and 5 years are currently underway.

Acknowledgements

We thank all the participating parents and children, the Amsterdam's Public Health Service for help with collecting the matched term born comparison group, and M.J.Wolf for her assistance in the design of this study and support during data collection.
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IBAIP improves independency in mobility at preschool age


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Chapter 3

The Infant Behavioral Assessment and Intervention Program
in very low birth weight infants; outcome on executive
functioning, behaviour and cognition at preschool age

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The study presented in this chapter, is a follow-up at preschool age of the multi-centre RCT of IBAIP versus usual care in VLBW infants. The RCT was performed in Amsterdam, The Netherlands (IBAIP RCT registered on controlled-trial.com number ISRCTN65503576).
ABSTRACT

Background: The Infant Behavioral Assessment and Intervention Program (IBAIP®) improved motor function at 24 months, and mental and behavioural development in high risk subgroups of very low birth weight (VLBW) infants.

Aim: To determine IBAIP’s effects on executive functioning, behaviour and cognition at preschool age.

Study design: Follow-up of a randomised controlled trial (RCT).

Subjects: At 44 months corrected age, all 176 VLBW infants were invited for follow-up. Forty-one term born children were assessed for comparison.

Outcome measures: Visual Attention Task (VAT), Gift delay, Peabody Picture Vocabulary Test III-NL (PPVT), Visual motor integration tests and Miller assessment for preschoolers. Parents completed Behavior Rating Inventory of Executive Function-Preschool (BRIEF-P) and Child Behavior Checklist (CBCL).

Results: At preschool age, 76 (88%) children of the intervention group and 75 (83%) children of the control group participated. There were no significant differences between the intervention and the control group. However, positive interaction effects between intervention and infants with bronchopulmonary dysplasia, infants born at gestational age < 28 weeks, and infants of low educated mothers were found on CBCL, CBCL and BRIEF-P, and PPVT respectively. Most interaction effects exceeded 1 standard deviation in favour of the intervention children. The 151 VLBW children performed significantly worse than the term born children on the VAT, BRIEF-P and CBCL.

Conclusion: IBAIP effects in VLBW children did not sustain until preschool age on executive functioning, behaviour and cognition. However, the most vulnerable children had a clinical relevant profit from IBAIP. VLBW children performed worse than the term born children.
INTRODUCTION

Children born very preterm and/or with very low birth weight (VLBW) experience significantly more problems with self regulation, executive functions, behaviour and cognition than term born peers. These problems become apparent during development and persist until adolescence. During infancy, self-regulatory competence refers to the ability to interact successfully with the environment without experiencing distress. Self-regulation at infant age is regarded as the foundation for the development of executive functions. Executive functions, in turn, are a collection of self-regulatory processes responsible for guiding, directing and managing cognitive, emotional, and behavioural functions particularly during novel problem solving and are crucial for the development of both cognitive and social capacities. These executive functions include inhibitory control and attention flexibility. Deficits in executive functions might lead to academic underachievement.

Early intervention programs assist parents to support the resilience of their very preterm infants, aiming to prevent developmental difficulties at a later age. The Infant Behavioral Assessment and Intervention Program (IBAIP©) aims to improve the infant's development by supporting the infant's self-regulation during interactions with the environment. Our group performed a multicentre randomised controlled trial (RCT) on the IBAIP in VLBW infants. The intervention implied that parents were guided by an IBAIP-trained paediatric physical therapist to observe their infant's attempts to approach and explore information and to regulate themselves during an interaction with the parent and/or a toy. The observations aimed to sensitize parents to their infant's strengths and needs to interact. Accordingly, parents were encouraged to offer co-regulation, to adjust the environment to their infant's needs, and to enjoy their infant's growing development and independency. Infants in the intervention group received one IBAIP intervention shortly before discharge and 6 to 8 interventions were provided at home, up to the corrected age (CA) of 6 months. The infants in the control group received standard care. A positive effect of the IBAIP was found on motor function, self-regulation, behaviour and mental development at the end of the intervention. At 24 months, IBAIP improved motor development, while for infants with bronchopulmonary dysplasia (BPD) and for infants with combined biological and social risk factors also improvements in mental and behavioural development were found. At 24 months no interaction was found between IBAIP and gestational age (GA) < 28 weeks, abnormal cranial ultrasound scanning (US) or low maternal education. To examine whether there was still an effect of the IBAIP just before the children start primary education we assessed them at 44 months CA and reported that IBAIP improved independency in mobility and sensory processing. Especially in children of the subgroups BPD, GA < 28 weeks, boys and the group with an abnormal US the IBAIP had effect at 44 months.
The aim of this follow-up study was to determine whether the IBAIP has effects on executive functions, behaviour and cognition at preschool age. In addition, we wanted to determine whether subgroups of VLBW children benefitted specifically from IBAIP and whether VLBW children differed from term born children.

PATIENTS AND METHODS

Participants and procedure

This study is a follow-up at preschool age of the multi-centre RCT of IBAIP versus usual care in VLBW infants. The Medical Ethics Committee of The Academic Medical Centre in Amsterdam approved this follow-up study. Recruitment of infants with a gestational age (GA) < 32 weeks and/or birth weight < 1500 gram took place between January 2004 and April 2006. Infants were randomised into the intervention group (IBAIP group) or control group with a computer-generated randomisation scheme, stratified for GA (< 30 and ≥ 30 weeks) and recruitment site, with twins assigned to the same group. One hundred seventy six infants participated; 86 infants received IBAIP and 90 infants received standard care.

A group of term born children matched with the VLBW group (IBAIP and control group combined) on the basis of country of birth of the mother, level of education of the mother (≤ 10 or >10 years of education), and gender was composed. Inclusion criteria for the term group were; born after at least 37 weeks of gestation, birth weight at least 2500 grams, no referral to psychologist, paediatrician or other physician because of developmental or health problems.

A few months before the 176 VLBW children reached the age of 3½ years, their parents were asked to participate in this follow-up study. The Amsterdam's Public Health Service sent 200 letters to all parents of term born children who would be 44 months old in a few months, asking them to participate. All term born children were consecutively included in the term group until the term group matched the VLBW group. The Child Behavior Checklist for ages 1½ - 5 years (CBCL) and the Behavior Rating Inventory of Executive Function-Preschool version (BRIEF-P) were sent to all participating parents.

During the home visit parents gave their written informed consent, answered questions about the child’s primary language and whether their child had received any paramedical support during the last 2 years. The children completed tests within 60 minutes while seated in a chair adjusted to their size. All tests were administered at home in the morning in a fixed order by the same assessor, an occupational therapist, who was blinded for group assignment of the VLBW children.
Testing started with word comprehension. If Dutch was not the child’s primary language, the assessor asked the parents to repeat the verbal instructions of the next assessments in the child’s first language. If parents did not understand the content of an item of the BRIEF-P and/or CBCL, the item was translated and/or explained.

Assessments

At 44 months (age range of 43.0 – 47.0 months) the following was assessed: executive functions, behaviour and for cognition; word comprehension, visual motor integration and cognitive skills.

Executive Functioning

Parents completed a Dutch translation of the BRIEF-P 15. This questionnaire assesses executive functioning at home and in preschool environments and measures 5 domains of executive functioning namely Inhibit, Shift, Emotional control, Working memory and Plan / organize. The Global Executive Composite (GEC) refers to the sum score of all items in the BRIEF-P. The raw scores of the domains and the GEC were converted into T scores based on a gender and age related norm of American children with a mean of 50 and standard deviation (SD) of 10. Higher scores refer to a higher degree of executive dysfunction 8. All scoring procedures were executed according to the manual 8.

The Visual Attention Task (VAT) of the Attention/Executive Functions domain of the Developmental neuropsychological assessment was administered 16. This paper and pencil visual search task records the speed and accuracy with which a child is able to select visual targets. The total completion time, the number of omissions and the number of commissions are recorded and composed into a total score. Based on an age related norm of American children a scaled score is calculated. The scaled score has a mean (SD) of 10 (3), range 1-19. A higher score reflects a more favourable performance.

The Gift delay task for delayed gratification measures behavioural inhibition in young children 17. Children sit in a chair turned 180° away from the experimenter and are instructed not to look while a gift is wrapped up for them. After 60 seconds, the child receives the wrapped up present. The procedure was recorded by camera to enable coding. Coding included peeking, yes or no, and the time until peeking. There are no norm data available for this task.
Behaviour

The child's behavioural and emotional functioning was assessed with the CBCL \(^\text{18}\). The CBCL is a questionnaire that consists of 99 statements about the child's behaviour. It yields scores for Internalizing behaviour problems, Externalizing behaviour problems and a Total problems score. In this study, the syndrome scales scores are reported as well (Emotional reactive, Anxious / depressed, Somatic complaints and Withdrawn of the Internalizing behaviour scale, Attention problems and Aggressive behaviour of the Externalizing behaviour scale). The raw scores of the scales were converted into T scores using the American norm data \(^\text{18}\). A higher score reflects more behavioural problems.

Word comprehension

Word comprehension was assessed with the Peabody Picture Vocabulary Test–III-NL (PPVT) \(^\text{19}\). The PPVT is a widely used norm-referenced test of receptive vocabulary for ages 2.5 to 90 years. Standard scores have a mean of 100 and a SD of 15. The PPVT is validated for the Dutch population \(^\text{19}\). Children with a non-Dutch primary language were excluded in the Dutch norm data.

Visual Motor Integration

The Beery-Buktenica Developmental Test of Visual-Motor Integration with the subtests Visual Motor Integration (VMI), Visual Perception (VP) and Motor Coordination (MC) were performed \(^\text{20}\). The standard scores have a mean (SD) of 100 (15). The VMI, VP and MC are not validated for the Dutch population, but broadly applied in clinical and research practice.

Cognitive skills

A selection of 8 out of 27 items of the Miller Assessment for Preschoolers (MAP) was used to screen the cognitive abilities of construction, figure-ground perception, stereognosis, copying and problem solving \(^\text{21}\). A child has a sufficient performance if he/she (1) constructs a tower of at least eight blocks out of sixteen (Tower), (2) copies two block constructions (Block design), (3) completes two puzzles within one minute each (Puzzle), (4) draws at least one part of a person within three minutes (Draw a person), (5) finds at least five of the seven hidden stars in a picture within one minute (Figure ground perception), (6) recognizes at least three of the four objects (Stereognosis), (7) imitates at least two out of three postures within three seconds each (Imitation of postures), and (8) imitates the handling of a maze within 5 seconds (Maze). A sufficient score for an item corresponds to more than 25\textsuperscript{th} percentile of the performance of American children \(^\text{21}\).
Data Analyses

Data were analysed using Statistical Package for the Social Sciences version 16.0. (SPSS Inc, Chicago, Illinois). Differences in sociodemographic and perinatal characteristics were analysed using independent samples t-tests or Chi-square tests. Analysis of Variance uncorrected as well as corrected for pre randomisation baseline differences was used to analyse group differences on VAT, Gift delay (peeking time), BRIEF-P, CBCL, PPVT, VMI, VP and MC. The Chi-square test was used to identify group differences on the MAP and Gift delay (peeking yes or no). To correct for multiple testing we used a significance level of 0.01.

Interaction effects were explored for intervention and BPD (definition according to Jobe), gender, gestational age less than 28 weeks, abnormal cranial ultrasound (defined as any degree of IVH, and/or PVL and/or ventricular dilatation), and mothers who received ≤ 10 years of education. To explore the interactions, multiple regression analyses on the measurements of executive functions, behaviour and cognition were performed by adding the interaction terms in separate analyses. Variables that differed at baseline were included in these multiple regression analyses. Because twins and triplets were assigned to the same group and this could have biased the outcomes, we repeated the analyses with only one, randomly chosen, multiplet member.

RESULTS

At a mean (SD) corrected age of 44 (0.5) months 151 children (86% of the original cohort) participated; 76 children of the IBAIP group (88%) and 75 of the control group (83%). Participants did not differ significantly from the 25 non-participants with respect to perinatal characteristics, socio-demographic factors, mental developmental index and psychomotor developmental index at 24 months of the Bayley Scales of Infant Development-II. However, children not participating were significantly less often first born (p < 0.005) and had significantly more often a father who was born outside the Netherlands (p < 0.002).

Despite randomisation, there were some significant differences in pre-randomisation perinatal characteristics between the IBAIP group and the control group (Table 1). More children in the IBAIP group were born < 28 weeks gestation than in the control group. In addition, more children in the IBAIP group were oxygen dependent for a period of more than 28 days, had septic periods before discharge, had received surfactant, and had received indomethacin. Comparisons between the VLBW groups were adjusted for these perinatal differences.

Between 6 and 24 months CA, significantly less children of the IBAIP had received paramedical support (paediatric physical therapy and/or occupational therapy and/or speech therapy compared to the control group 10 (13%) versus 21 (24%) (p < 0.038). At 44 months CA, 18 (24%) children
of the IBAIP group versus 26 (35\%) children of the control group had received paramedical support during the last 2 years (\(p = .138\)).

**Table 1: Sociodemographic and perinatal characteristics**

<table>
<thead>
<tr>
<th></th>
<th>IBAIP N=76</th>
<th>Control N=75</th>
<th>(p)</th>
<th>Term N=41</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Social factors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maternal age mean (SD), years</td>
<td>32 (5.3)</td>
<td>32 (5.4)</td>
<td>.906</td>
<td>n.a.</td>
</tr>
<tr>
<td>Paternal age mean (SD), years</td>
<td>36 (7.4)</td>
<td>36 (6.6)</td>
<td>.915</td>
<td>n.a.</td>
</tr>
<tr>
<td>Firstborn child (%)</td>
<td>57 (75)</td>
<td>49 (65)</td>
<td>.216</td>
<td>n.a.</td>
</tr>
<tr>
<td>Mother not born in the Netherlands (%)</td>
<td>28 (37)</td>
<td>31 (41)</td>
<td>.619</td>
<td>16 (39)</td>
</tr>
<tr>
<td>Father not born in the Netherlands (%)</td>
<td>29 (38)</td>
<td>31 (41)</td>
<td>.738</td>
<td>n.a.</td>
</tr>
<tr>
<td>Maternal education: ≤10 years of education (%)</td>
<td>27 (35)</td>
<td>28 (37)</td>
<td>.867</td>
<td>14 (36)</td>
</tr>
<tr>
<td>Paternal education: ≤10 years of education (%)</td>
<td>28 (39)</td>
<td>27 (36)</td>
<td>.865</td>
<td>n.a.</td>
</tr>
<tr>
<td>Gender: Male (%)</td>
<td>43 (57)</td>
<td>32 (43)</td>
<td>.104</td>
<td>21 (51)</td>
</tr>
<tr>
<td>Family status of 2 parents (%)</td>
<td>62 (82)</td>
<td>68 (91)</td>
<td>.157</td>
<td>n.a.</td>
</tr>
<tr>
<td><strong>Perinatal factors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gestation (weeks), mean (SD)</td>
<td>29.6 (2.2)</td>
<td>30.0 (2.1)</td>
<td>.261</td>
<td>n.a.</td>
</tr>
<tr>
<td>Gestation &lt; 28 weeks (%)</td>
<td>20 (26)</td>
<td>8 (11)</td>
<td>.020</td>
<td>0</td>
</tr>
<tr>
<td>Birth weight (grams), mean (SD)</td>
<td>1228 (345)</td>
<td>1311 (322)</td>
<td>.193</td>
<td>n.a.</td>
</tr>
<tr>
<td>Antenatal steroid use (%)</td>
<td>55 (72)</td>
<td>55 (73)</td>
<td>1.00</td>
<td>n.a.</td>
</tr>
<tr>
<td>Indomethacin use (%)</td>
<td>17 (22)</td>
<td>7 (9)</td>
<td>.044</td>
<td>0</td>
</tr>
<tr>
<td>APGAR score 5 minutes, mean (SD)</td>
<td>8.5 (1.6)</td>
<td>8.5 (1.4)</td>
<td>.937</td>
<td>n.a.</td>
</tr>
<tr>
<td>Artificial ventilation (%)</td>
<td>37 (49)</td>
<td>26 (35)</td>
<td>.099</td>
<td>0</td>
</tr>
<tr>
<td>Surfactant (%)</td>
<td>31 (41)</td>
<td>17 (23)</td>
<td>.023</td>
<td>0</td>
</tr>
<tr>
<td>Oxygen therapy ≥ 28 days (%)</td>
<td>32 (42)</td>
<td>15 (20)</td>
<td>.005</td>
<td>0</td>
</tr>
<tr>
<td>Oxygen therapy at 36 weeks post menstrual age (%)</td>
<td>22 (29)</td>
<td>8 (11)</td>
<td>.007</td>
<td>0</td>
</tr>
<tr>
<td>Postnatal steroid use (%)</td>
<td>5 (7)</td>
<td>2 (3)</td>
<td>.442</td>
<td>0</td>
</tr>
<tr>
<td>PVL grade 1 / 2+3</td>
<td>9 / 1</td>
<td>8 / 2</td>
<td>1.00</td>
<td>0</td>
</tr>
<tr>
<td>Ventricular dilatation (%)</td>
<td>1 (1)</td>
<td>3 (4)</td>
<td>.367</td>
<td>0</td>
</tr>
<tr>
<td>IVH grade I + II / III + IV b</td>
<td>13 / 5</td>
<td>8 / 3</td>
<td>1.00</td>
<td>0</td>
</tr>
<tr>
<td>Cranial ultrasound (US) abnormal (%) c</td>
<td>27 (35)</td>
<td>19 (26)</td>
<td>.191</td>
<td>0</td>
</tr>
<tr>
<td>Necrotizing enterocolitis (%)</td>
<td>4 (5)</td>
<td>1 (1)</td>
<td>.367</td>
<td>0</td>
</tr>
<tr>
<td>Septic periods before discharge (%)</td>
<td>46 (60)</td>
<td>30 (40)</td>
<td>.015</td>
<td>0</td>
</tr>
<tr>
<td><strong>At Discharge</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Days post menstrual age, mean (SD)</td>
<td>266 (17)</td>
<td>263 (17)</td>
<td>.241</td>
<td>n.a.</td>
</tr>
<tr>
<td>Length of hospitalizations days, mean (SD)</td>
<td>59 (30)</td>
<td>51 (25)</td>
<td>.080</td>
<td>n.a.</td>
</tr>
<tr>
<td>Weight (grams), mean (SD)</td>
<td>2430 (455)</td>
<td>2370 (418)</td>
<td>.402</td>
<td>n.a.</td>
</tr>
<tr>
<td>Oxygen supply at discharge (%)</td>
<td>5 (7)</td>
<td>3 (4)</td>
<td>.719</td>
<td>0</td>
</tr>
<tr>
<td><strong>At 44 months</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Children as twins or triplets included in study (%)</td>
<td>23 (30)</td>
<td>22 (29)</td>
<td>.901</td>
<td>0</td>
</tr>
</tbody>
</table>

Data are given in number with % or means with standard deviation (SD)
\(p\): \(p\) value IBAIP versus Control group

\(a\) periventricular leukomalacia was defined according to de Vries et al 1992 29

\(b\) Cerebral haemorrhage (IVH) was define according to Papile et al 1983 30

\(c\) defined as not normal ultrasound scan; IVH and/or PVL and/or ventricular dilatation

n.a.: not available
At 44 months CA, eight children (5%) of the VLBW group were diagnosed with cerebral palsy by a paediatrician or child neurologist, 5 in the control group and 3 in the IBAIP group \( (p \approx 0.494) \).

From the 57 parents of term born children who were willing to participate 42 were consecutively matched with the VLBW group and their children formed the term group. One of the 42 term born children was excluded from the analyses because he was referred to a physician due to a developmental delay. The term group consisted of 21 boys (51%) with a mean (SD) age of 44 (0.4) months. Of the term group, 14 (36%) mothers had received ≤ 10 years of education and 16 (39%) were born abroad. The proportions of children with a non-Dutch primary language were not significantly different between the groups; 11 (15%) in the IBAIP group versus 14 (19%) in the control group \( (p \approx 0.465) \) and 10 (24%) in the term group versus 25 (17%) in the group of all 151 VLBW children \( (p \approx 0.249) \). The Figure shows a flowchart of the assessed children in this study and the number of assessed children for each test.

**Figure:** Overview of the number of assessments in the 3 groups. Behaviour Rating Inventory of Executive Function-Preschool version (BRIEF-P); Visual Attention Task of NEPSY (VAT); Child Behavior Checklist for ages 1 ½ - 5 years (CBCL); Peabody Picture Vocabulary Test-III-NL (PPVT); Beery Buktenica Developmental Test of Visual-Motor Integration (VMI); Developmental Test of Visual Perception (VP); Developmental Test of Motor Coordination (MC); Miller Assessment for Preschoolers (MAP).
Table 2: Outcome at 44 months corrected age

<table>
<thead>
<tr>
<th></th>
<th>IBAIP Adjusted means (SD)</th>
<th>Control</th>
<th>p</th>
<th>VLBW (all) Means (SD)</th>
<th>Term</th>
<th>p'</th>
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</thead>
<tbody>
<tr>
<td><strong>EXECUTIVE FUNCTIONS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Behavior Rating Inventory of Executive Function-Preschool version (BRIEF-P)*</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Inhibit</td>
<td>48.3 (11.4)</td>
<td>48.0 (11.4)</td>
<td>.885</td>
<td>48.1 (11.2)</td>
<td>45.1 (7.7)</td>
<td>.046</td>
</tr>
<tr>
<td>Shift</td>
<td>47.6 (10.1)</td>
<td>48.8 (10.1)</td>
<td>.485</td>
<td>48.2 (9.8)</td>
<td>45.4 (6.8)</td>
<td>.038</td>
</tr>
<tr>
<td>Emotional control</td>
<td>45.4 (9.2)</td>
<td>46.5 (9.3)</td>
<td>.462</td>
<td>45.9 (8.9)</td>
<td>42.8 (5.6)</td>
<td>.006</td>
</tr>
<tr>
<td>Working memory</td>
<td>49.9 (12.4)</td>
<td>51.2 (12.4)</td>
<td>.539</td>
<td>50.5 (12.1)</td>
<td>46.0 (8.8)</td>
<td>.009</td>
</tr>
<tr>
<td>Plan / organize</td>
<td>49.0 (11.5)</td>
<td>45.9 (11.5)</td>
<td>.107</td>
<td>47.5 (11.2)</td>
<td>43.4 (7.1)</td>
<td>.006</td>
</tr>
<tr>
<td>Global executive Composite</td>
<td>47.5 (11.9)</td>
<td>47.8 (11.9)</td>
<td>.861</td>
<td>47.7 (11.5)</td>
<td>43.1 (6.9)</td>
<td>.002</td>
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<tr>
<td><strong>Inhibition:</strong></td>
<td></td>
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<tr>
<td>Visual Attention Task (VAT) of NEuroPSYchological Assessment (NEPSY) #</td>
<td></td>
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<td></td>
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<tr>
<td>Scaled score</td>
<td>10.6 (2.3)</td>
<td>10.6 (2.3)</td>
<td>.895</td>
<td>10.6 (2.2)</td>
<td>11.6 (2.0)</td>
<td>.010</td>
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<tr>
<td><strong>BEHAVIOUR</strong></td>
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<tr>
<td>Child Behavior Checklist for ages 1 ½ - 5 years (CBCL 1 ½ - 5)*</td>
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<tr>
<td>Emotional reactive</td>
<td>53.9 (5.6)</td>
<td>53.5 (5.6)</td>
<td>.670</td>
<td>53.8 (5.4)</td>
<td>54.2 (5.5)</td>
<td>.648</td>
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<tr>
<td>Anxious / depressed</td>
<td>51.8 (4.7)</td>
<td>52.6 (4.7)</td>
<td>.364</td>
<td>52.2 (4.6)</td>
<td>51.1 (2.0)</td>
<td>.030</td>
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<tr>
<td>Somatic complaints</td>
<td>52.9 (5.8)</td>
<td>55.3 (5.8)</td>
<td>.013</td>
<td>54.0 (5.7)</td>
<td>55.9 (7.2)</td>
<td>.114</td>
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<td>Withdrawn</td>
<td>54.0 (6.3)</td>
<td>54.5 (6.3)</td>
<td>.636</td>
<td>54.3 (6.1)</td>
<td>53.5 (4.7)</td>
<td>.448</td>
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<tr>
<td>Sleep problems</td>
<td>55.2 (7.1)</td>
<td>52.7 (7.1)</td>
<td>.034</td>
<td>53.9 (7.1)</td>
<td>52.0 (4.1)</td>
<td>.030</td>
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<tr>
<td>Attention problems</td>
<td>54.3 (7.1)</td>
<td>54.1 (7.1)</td>
<td>.853</td>
<td>54.2 (6.8)</td>
<td>51.9 (2.7)</td>
<td>.001</td>
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<tr>
<td>Aggressive behaviour</td>
<td>53.2 (6.0)</td>
<td>53.0 (6.0)</td>
<td>.804</td>
<td>53.1 (5.8)</td>
<td>52.2 (3.6)</td>
<td>.379</td>
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<tr>
<td>Intern problems</td>
<td>46.3 (11.1)</td>
<td>47.9 (11.1)</td>
<td>.386</td>
<td>46.7 (10.9)</td>
<td>48.2 (9.8)</td>
<td>.398</td>
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<tr>
<td>Extern problems</td>
<td>47.9 (11.2)</td>
<td>46.5 (11.2)</td>
<td>.459</td>
<td>47.2 (11.0)</td>
<td>47.0 (8.3)</td>
<td>.871</td>
</tr>
<tr>
<td>Total problems</td>
<td>46.9 (11.0)</td>
<td>46.9 (11.0)</td>
<td>.984</td>
<td>47.0 (10.8)</td>
<td>46.6 (8.7)</td>
<td>.854</td>
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<td><strong>WORD COMPREHENSION</strong></td>
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<tr>
<td>Peabody Picture Vocabulary Test- III- NL (PPVT)#</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WCQ (chronological age)</td>
<td>94.7 (16.5)</td>
<td>101.9 (17.0)</td>
<td>.015</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WCQ (corrected age)</td>
<td>99.4 (17)</td>
<td>97.3 (17)</td>
<td>.456</td>
<td>98.4 (16.7)</td>
<td>101.9 (17.0)</td>
<td>.235</td>
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</table>
**VISUAL MOTOR INTEGRATION**

<table>
<thead>
<tr>
<th></th>
<th>VMI (chronological age)</th>
<th>VMI (corrected age)</th>
<th>Visual perception (VP) #</th>
<th>VP (chronological age)</th>
<th>VP (corrected age)</th>
<th>Motor Coordination (MC) #</th>
<th>MC (chronological age)</th>
<th>MC (corrected age)</th>
</tr>
</thead>
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<tr>
<td></td>
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<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>97.4 (12.8)</td>
<td>101.5 (14)</td>
<td>100.2 (21.3)</td>
<td>102.3 (22)</td>
<td>90.2 (17)</td>
<td></td>
<td>88.3 (17.0)</td>
<td>88.9 (17.0)</td>
</tr>
<tr>
<td></td>
<td>106.4 (13)</td>
<td>100.1 (14)</td>
<td>109.1 (19.7)</td>
<td>99.8 (22)</td>
<td>87.5 (17)</td>
<td></td>
<td>94.7 (12.9)</td>
<td>94.7 (12.9)</td>
</tr>
<tr>
<td></td>
<td>&lt;.001</td>
<td>.684</td>
<td>.018</td>
<td>.515</td>
<td>.331</td>
<td></td>
<td>.029</td>
<td>.046</td>
</tr>
</tbody>
</table>

Adjusted means and standard deviations (SD) used for comparison IBAIP versus control group. Means adjusted for pre-randomisation differences; use of surfactant, indomethacin, Oxygen ≥ 28 days, sepsis before discharge, <28 weeks of gestation. *p* values corrected for pre-randomisation differences between the IBAIP group and control group calculated with ANOVA.

* Lower scores represent better performance
# Higher scores represent better performance

Corrected age; age corrected for preterm birth
WCQ: Word comprehension quotient
IBAIP group versus control group (Table 2)

For BRIEF-P high inconsistency scores were comparable; 3 in the IBAIP group versus 2 in the control group ($p = 1.00$). All BRIEF-P results were considered valid.

After adjustment for pre-randomisation differences there were no significant differences between the IBAIP group and control group on any of the assessments of executive functioning, behaviour, word comprehension and visual motor integration (Table 2). In addition, the percentages of children not peeking within one minute during the Gift delay were comparable between groups; 43% in the IBAIP group and 44% in the control group. Further, also for the cognitive skills assessed with the MAP, the proportions of children receiving sufficient scores were comparable between the IBAIP and the control group.

The analyses which included only one multiplet member revealed no significant differences between IBAIP and control group on any assessment.

Interaction between intervention and risk factors (Table 3)

Positive significant interaction effects were found between the intervention and BPD for the CBCL's domain Withdrawn. The mean difference of the intervention children with BPD was 8.8 points (>1 SD) higher than the control children with BPD. Positive significant interaction effects were found between the intervention and GA < 28 weeks on the CBCL's domain Emotional reactive with a mean difference of 7 (>1 SD) higher. Also for 5 of the 6 BRIEF-P's domains positive interaction effects between the intervention and GA < 28 weeks were found with mean differences exceeding 1 SD for 4 domains. Positive significant interaction effects were also found between the intervention and mothers who received ≤ 10 years of education on the PPVT with a mean difference of nearly 0.3 SD. For abnormal ultrasound and for gender no significant interaction effects with the intervention were found. The analyses which included only one multiplet member revealed generally comparable interaction effects.
Table 3: Interaction effects of the IBAIP intervention at 44 months corrected age; p value and Mean Difference

<table>
<thead>
<tr>
<th></th>
<th>BPD (Mean Difference)</th>
<th>GA&lt;28 wk (Mean Difference)</th>
<th>Mother low educated (Mean Difference)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EXECUTIVE FUNCTIONS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Behavior Rating Inventory of Executive Function-Preschool version (BRIEF-P)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inhibit</td>
<td></td>
<td>.001 (15.2)</td>
<td>-</td>
</tr>
<tr>
<td>Shift</td>
<td></td>
<td>-.001 (14.9)</td>
<td>-</td>
</tr>
<tr>
<td>Emotional Control</td>
<td></td>
<td>.013</td>
<td>-</td>
</tr>
<tr>
<td>Working Memory</td>
<td></td>
<td>.001 (17.4)</td>
<td>-</td>
</tr>
<tr>
<td>Plan / Organize</td>
<td></td>
<td>.010 (8.9)</td>
<td>-</td>
</tr>
<tr>
<td>Global executive Composite</td>
<td></td>
<td>-.001 (17.9)</td>
<td>-</td>
</tr>
<tr>
<td><strong>BEHAVIOUR</strong> (positive interaction with BPD and GA &lt; 28 wk)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Child Behavior Checklist for ages 1 ½ - 5 years (CBCL 1 ½ - 5)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emotional reactive</td>
<td>.013</td>
<td>.002 (7.0)</td>
<td>-</td>
</tr>
<tr>
<td>Anxious / depressed</td>
<td>.074</td>
<td>.072</td>
<td>-</td>
</tr>
<tr>
<td>Somatic complaints</td>
<td>.042</td>
<td>.797</td>
<td>-</td>
</tr>
<tr>
<td>Withdrawn</td>
<td>.001 (8.8)</td>
<td>.039</td>
<td>-</td>
</tr>
<tr>
<td>Sleep problems</td>
<td>.248</td>
<td>.167</td>
<td>-</td>
</tr>
<tr>
<td>Attention problems</td>
<td>.155</td>
<td>.071</td>
<td>-</td>
</tr>
<tr>
<td>Aggressive behaviour</td>
<td>.544</td>
<td>.031</td>
<td>-</td>
</tr>
<tr>
<td>Intern problems</td>
<td>.030</td>
<td>.063</td>
<td>-</td>
</tr>
<tr>
<td>Extern problems</td>
<td>.109</td>
<td>.078</td>
<td>-</td>
</tr>
<tr>
<td>Total problems</td>
<td>.033</td>
<td>.038</td>
<td>-</td>
</tr>
<tr>
<td><strong>WORD COMPREHENSION</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Peabody Picture Vocabulary Test- III- NL (PPVT)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WCQ (corrected age)</td>
<td></td>
<td>-</td>
<td>.002 (4.9)</td>
</tr>
</tbody>
</table>

Interaction effects were calculated with multiple regression analyses, differences at baseline were included in these multiple regression analyses: use of surfactant, indomethacin, Oxygen ≥ 28 days, sepsis before discharge, <28 weeks of gestation.

In case of a significant interaction term with \( p < .01 \) the mean difference is presented between the intervention and control children with the specific risk factor, i.e. having bronchopulmonary dysplasia (BPD), Gestational Age (GA) < 28 weeks, low educated mother.

WCQ: Word comprehension quotient.

**VLBW children versus term born children (Table 2)**

As no overall group differences were found between the IBAIP group and control group on any of the assessments, we combined these groups into one VLBW group. The results of the 151 VLBW children were compared with the results of the 41 term born children. For BRIEF-P no inconsistencies were found. The VLBW group performed significantly less compared to the term group on executive functioning measured with the BRIEF-P and the VAT, and on behaviour with the CBCL's Attention problems. On visual motor integration the VLBW group performed significantly lower only for the VMI subtest's score for the chronological age. On the MAP's Figure ground perception, 100% of the term group versus 88% of the VLBW group \( (p = .009) \) received
a sufficient score. The analyses which included only one multiplet member revealed generally comparable differences.

**DISCUSSION**

In this study, we did not find an effect of the post-discharge IBAIP intervention in VLBW infants on executive functioning, behaviour and cognition at 44 months CA. However, specific subgroups still benefitted at 44 months CA from the intervention. These positive effects concern behaviour for infants with BPD, executive functioning and behaviour for infants with GA < 28 weeks, and word comprehension for infants born to low educated mothers.

The VLBW children had significantly worse outcomes than the children in the matched term group on measurements of executive functioning (VAT and BRIEF-P), Attention problems (CBCL), Visual-motor integration (VMI) and MAP's Figure ground perception.

It appears that the positive 6 months' results of the IBAIP on self-regulation, behaviour, cognition and motor development sustained in better motor abilities at 24 months and in more independency in mobility at 44 months, but not in better executive functioning, behaviour and cognition at 44 months. Our results differ from the outcomes of other recent studies that found positive results of early intervention on mental development and behaviour. A modified version of the Mother-Infant Transaction Program did not improve motor development, but had a positive effect on full-scale IQ score at 5 years of age. Another study on an early intervention program, supporting preterm infants and their families during the first 12 months of life, found positive results on the child's behaviour at 24 months of age, but not on motor and mental development. However, follow-up results of this study at preschool age are not yet available. Possibly, early neurodevelopmental improvements of post discharge intervention may fade away if they do not extend to the sensitive period during which the behavioural and mental domain primarily develop. Whether it is useful to continue our intervention after 6 months with age-specific experiences that focus on behavioural and mental development warrants further study.

Our results confirm the earlier findings of this RCT at 24 months CA that IBAIP may be particularly effective in subgroups of the most vulnerable preterm born children. At preschool age, VLBW infants with BPD, and infants born with a GA less than 28 weeks appeared to profit specifically from the intervention in terms of more favourable behavioural and executive functioning. The intervention effects in the subgroups were not only significant but also clinically relevant because the mean differences of these domains mostly exceed 1 SD in favour of the
intervention children. However, on BRIEF-P's domain Plan and organize a mean difference of > 0.5 SD was found. A difference > 0.5 SD is generally considered a medium, and above 0.8 SD a large effect size. For infants born to low educated mothers an intervention effect on word comprehension was found. However, the effect size was only small: 0.3 SD. It seems that the support of self-regulation by IBAIP translates at preschool age into less behavioural problems in children with BPD and children with GA< 28 weeks, and better executive functioning in children with GA< 28 weeks. The IBAIP may have been particularly effective in these most vulnerable infants as they will probably have the most problems with self-regulation and their parents are most likely to need specific sensitivity and nurturing qualities. However, we cannot draw firm conclusions because these subgroups are small and members of the subgroups were not equally assigned to the IBAIP and control groups.

This study showed that at the corrected age of 44 months VLBW children perform less on executive functioning and attention compared to term born children. These findings confirm that executive functioning and attention are areas of weakness for VLBW children and are already detectable at preschool age. Further research on the abilities of the VLBW children in these domains is valuable because executive functioning is related to academic achievement. For the subtest Visual motor integration (VMI) a significant difference was found between the VLBW group and the term group. This difference was only significant when using scores for chronological age. This indicates that visual motor integration is still developing quickly at preschool age. Therefore, to have a realistic picture of the VLBW preschooler's visual motor integration, interpreting scores both on the basis of the calendar age and the corrected age is important when comparing these abilities with age related peers.

A limitation of this study is that USA norm data were used for all assessments. Only for the PPVT we used Dutch norm data. However, all children performed the same assessments and the VLBW groups were compared to the term group instead of to norm data. Another limitation of this study may be that the tests we used did not capture all aspects of executive functioning and cognition. Moreover, inter-individual differences in developmental trajectories of the abilities in the assessed domains may make it difficult to detect changes at preschool age. Therefore, further study at a more advanced age is needed to determine the full impact of the IBAIP intervention specifically and of very preterm birth in general on the development of executive functions, behaviour and cognition in this cohort. Further follow-up studies evaluating the effect of the IBAIP at 5 years are currently in progress.
There are several strengths of our follow-up study. We attained a high response rate of 86% and used a matched term comparison group. The response rate is notable for a cohort of which 39% percent of the mothers were born outside the Netherlands.

To conclude, IBAIP effects in VLBW children did not sustain until preschool age on executive functioning, behaviour and cognition. However, the most vulnerable children still profited from IBAIP with clinically relevant better behavioural and executive functioning.

**Conflict of interest statement**

The authors declare that there is no potential conflict of interest that could inappropriately influence this work.

**Acknowledgements**

We thank all the participating parents and children, Richard van Seenus Nederland BV for their supplying the ALVEMA MAXIT chair, the Amsterdam’s Public Health Service for help with collecting the matched term group, and M.J.Wolf for her assistance in the design of this study and support during data collection. This study was funded by Zorg Onderzoek Nederland (ZonMw project 622300032) and Innovatiefonds Zorgverzekeraars (project 576).
REFERENCES


Chapter 4

Attention problems in very low birth weight children prior to school entry and the relationship to educational placement at 66 months of age

Submitted

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**ABSTRACT**

**Background:** It is unclear if attention problems in very low birth weight (VLBW) children are already present at preschool age and whether they are associated with future educational placement.

**Aim:** To compare attention scores of VLBW children at 44 months corrected age (CA) with matched controls, and to explore the association with educational placement 22 months later.

**Method:** One hundred and fifty-one VLBW children of 44 months CA and 41 healthy term born peers were assessed. Attention was explored using six measures. The children performed the Visual Attention test of the Developmental neuropsychological assessment and the Gift delay test. The parents completed the Attention Problems domain of the Child Behavior Checklist (CBCL-AP), the Inhibit domain of the Behavior Rating Inventory of Executive Function (BRIEF-preschool version), and the Inattention/Distractibility scale of the Sensory Profile (SP). The assessor completed the attention domain within the Behavior During Testing (BDT-AD) of the Miller assessment for preschoolers. Mean scores and abnormal scores were calculated. Attention scores were associated with the educational placement at 66 months CA.

**Results:** VLBW children performed significantly worse than their term born peers on all attention measures except for the SP. On the CBCL-AP and the BDT-AD, significantly more abnormal scores were found in the VLBW group than in the term group. Abnormal scores on the BDT-AD and the SP were significantly associated with lower levels of participation in mainstream educational curricula at 66 months CA.

**Conclusions:**
The results of this study confirm that VLBW children perform worse on attention measures than their term born peers at 44 months CA. The BDT-AD is also associated with later school problems, therefore this may be a valuable tool for identifying children in need of intervention at preschool age. Further studies on this attention measurement are warranted.
INTRODUCTION

Reviews conclude that very low birth weight (VLBW) children are at an increased risk of attention problems 1-3. Attention underlies and maintains the activity of cognitive functions 4. Therefore, attention problems can interfere with cognitive development 5. The identification of attention problems before children start school is important, since such problems hinder academic achievement 6-9. This identification at 3-4 years of age involves the assessment of a child’s ability to orientate to, shift between and maintain focus on events, objects, tasks, and problems in the external world 3. Because this demands such a broad spectrum of abilities, various instruments are used to assess different aspects of attention: performance based tests 10,11, questionnaires to be completed by parents or care takers 10, and systematic professional observations of attention behaviour 10.

Different modalities of attention assessments may yield different outcomes. In addition, it is not clear which measurements are most effective for assessing the attention of VLBW at preschool age. Therefore, the objective of this study is to compare VLBW children at 44 months of corrected age (CA) with term born peers using multiple instruments covering different aspects of attention, and to explore the association with later educational placement.

PATIENTS AND METHODS

Participants and procedure

VLBW children and a comparison group of healthy term born peers were assessed at 44 months corrected age (CA). This age was chosen because in the Netherlands children start school at 4 years of uncorrected age.

A cohort of 176 VLBW children who participated in a multicenter randomised controlled trial (RCT), which studied the effect of an early neurobehavioral intervention program with long-term follow up, was used 12. For this RCT, 176 VLBW infants born with a birth weight < 1500 g and/or gestational age of < 32 weeks were recruited in seven hospitals in Amsterdam, the Netherlands in 2003-2006. Eighty-six VLBW children received the intervention and 90 children received standard care. Parents of all 176 VLBW children were invited to participate in the follow up study at 44 months CA 13,14 and at 66 months (5.5 years) CA 15.

Healthy term born children were recruited through Amsterdam’s Public Health Service. Two hundred parents were invited to participate in the study. Inclusion criteria for the healthy term group were: being born after ≥ 37 weeks of gestation and birth weight ≥ 2500 g. Children who
were referred to a psychologist, paediatrician or physician because of developmental or health problems were excluded. Via a process of consecutive selection, the comparison group of term born children and their parents matched the distribution of the VLBW group with respect to male gender, maternal education ≤ 10 years and mother born abroad.

After the written informed consent of the parents, assessments of children at 44 months CA were conducted during home visits between August 2007 and February 2010. All children were seated in a chair with a table top adjusted to their size, and fastened with a safety rod at waist height. The assessments were administered in the same order by the same assessor, who was aware of the birth status of the child.

**Measurements**

Attention was assessed using two performance tests, three parental questionnaires, and a structured observation of behaviour by the assessor: an experienced occupational therapist MSc.

**Performance tests:**

The children performed the Visual Attention Test (VAT) of the Developmental Neuropsychological Assessment (NEPSY) and the Gift delay test. The VAT records the speed and accuracy with which a child is able to focus selectively on, and maintain attention to, visual targets. The total score was compared with the age-related norm of American children with a mean of 10 (SD = 3). A score below < 7 (1 SD) is considered as abnormal.

The Gift delay test assesses the child’s ability to inhibit a predisposed response. The child sits in the chair which is turned 180 degrees away from the investigator and is instructed not to look while a gift is wrapped for him/her. After 60 s, the child receives the wrapped gift. The procedure was recorded by a video camera in order to be able to calculate the time until peeking. There are no standardised norm data available for this test. The performance of those children who were unable to wait longer than the 84th percentile (1 SD) was considered abnormal.

**Questionnaires:**

The parents completed three questionnaires containing different domains of attention.

The Attention Problems scale of the Dutch version of the Child Behavior Checklist for ages 1.5 to 5 years was administered (CBCL-AP). The CBCL-AP consists of several statements about the child’s attention: focussing attention, maintaining attention and inhibition. Raw scores were converted into a T-score using the American norm data which are also valid for Dutch children (www.aseba.nl). Scores ≥ 65 (1.5 SD) are in the clinical range.

The Inhibit scale of the Dutch translation of the Behavior Rating Inventory of Executive Function-Preschool version (BRIEF-P) was administered. The BRIEF-P’s Inhibit scale consists of 16 items about inhibition. Raw scores were converted into a T-score based on the gender and age-
related American norms, with a mean of 50 and SD of 10. Scores above the 90th percentile (1.5 SD) are considered to be potentially clinically significant.

The Inattention/Distractibility scale of the Dutch translation of the Sensory Profile (SP-ID) was administered. The Sensory Profile assesses children’s responses to naturally occurring sensory experiences in their everyday environment. The SP-ID consists of seven items, five of which comprise listening behaviour and being distracted by auditory stimuli. Scores below 26 (1 SD) are considered to be potentially clinically significant. The SP is shown to be a reliable and valid measure for the USA, but has not been validated for the Dutch population.

**Structured observation:**

In addition to the VAT and Gift delay tasks, the children performed cognitive and fine motor tasks within one hour (see for details Verkerk et al 2012). Directly after the assessment of every child the assessor completed the attention domain of Behavior During Testing (BDT-AD). The BDT-AD is part of the Miller assessment for preschoolers and covers four items: activity level, concentration, ability to structure time/complete tasks, and need for reward/ability to delay gratification. The response options were converted to an ordinal 3-point scale as follows: 1 = severe dysfunction, 2 = moderate dysfunction and 3 = normal behaviour. Thus, the total BDT-AD score ranged between 4 and 12 points. There are no norms available for the total BDT-AD score. Scores below 1 SD of the mean score of all assessed children were considered abnormal. The validity and the reliability of the BDT-AD have not been assessed.

**Educational placement at 66 months CA**

At 66 months CA, parents were asked whether their child(ren) followed (1) mainstream education at age-appropriate level or (2) special education and/or had grade retention.

**Data analyses**

All statistical analyses were performed using the Statistical Package for Social Sciences version 16.0 for Windows (SPSS Inc, Chicago, Illinois).

In the follow up study of the RCT, the attention outcomes at 44 months CA on four of the six measures were comparable for the VLBW intervention group and the VLBW control group. To be able to pool the data of all six attention measures, we investigated, using the Analyses of Variance (ANOVA), if the results on the SP-ID and the BDT-AD differed between the VLBW intervention group and the VLBW control group.

Independent samples t-tests were used to compare the mean attention outcomes between the VLBW group and the term group, except for the BDT-AD. Mann Whitney U test was used for BDT-AD because of the skewed distribution of the BDT-AD data.
Chi-squared tests were used to compare proportions of abnormal scores between the VLBW group and the term group. Missing data were coded as a normal test score. To explore which aspects of attention were specifically troublesome for the VLBW group, chi-squared tests or Mann-Whitney U tests were performed on the separate items of the assessments, for which significantly more abnormal scores were observed in the VLBW group compared to the term group.

Chi-squared tests were used to examine the association between attention and educational placement. The proportions of abnormal attention outcomes were compared between the group who followed mainstream education, versus the group who followed special education and/or had grade retention. Stepwise multiple logistic regression analysis was performed to explore whether any of the attention measures were significant risk factors for educational placement at 66 months. The intervention was included as a covariate in the regression analysis. Differences with \( p < .05 \) were regarded as significant.

**RESULTS**

Data of 151 VLBW children (86% of the original cohort) at a mean (SD) corrected age of 44 (0.5) months were collected. Reasons for dropping out of the study were death (\( n = 2 \)), moving abroad (\( n = 6 \)), lost to follow-up (\( n = 6 \)), and parental withdrawal (\( n = 11 \)). The perinatal characteristics did not differ significantly between the VLBW children who participated and those who dropped out. However, children with a father born outside the Netherlands discontinued participation significantly more often (\( p = .002 \)), and first born children continued to participate significantly more frequently (\( p = .005 \)).

Outcomes on the SP-ID and the BDT-AD did not differ significantly between the VLBW intervention group and the VLBW control group. Because there were no significant differences between VLBW groups on any outcome measure, the results were pooled.

Fifty seven parents of term born children were willing to participate. Sixteen term born children from highly educated mothers who applied for participation were not invited, in order to ensure a similar distribution with respect to maternal education in both groups. The VLBW group and the term group (\( n = 41 \)) had the same mean age 44 months (SD 0.4), proportion of boys (51%), maternal education \( \leq 10 \) years (36%), and mothers born abroad (39%).

The perinatal characteristics and the socio-demographic factors of the VLBW group are shown in Table 1.
Table 1: Peri-ante-neonatal and socio-demographic characteristics of VLBW children (n=151)

<table>
<thead>
<tr>
<th>Perinatal factors</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Weeks of gestation, mean (SD)</td>
<td>29.8 (2.1)</td>
</tr>
<tr>
<td>Gestation &lt; 28 weeks, n (%)</td>
<td>24 (16)</td>
</tr>
<tr>
<td>Birth weight in grams, mean (SD)</td>
<td>1269 (335)</td>
</tr>
<tr>
<td>Birth weight below 1000 grams, n (%)</td>
<td>39 (26)</td>
</tr>
<tr>
<td>Antenatal steroid use, n (%)</td>
<td>110 (73)</td>
</tr>
<tr>
<td>Received oxygen therapy at 36 weeks postmenstrual age, n %</td>
<td>30 (20)</td>
</tr>
<tr>
<td>Abnormal cranial ultrasound*, n %</td>
<td>46 (30)</td>
</tr>
<tr>
<td>Septic periods before discharge, n (%)</td>
<td>76 (50)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>75 (50)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Social factors</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>First born child, n (%)</td>
<td>107 (70)</td>
</tr>
<tr>
<td>Singleton, n (%)</td>
<td>106 (70)</td>
</tr>
<tr>
<td>Maternal age in years, mean (SD)</td>
<td>32.4 (5.2)</td>
</tr>
<tr>
<td>Paternal age in years, mean (SD)</td>
<td>36.0 (6.8)</td>
</tr>
<tr>
<td>Mother born in the Netherlands, n (%)</td>
<td>92 (61)</td>
</tr>
<tr>
<td>Maternal education ≤ 10 years, n (%)</td>
<td>54 (36)</td>
</tr>
<tr>
<td>Father born in the Netherlands, n (%)</td>
<td>91 (61)</td>
</tr>
<tr>
<td>Family status of 2 parents, n (%)</td>
<td>130 (86)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>At Discharge</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitalisation days, mean (SD)</td>
<td>55.3 (28)</td>
</tr>
<tr>
<td>Oxygen supply at discharge, n (%)</td>
<td>8 (5)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>At 44 months corrected age</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosed with cerebral palsy, n (%)</td>
<td>8 (5)</td>
</tr>
</tbody>
</table>

*Abnormal cranial ultrasound defined as any grade of Intra Ventricular Haemorrhage (IVH) and/or periventricular leucomalacia (PVL) and/or ventricular dilatation. IVH was defined according to Papile et al \(^{24}\) and PVL was defined according to de Vries et al \(^{25}\).

**VLBW-Term comparisons**

The VLBW group had significantly lower mean scores than the term group on all attention outcomes, except for the SP-ID (Table 2).

Abnormal scores on the CBCL-AP and on the BDT-AD were significantly more often present in the VLBW group, than in the term group (Table 3).

On the BDT-AD item ‘Ability to structure time/complete tasks’, the children in the VLBW group more often showed abnormal scores than those in the term group (\(p = .051\)) (Table 3). There were no significant differences between the VLBW group and the term group in the scores of other BDT-AD items or CBCL-AP items.
### Table 2: Average attention outcomes at 44 months corrected age

<table>
<thead>
<tr>
<th></th>
<th>Number of completed measurements</th>
<th>VLBW</th>
<th>Term</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>VAT* mean (SD)</td>
<td>149 / 40</td>
<td>10.6 (2.2)</td>
<td>11.6 (2.0)</td>
<td>.010</td>
</tr>
<tr>
<td>Gift delay* mean (SD)</td>
<td>148 / 40</td>
<td>37 (23.5)</td>
<td>44.5 (20.2)</td>
<td>.047</td>
</tr>
<tr>
<td>CBCL-AP** mean (SD)</td>
<td>150 / 41</td>
<td>54.3 (6.8)</td>
<td>51.9 (2.7)</td>
<td>.001</td>
</tr>
<tr>
<td>BRIEF-P Inhibit** mean (SD)</td>
<td>150 / 41</td>
<td>48.1 (11.2)</td>
<td>45.1 (7.7)</td>
<td>.046</td>
</tr>
<tr>
<td>SP-ID* mean (SD)</td>
<td>149 / 40</td>
<td>28.8 (4.5)</td>
<td>29.5 (3.7)</td>
<td>.626</td>
</tr>
<tr>
<td>BDT-AD* ^1 median (range)</td>
<td>151 / 41</td>
<td>12 (7-12)</td>
<td>12 (10-12)</td>
<td>.012</td>
</tr>
</tbody>
</table>

Very Low Birth Weight (VLBW) children compared with term born peers with independent sample t-tests. Visual Attention Task (VAT) of Developmental NEuroPSYchological Assessment (NEPSY); Attention problems syndrome scale score of Child Behavior Checklist for ages 1 ½ - 5 years (CBCL-AP); Inhibit domain of Behaviour Rating Inventory of Executive Function-Preschool version (BRIEF-P); Inattention / distractibility factor scale of Sensory Profile (SP-ID); Attention domain of Behaviour during testing (BDT-AD) of Miller Assessment for Preschoolers.

* A higher score corresponds with better attention
** A lower score corresponds with better attention
1 Mann-Whitney U test: median (range)

### Table 3: Number of VLBW and term born children with abnormal attention outcomes at 44 months corrected age

<table>
<thead>
<tr>
<th>Assessment (cut of value)</th>
<th>VLBW (n =151)</th>
<th>Term (n = 41)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>VAT (score &lt; 7)</td>
<td>3 (2)</td>
<td>0 (0)</td>
<td>1.00**</td>
</tr>
<tr>
<td>Gift delay (score &lt; 10 seconds)</td>
<td>26 (17)</td>
<td>3 (7)</td>
<td>.116*</td>
</tr>
<tr>
<td>CBCL-AP (score ≥ 65)</td>
<td>19 (13)</td>
<td>0 (0)</td>
<td>.015**</td>
</tr>
<tr>
<td>BRIEF-P Inhibit (score ≥ 65)</td>
<td>13 (9)</td>
<td>1 (2)</td>
<td>.309**</td>
</tr>
<tr>
<td>SP-ID (score &lt; 25)</td>
<td>32 (21)</td>
<td>7 (17)</td>
<td>.581*</td>
</tr>
<tr>
<td>BDT-AD (total score ≤ 11)</td>
<td>28 (19)</td>
<td>1 (2)</td>
<td>.011***</td>
</tr>
</tbody>
</table>

BDT-AD Item scores < 3:
- activity level
  - 3 (2)         | 0 (0)         | 1.00**  |
- concentration
  - 10 (7)       | 0 (0)         | .123**  |
- ability to structure time / complete tasks
  - 21 (14)      | 1 (2)         | .051**  |
- need for reward / ability to delay gratification
  - 12 (8)       | 1 (2)         | .306**  |

Visual Attention Task (VAT) of Developmental NEuroPSYchological Assessment (NEPSY); Attention problems syndrome scale score of Child Behavior Checklist for ages 1 ½ - 5 years (CBCL-AP); Inhibit domain of Behavior Rating Inventory of Executive Function-Preschool version (BRIEF-P); Inattention/distactibility factor scale of Sensory Profile (SP-ID); Attention domain of Behavior during testing (BDT-AD) of Miller assessment for preschoolers.

p values of: * Pearson Chi square test, ** Fisher’s exact test, *** comparison of the distribution of abnormal scores between the VLBW group and the term group performed with Mann-Whitney U test.
**Association with educational placement at 66 months CA**

Of the 151 VLBW children assessed at follow up at 44 months, information on educational placement was available for 124 children at 5.5 years CA. Of these 124 children, 79 followed mainstream education and 45 followed special education or had grade retention. Children with abnormal scores on BDT-AD and SP-ID were found to have a significantly lower rate of participation in mainstream education (Table 4). Multiple logistic regression analyses revealed that only the BDT-AD was significantly associated with educational placement, when controlling for intervention allocation, (Odds Ratio (OR) of 5.1 (95% CI; 1.9-13.9) Nagelkerke R Square is .12).

**Table 4: Association between attention measurement at 44 months and educational placement at 5.5 years (n = 124 including 7 children with CP)**

<table>
<thead>
<tr>
<th></th>
<th>Mainstream</th>
<th>Special education/grade retention</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>VAT normal</td>
<td>122</td>
<td>77 (63%)</td>
<td>45 (37%)</td>
</tr>
<tr>
<td>VAT abnormal</td>
<td>2</td>
<td>2 (100%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Gift delay normal</td>
<td>103</td>
<td>68 (66%)</td>
<td>35 (34%)</td>
</tr>
<tr>
<td>Gift delay abnormal</td>
<td>21</td>
<td>11 (52%)</td>
<td>10 (48%)</td>
</tr>
<tr>
<td>CBCL-AP normal</td>
<td>106</td>
<td>69 (65%)</td>
<td>37 (35%)</td>
</tr>
<tr>
<td>CBCL-AP abnormal</td>
<td>18</td>
<td>10 (56%)</td>
<td>8 (44%)</td>
</tr>
<tr>
<td>BRIEF-P Inhibit normal</td>
<td>113</td>
<td>73 (65%)</td>
<td>40 (35%)</td>
</tr>
<tr>
<td>BRIEF-P Inhibit abnormal</td>
<td>11</td>
<td>6 (55%)</td>
<td>5 (45%)</td>
</tr>
<tr>
<td>SP-ID normal</td>
<td>96</td>
<td>66 (69%)</td>
<td>30 (31%)</td>
</tr>
<tr>
<td>SP-ID abnormal</td>
<td>28</td>
<td>13 (46%)</td>
<td>15 (54%)</td>
</tr>
<tr>
<td>BDT-AD normal</td>
<td>102</td>
<td>72 (71%)</td>
<td>30 (29%)</td>
</tr>
<tr>
<td>BDT-AD abnormal</td>
<td>22</td>
<td>7 (32%)</td>
<td>15 (68%)</td>
</tr>
</tbody>
</table>

Visual Attention Task (VAT) of Developmental NEuroPSYchological Assessment (NEPSY); Attention problems syndrome scale score of Child Behavior Checklist for ages 1 ½ - 5 years (CBCL-AP); Inhibit domain of Behavior Rating Inventory of Executive Function-Preschool version (BRIEF-P); Inattention / distractibility factor scale of Sensory Profile (SP-ID); Attention domain of Behavior during testing (BDT-AD) of Miller assessment for preschoolers.

Pearson Chi square test.

*: Fisher’s exact test.
DISCUSSION

The results of this study showed that VLBW children performed less well compared to their term born peers on all aspects of attention except for distraction by auditory stimuli. According to parental observation in daily life and professional observation of attention during assessment, abnormal attention scores were shown significantly more in VLBW children than term born children. The professional observation of attention problems was significantly associated with lower participation in mainstream education at 66 months CA.

Our findings confirm the results of other studies which found attention problems in VLBW children at 3-4 years of age \textsuperscript{10,11,26}. Nevertheless, in the current study, the VLBW children and the healthy term born peers had comparable outcomes on the SP-ID. Relative to other measures, the SP-ID contains more questions about distraction caused by auditory stimuli. The results of this study suggest that this specific attention behaviour is comparable for VLBW children and term born peers at 44 months CA.

The VLBW children significantly more often had scores in the abnormal/clinical range than the term born peers on the CBCL-AP. This scale assesses focussing, maintaining attention, and inhibition. In addition during assessment, significantly more abnormal attention behaviour was found in the VLBW children with the BDT-AD. The VLBW children had specifically more difficulty maintaining attention during the assessments. This is in line with the findings of a study which involved a visual search task with 4 year old VLBW children \textsuperscript{11}. In this study \textsuperscript{11} the VLBW children were less successful in staying on the task and therefore did not complete all of the test trials within the visual search task. In addition, another study found that at 4 years of age, VLBW children performed significantly worse on sustained attention when undertaking problem solving tasks which were measured by systematic professional observation \textsuperscript{10}.

In the present study, at 44 months CA, difficulty with maintaining attention during assessment, and parental observations of distractibility (mainly by auditory stimuli), were shown to be significantly associated with a lower rate of participation in a mainstream educational curriculum. Of these two measures, it was the problems observed by the professional during test performance that was most strongly associated with future educational placement. Children experiencing attention difficulties during assessment have a twofold increased risk of being unable to participate in a mainstream educational curriculum. Attention is an important regulatory skill needed for information processing and, therefore, for learning \textsuperscript{4,5,27}. Therefore, it is not surprising that the observation of attention by a professional during cognitive and fine motor tasks is associated with educational placement. The amount of variance of educational placement explained by the attention observation was 12%. This indicates that there are other factors
Attention in VLBW children at preschool age

contributing to a VLBW child’s ability to participate in a mainstream educational curriculum. This means that in addition to attention problems they may have other difficulties.

Attention problems as measured by the CBCL (parent report) were not related to educational placement. The CBCL-AP items cover over-activity and impulsive behaviour as well as inattentiveness. Deutscher & Fewell 28 found that, in low birth weight children, the professional observation of inattention, rather than impulsivity or over-activity at 30 months, predicted the need for special education at 8 years of age. Jaekel et al 29 assessed academic achievement in 13 year old VLBW children and aspects of their attention at 6 and 8 years of age. They concluded that poor attention, rather than hyperactivity/impulsivity, is an independent predictor of academic underachievement. It seems that the majority of the CBCL-AP items cover over-activity and impulsivity instead of inattentiveness. This might explain why the CBCL-AP did not predict educational placement at 66 months in our study.

Strengths and limitations

The strength of this study is that attention was comprehensively assessed using three sources: the performance of the child on two tests, the observations by the parents using three different questionnaires, and the structured observation by the assessor. The study results represent 151 VLBW children of the original cohort of 176. This response rate of 86% is relatively high for a cohort of which 39% were non-Dutch mothers and 36% were low educated mothers. Other strengths of the study are that there were no missing values for the BDT-AD and the assessor was unaware of the child’s educational placement at 66 months CA.

This study also has some limitations. The parents and the assessor were both aware of the child’s birth status and therefore may have been biased in their observations. However, significant differences in the abnormal scores between the VLBW group and the term group were found only on the Attention problems scale of the CBCL. If parents were biased, differences between groups would be expected on the other CBCL scales as well. Moreover, the present results on the CBCL-AP are consistent with the conclusions of a meta-analysis, which found almost a medium effect size for parent and teacher ratings on CBCL-AP 1. With respect to the performance tests and observation, the assessor carefully followed the test protocols in order to minimise bias.

The exclusion of term born children with developmental problems may have produced a selective term sample. However, the CBCL scores of the term group were in the average range which indicates a representative sample 14.
**Clinical Relevance**

Sustaining attention is crucial for a child’s cognitive development and academic performance. Therefore, the early detection of attention problems and timely referral for intervention are important. This study suggests that the observation of a VLBW child’s ability to maintain attention during task-directed behaviour, before s/he begins school, is associated with future educational placement. Observations of a child’s attention abilities can easily complement the standardised follow-up assessments. However, additional studies are warranted to validate the observation of attention during these follow-up assessments.

Intervention studies, directed at improving attention abilities at preschool age in VLBW children, are required.

**Acknowledgements**

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REFERENCES


Chapter 5

Assessing independency in daily activities in very preterm children at preschool age

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ABSTRACT

This study investigates whether very low birth weight (VLBW) preschoolers experience disability in daily activities and what the risk factors for disability in daily activities are.

The Dutch Pediatric Evaluation of Disability Inventory (PEDI-NL) was used to detect disability in daily activities in 143 VLBW children without cerebral palsy (CP) at 44 months of corrected age (CA). Data from the psychomotor-developmental index (PDI) and the mental developmental index (MDI) of the Bayley Scales of Infant Development II (BSID II) at 24 months CA, and data relating to perinatal and socio-economic status were available. Disability in daily activities was found in 27 (19%) VLBW children without CP. High frequencies of disability were found in 19 (13%) children on the mobility domain and in 12 (8%) children on the social functioning domain. The multiple logistic regression analyses showed that low BSID II outcomes (< 2SD) were risk factors for disability in the mobility domain, but not for disability in the social functioning domain. The predictive value of the BSID II outcomes is moderate, 46% of the VLBW children with a low PDI and 44% with a low MDI developed a disability in the mobility domain. This study showed a higher frequency of disability in daily activities in VLBW preschoolers compared to term born peers. Therefore, it is suggested to assess VLBW children’s performance of daily activities before they start school.
INTRODUCTION

Research shows that at 3 to 4 years of age, very low birth weight (VLBW) children experience difficulties in cognition, language, attention, executive functions, motor development and neuromotor development. Furthermore, these children also experience behavioural difficulties.

The above studies assessed bodily functions and psychomotor activities, rather than the ability to participate in daily activities. Adequately performing daily activities, such as self-care, mobility, and social functioning, enables VLBW children to participate in family life, preschool programmes and interact with their peers. Although participation is considered to be an important aspect of child development, studies measuring this in VLBW children are scarce. Effective performance of daily activities is associated with a higher health related quality of life and promotes general health and well-being.

The Pediatric Evaluation of Disability Inventory (PEDI) is an instrument that measures independency in daily living and covers essential daily activities in self-care, mobility and social functioning. In the Netherlands the Dutch PEDI (PEDI-NL) was used in a follow-up study which examined the effect of an early intervention programme for VLBW infants: the Infant Behavioral Assessment and Intervention Program (IBAIP©). The PEDI-NL formed part of the follow-up assessment when children were assessed at 44 months of corrected age (CA). The corrected age is the actual age minus the days born premature. Despite better mean scores in the mobility scales of the PEDI-NL in children who received the intervention, both the intervention and control VLBW children performed significantly worse than their term born peers on most of the PEDI-NL scales at 44 months CA. Limitations in independency may hinder the participation of VLBW children in daily activities. Further exploration of these problems is therefore needed.

Two earlier studies, evaluated daily activities of VLBW children at the age of 2-3 years and 5 years respectively. However, these studies included VLBW children with cerebral palsy (CP), who are known to be at risk of disability in self-care, mobility and to a lesser extent in social functioning.

In this study, we aimed to determine the frequency of disability in daily activities in a cohort of VLBW children, <32 weeks and/or <1500 grams, without CP. These children were part of the above mentioned IBAIP follow-up study: a multicentre randomised controlled trial (RCT). In addition, we investigated whether low scores on the Bayley Scales of Infant Development II (BSID II) at 24 months of CA were risk factors for disability in daily activities at preschool age, taking perinatal and socio-economic status into account.
METHODS

Participants
The parents of VLBW infants who participated in the multicentre RCT on the IBAIP \(^{13,14}\) were asked to take part in a follow-up study with their children at 44 months CA. For this RCT, 176 VLBW infants born with a birth weight < 1500 gram and/or gestational age < 32 weeks were included. The VLBW infants were born in 7 hospitals in Amsterdam, the Netherlands. Infants with severe congenital abnormalities, those whose mothers had a documented history of illicit drug use or severe physical or mental illness, infants from non-Dutch speaking families for whom an interpreter could not be arranged, and infants who participated in other trials were excluded from the RCT.

Data on perinatal characteristics and socio-economic status of the included children were available, together with data from the Bayley Scales of Infant Development (BSID II) at 24 months CA.

Procedure
Parents of the VLBW children who gave their informed consent to participate in the follow-up study were interviewed about the daily activities of their children by one assessor, an occupational therapist. The assessor has been trained in the use of the Dutch Pediatric Evaluation of Disability Inventory (PEDI-NL) \(^{19}\). The assessments were administered at home between August 2007 and February 2010 at the children’s corrected age of 3 years and 8 months. This is just before the VLBW children start school in the Netherlands, at 4 years of uncorrected age.

Measurements

PEDI-NL
The PEDI is designed to assess the individual performance of essential daily activities in all children who show potential delays in the development of daily activities. It is particularly appropriate for children with physical or combined physical and cognitive impairments \(^{12}\). The PEDI has been used for children with several diagnoses including CP, acquired brain injury, Down’s syndrome, musculoskeletal disorders and developmental coordination disorder and is translated into multiple languages \(^{20}\). The PEDI involves a structured interview with a parent or caregiver and is appropriate for children from 6 months to 7.5 years of age. The PEDI consists of approximately 200 items categorised into three domains: self care, mobility and social functioning, and administration takes 45-60 min. According to the International Classification of Function, Disability and Health, Children and Youth version (ICF-CY) \(^{9}\) terminology, both the capacity and
the performance of essential daily activities in the domains are measured. Capacity is measured by identifying the daily activities which the child has shown to perform independently. Results of capacity are reflected in the skills scale scores for each of the three domains. Performance is measured by assessing the level of assistance, given to the child by the caregiver, which is needed to accomplish the daily activity. Results of performance are reflected in the assistance scale scores of the domains. Thus, the PEDI consists of 6 scales each with a mean score of 50 and a standard deviation (SD) of 10. For each PEDI scale there are norm scores comprising age bands of 6 months. The Dutch version of the PEDI (PEDI-NL) is a cross-cultural adaptation of the USA version with good psychometric properties 19,21. The intraclass correlation coefficients (ICC) for the inter-rater reliability were .99 for all PEDI-NL scales. The ICC for test-retest reliability varied between .91 and .98 19,21. The PEDI-NL has the same domains as the PEDI. A score below 2 SD of the norm represents a disability in daily activity of the assessed domain.

Perinatal and socio-demographic risk factors

For the assessment of potential risk factors for disability in daily activities, we selected several perinatal and socio-demographic characteristics which are established in other studies. As risk factors we selected gestational age < 28 weeks 22; birth weight < 1000 grams 23; bronchopulmonary dysplasia (BPD) 24 defined as received oxygen therapy at 36 weeks post menstrual age 25; abnormal cranial ultrasound scan 26,27 defined as any degree of intra ventricular haemorrhage, and/or periventricular leukomalacia and/or ventricular dilatation, sepsis 28; male gender 29; first child; low education level of the mother 29, and having a mother not born in the Netherlands 29.

Bayley Scales of Infant Development (BSID II)

The BSID II has been used to identify those infants and toddlers with a developmental delay 18. It is recommended for the follow-up care of VLBW infants at 24 months CA 30. The VLBW children of this RCT were assessed at 24 months CA using the Dutch version of the BSID II 14,31. The BSID II’s Psychomotor Developmental Index (PDI) and the Mental Developmental Index (MDI) were both used in this study. The PDI evaluates the level of fine and gross motor development, and the MDI assesses the child’s cognitive, language and social development 18. The Dutch version of the BSID-II is a valid instrument 32. The reliability is good: the ICC for test-retest reliability was .75 for the MDI and .80 for the PDI. The ICC for inter-rater reliability was .81 for MDI and .77 for PDI 32. The PDI and the MDI scores have a mean of 100 and a SD of 15. The PDI and MDI scores were dichotomised: scores below 70 (< 2 SD) were regarded as low.
**Analyses**

All statistical analyses were performed using the Statistical Package for Social Sciences version 16.0 for Windows (SPSS Inc, Chicago, Illinois).

The number and percentage of VLBW children who have a disability in daily activities were calculated for each of the 6 PEDI-NL scales.

Univariate and stepwise multiple logistic regression analyses were performed to explore risk factors, but only for the PEDI-NL's scales, for which a high frequency (> 5%) of disability was found. The selected perinatal and socio-demographic risk factors, low PDI and low MDI scores were included in the logistic regression analyses. We also included the IBAIP as a covariate because in the follow up of the RCT the mean scores on PEDI-NL's mobility scales were significantly better in the IBAIP group than in the control group 15.

Agreement between a disability in daily activities and low PDI and/or low MDI was calculated only when PDI and/or MDI were significant risk factors in the multiple logistic regression analyses. A *p*-value less than .05 was considered significant.

**RESULTS**

**Participants**

Data from the PEDI-NL in 151 VLBW children (86% of the original cohort) were collected at a mean corrected age (SD) of 44 (0.5) months. Reasons for non-participation were the relocation to another country for six children and withdrawal of eleven children. Two children had died and six children were untraceable.

Perinatal characteristics and socio-demographic factors did not differ significantly between the participants and the 25 non-participants. However, children with a father not born in the Netherlands withdrew significantly more often (*p* = .002) and first children continued to participate significantly more often (*p* = .005). Of the 151 participants, 8 children (5%) were excluded because of cerebral palsy (CP). For one child, only one of the six PEDI-NL scales (namely self-care skills) was completed. The characteristics of the participants are shown in table 1.
Table 1: Perinatal and socio-demographic characteristics of the VLBW sample (n=143)

<table>
<thead>
<tr>
<th>Perinatal factors</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weeks of gestation, mean (SD)</td>
<td>29.9 (2.1)</td>
</tr>
<tr>
<td>Gestation &lt; 28 weeks, n (%)</td>
<td>21 (15)</td>
</tr>
<tr>
<td>Birth weight in grams, mean (SD)</td>
<td>1284 (338)</td>
</tr>
<tr>
<td>Birth weight below 1000 grams, n (%)</td>
<td>36 (25)</td>
</tr>
<tr>
<td>Received oxygen therapy at 36 weeks postmenstrual age, n %</td>
<td>25 (18)</td>
</tr>
<tr>
<td>Abnormal cranial ultrasound a, n %</td>
<td>39 (27)</td>
</tr>
<tr>
<td>Septic periods before discharge, n (%)</td>
<td>68 (48)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>70 (49)</td>
</tr>
<tr>
<td>Part of twin or triplet, n (%)</td>
<td>35 (25)</td>
</tr>
<tr>
<td>First born child, n (%)</td>
<td>102 (71)</td>
</tr>
<tr>
<td>Social factors</td>
<td></td>
</tr>
<tr>
<td>Maternal education ≤ 10 years, n (%)</td>
<td>55 (39)</td>
</tr>
<tr>
<td>Maternal education &gt; 10 years, n (%)</td>
<td>88 (61)</td>
</tr>
<tr>
<td>Maternal age in years, mean (SD)</td>
<td>32.2 (5.3)</td>
</tr>
<tr>
<td>Paternal age in years, mean (SD)</td>
<td>35.9 (7.1)</td>
</tr>
<tr>
<td>Mother born in the Netherlands, n (%)</td>
<td>92 (61)</td>
</tr>
<tr>
<td>Father born in the Netherlands, n (%)</td>
<td>86 (60)</td>
</tr>
<tr>
<td>Family status of 2 parents, n (%)</td>
<td>122 (85)</td>
</tr>
<tr>
<td>At Discharge</td>
<td></td>
</tr>
<tr>
<td>Hospitalisation days, mean (SD)</td>
<td>53.0 (26)</td>
</tr>
<tr>
<td>Oxygen supply at discharge, n (%)</td>
<td>5 (4)</td>
</tr>
<tr>
<td>Infant Behavioral Assessment and Intervention Program until 6 months CA, n (%)</td>
<td>73 (51)</td>
</tr>
</tbody>
</table>

Data are given in number with % of means with standard deviation (SD)

a abnormal ultrasound scan defined as; Intraventricular haemorrhage (IVH), and/or periventricular leukomalacia (PVL) and/or ventricular dilatation

IVH was defined according to Papile et al 33.

PVL was defined according to de Vries et al 34.

Disability in daily activities

Analyses showed that 19% of the 143 VLBW children were assessed as having at least one disability on any of the 6 PEDI-NL’s scales. A disability on at least 2 scales was found for 6% of the children. Disability was most frequently present on the mobility skills scale (13%) followed by the social functioning assistance scale (8%) (Table 2). Five children (4%) had disability on both the mobility skills scale and the social functioning assistance scale.
Table 2: Disability in daily activities of 143 VLBW preschoolers, children with CP excluded, as measured with Pediatric Evaluation of Disability Inventory (PEDI-NL)

<table>
<thead>
<tr>
<th>Scales</th>
<th>Scores &lt; 1 SD</th>
<th>Disability (scores &lt; 2 SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self care skills</td>
<td>18 (13)</td>
<td>4 (3)</td>
</tr>
<tr>
<td>Self care assistance</td>
<td>31 (22)</td>
<td>3 (2)</td>
</tr>
<tr>
<td>Mobility skills</td>
<td>92 (65)</td>
<td>19 (13)</td>
</tr>
<tr>
<td>Mobility assistance</td>
<td>19 (13)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Social function</td>
<td>15 (11)</td>
<td>0</td>
</tr>
<tr>
<td>Social function assistance</td>
<td>81 (57)</td>
<td>12 (8)</td>
</tr>
</tbody>
</table>

Number (percentage).
Norm population: 16% of scores fall below 1 SD and 2.5% of scores fall below 2 SD.

Risk factors for disability in daily activities

Complete data from the BSID II for 134 children were available. Univariate logistic regression analyses showed several significant risk factors for disability on the mobility skills scale and disability on the social functioning assistance scale (Table 3).

For disability on the mobility skills scale the multiple logistic regression analyses showed that a low MDI combined with a low PDI were risk factors: Odds ratio for MDI is 6.6 (95% CI; 1.8-23.7) \( p = .004 \) and for PDI is 4.8 (95% CI: 1.1-21.3) \( p = .04 \), Nagelkerke R Square is .22.

For disability on the social functioning assistance scale the multiple logistic regression analyses showed that having a mother of non-Dutch origin was a risk factor: Odds ratio is 6.9 (95% CI: 1.4-34.1) \( p = .02 \), Nagelkerke R square is .13.

Table 3: Univariate logistic regression analyses of 142 VLBW preschoolers; children with cerebral palsy excluded

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Mobility skills &lt; 2 SD</th>
<th>Social function assistance &lt; 2 SD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Exp B (95% CI for B)</td>
<td>Exp B (95% CI for B)</td>
</tr>
<tr>
<td>Birth weight &lt; 1000 grams</td>
<td>3.4 (1.2 – 9.1) ( ^a )</td>
<td>1.0 (.26 – 4.0)</td>
</tr>
<tr>
<td>Gestational age &lt; 28 weeks</td>
<td>1.6 (.33 – 7.3)</td>
<td>1.2 (.24 – 5.8)</td>
</tr>
<tr>
<td>Bronchopulmonary dysplasia (BPD)</td>
<td>3.6 (1.3 – 10.5) ( ^a )</td>
<td>.98 (.20 – 4.8)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>2.1 (.76 – 5.6)</td>
<td>1.6 (.48 – 5.2)</td>
</tr>
<tr>
<td>Abnormal Cranial ultrasound</td>
<td>1.3 (.44 – 3.6)</td>
<td>.87 (.22 – 3.4)</td>
</tr>
<tr>
<td>Infant Behavioral Assessment and Intervention Program (IBAIP)</td>
<td>.65 (.24 – 1.7)</td>
<td>.65 (.20 – 2.2)</td>
</tr>
<tr>
<td>MDI &lt; 70 at 24 months CA</td>
<td>8.7 (2.7 – 28.4) ( ^c )</td>
<td>3.3 (.78 – 14.0)</td>
</tr>
<tr>
<td>PDI &lt; 70 at 24 months CA</td>
<td>7.7 (2.0 – 29.1) ( ^b )</td>
<td>1.1 (.13 – 9.7)</td>
</tr>
<tr>
<td>First born</td>
<td>.63 (.23 – 1.7)</td>
<td>1.2 (.31 – 4.7)</td>
</tr>
<tr>
<td>Male</td>
<td>1.5 (.58 – 4.1)</td>
<td>2.3 (65 – 7.9)</td>
</tr>
<tr>
<td>Mother’s education ≤ 10 years</td>
<td>1.2 (.46 – 3.2)</td>
<td>1.7 (.52 – 5.6)</td>
</tr>
<tr>
<td>Mother non-Dutch origin</td>
<td>1.9 (.70 – 4.9)</td>
<td>5.3 (1.4 – 20.6) ( ^a )</td>
</tr>
</tbody>
</table>

\( ^a \) \( p < .05 \) \( ^b \) \( p < .01 \) \( ^c \) \( p < .001 \)
**Predictive value of the low PDI and low MDI scores for disability in mobility (Table 4)**

Forty six percent of the VLBW children with a low PDI were assessed as having a disability on the mobility skills scale at 44 months CA. Forty four percent of the children with a low MDI were assessed as having a disability on the mobility skills scale. However, of the VLBW children with PDI or MDI scores ≥ 70, 10% and 8% respectively were assessed as having a disability on the mobility skills scale.

**Table 4:** Disability in the mobility skills of the PEDI-NL at 44 months of CA, in relation to the PDI and MDI of the BSID II at 24 months of CA

<table>
<thead>
<tr>
<th>BSID II scores</th>
<th>n =142</th>
<th>PEDI-NL Mobility skills no disability: 123 (87)</th>
<th>PEDI-NL Mobility skills disability: 19 (13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PDI at 24 months CA</td>
<td>134 Missing: 6</td>
<td>Missing: 2</td>
<td></td>
</tr>
<tr>
<td>PDI at 24 months CA ≥ 70</td>
<td>123 111 (90)</td>
<td>12 (10)</td>
<td></td>
</tr>
<tr>
<td>PDI at 24 months CA &lt; 70</td>
<td>11 6 (54)</td>
<td>5 (46)</td>
<td></td>
</tr>
<tr>
<td>MDI at 24 months CA</td>
<td>138 Missing: 2</td>
<td>Missing: 2</td>
<td></td>
</tr>
<tr>
<td>MDI at 24 months CA ≥ 70</td>
<td>122 112 (92)</td>
<td>10 (8)</td>
<td></td>
</tr>
<tr>
<td>MDI at 24 months CA &lt; 70</td>
<td>16 9 (56)</td>
<td>7 (44)</td>
<td></td>
</tr>
</tbody>
</table>

Number and (percentages)

**DISCUSSION**

**Disability in daily activities**

This study demonstrates that approximately one fifth of VLBW children, without CP, had disability in daily activities when they start school. Disability was highest in relation to mobility (13%), and social functioning (8%). As evaluation of daily activities forms no standard part of follow-up programmes in the Netherlands these outcomes reveal hidden disabilities at the time of school entry which may hinder effective age related participation. The detection of these disabilities is relevant as these children may not get the support they need to optimise their daily activities.

On the mobility skills scale disability was frequently found, still only 1% of the VLBW children required help for mobility according to the mobility assistance scale. An explanation for this discrepancy is that the mobility skills scale specifically questions the speed of a child’s mobility whilst the mobility assistance scale does not. This confirms the findings of other studies which showed that VLBW children performed motor skills more slowly than their term born peers. 35,36.
This study showed that the VLBW children have adequate social skills but need assistance to use them in daily situations. The less well developed executive functions found in these children may have contributed to their increased need for assistance with social functioning. Executive functions, for example, the ability to stay focused despite ever-present distractions, display self-control, multitask, or perform multistep procedures, even when interrupted are needed to participate in different social situations.

In the VLBW children a low frequency of disability in self-care was found. An earlier study of 425 five year old VLBW children, including children with CP (13%), born between 1988 and 1992, found 12% scoring below 2 SD on PEDI self care skills. It could therefore be argued that a disability in self-care is mostly found in VLBW children diagnosed with CP. Another explanation for this difference in disability in self-care skills, is that it may not be detectable at 44 months of age because at this age self-care is to a large extent, guided by the parents. The problems in self-care may arise when the VLBW children go to school and are required to become more independent in activities such as using the toilet, dressing themselves, etcetera. Longitudinal studies in VLBW children until school age are necessary to evaluate the development in their daily activities.

**Risk factors for disability in daily activities**

The univariate logistic regression analyses showed several significant risk factors. The IBAIP was not a significant factor, even though earlier research found a positive effect from this intervention on the mean scores in independency in mobility. It seems that the IBAIP improves independency in mobility, but does not prevent disability in mobility.

The multiple logistic regression analysis for disability in mobility showed that a low MDI and low PDI were significant risk factors. Apparently, children with a low developmental level at 24 months of age are at risk of being less independent in mobility at 44 months. Regarding disability in social functioning, being born to a non-Dutch mother was found to be a significant risk factor. One explanation for this finding is that children born to a non-Dutch mother may have less well developed Dutch language skills.

The explained variances of the multiple logistic regression analyses were small and varied between 13% and 22%. This supports the assumption of the ICF-CY that disability in daily activities is not only determined by diseases or difficulties concerning bodily functions, but should be viewed in the context of the child. Personal factors, for example, the coping style and the individual character, together with environmental factors, also influence the performance of daily activities.
Predictive value of the PDI and MDI

Forty-six percent of the VLBW children with a low PDI, and 44% with a low MDI did not have a disability in mobility at 44 months CA. Only 10% of the VLBW children with a normal PDI score (≥ 70) and 8% with a normal MDI score (≥ 70) showed disability in their mobility. Thus, a normal PDI and/or MDI score would seem to be a good predictor of a child having no disability in mobility at 44 months CA. However, low PDI and/or MDI scores alone, are not necessarily adequate predictors of disability in mobility at 44 months CA and do not predict disability in social functioning.

As predictors for disability in daily activities are insufficient, an assessment of the performance of daily activities is necessary in order to identify VLBW children with such a disability. Prior to their enrolment in school they may benefit from interventions directed to support participation in family life, primary school, and with peers. Future research is necessary to evaluate the effect of intervention aimed at improving daily activities in VLBW children.

Limitations

It is difficult to compare the results of this study with the two other studies that used the PEDI with VLBW children because they utilised only 3 of the 6 PEDI scales, included children with CP and examined them at a different age. In addition, the validity of PEDI for children whose delays are primarily behavioural or social, is not well established. Therefore, more studies relating to the performance of VLBW children on the PEDI are warranted in order to obtain further insight into levels of independency in daily activities and the need for support.

Conclusions

This study shows that one in five VLBW children without CP requires extra support in daily activities of self care, mobility and social functioning when starting to attend school. Risk factors for disability in daily activities comprise both child and environmental factors. Accordingly, the predictive value of the MDI and the PDI collected at 2 years of age for disability in daily activities is limited. Therefore, assessing independency in daily activities at the time of school entry is needed to identify those children who may benefit from interventions to support participation in family life, in school programmes and with peers. Our findings support the monitoring of daily activities with the PEDI. Additional studies on the performance of VLBW children on the PEDI and on the effect of intervention to improve daily activities are warranted.
Acknowledgements

We thank all the participating parents and children and M.J.Wolf for her assistance in the planning of this study and support during data collection.

Conflict of interest

None of the authors has a conflict of interest or financial disclosure relevant to this manuscript.
REFERENCES


Chapter 6

The relationship between multiple developmental difficulties in very low birth weight children at 3½ years of age and the need for learning support at 5 years of age

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ABSTRACT

This study investigated whether multiple developmental difficulties are more frequent in very low birth weight (VLBW) children than in those born full term. The association between multiple developmental difficulties assessed at 3½ years of age and educational provision for the child at 5½ years was also investigated, with ‘educational provision’ referring to the curriculum, school placement and the level of learning support. There were 143 VLBW children without cerebral palsy (CP) and 41 term-born peers assessed at 3½ years of age. The assessment included 6 measures of development: word comprehension, visual motor integration, visual perception, motor coordination, executive functioning and behaviour. Educational provision was determined at age 5½ years. A mildly abnormal score (score <1 standard deviation) was considered to indicate developmental difficulty. Scores from the six measures of development were analysed to determine the difficulty frequency and the presence of multiple difficulties (>1 difficulty score) in each child. This study showed that at 3½ years of age, the VLBW children had significantly more difficulty with motor coordination than their term-born peers. In addition, 27% of the VLBW children had multiple difficulties compared to 10% in the term-born group. Multiple logistic regression analyses showed that of the difficulties, impaired motor coordination was most strongly associated with the requirement for learning support two years later. Regression analyses showed that having multiple difficulties was significantly associated with the need for learning support (Odds Ratio of 3.4 (95% CI 1.5–7.8). These results show that the presence of multiple difficulties in a preschool-age child can impact the child’s educational provision two years later.
INTRODUCTION

The number of very low birth weight (VLBW) children with severe neonatal morbidities is decreasing worldwide. However, VLBW children are at risk of neurodevelopmental problems. Meta-analyses and reviews show that VLBW children, mainly those ≥ 4 years of age, do not perform as well as their term-born peers in domains such as word comprehension, visual motor integration, visual perception, motor coordination and executive functioning. VLBW children also have more behavioural difficulties. Further, a number of studies show that VLBW children older than 4 years of age are at increased risk of difficulty in multiple developmental domains, with ‘difficulty’ defined as a score < 1 standard deviation (SD).

Impaired development becomes more apparent in VLBW children as they get older, and having multiple difficulties can significantly impact a child’s educational achievement. Therefore, early detection of difficulties in multiple developmental domains, together with the identification of appropriate interventions, are important steps for helping ensure that a child is able to reach his or her learning potential.

This study compared VLBW children with their term-born peers with respect to the frequency of difficulties (scores < 1 SD), the presence of multiple difficulties (difficulty score > 1) and the cumulative level of difficulty across several developmental domains at 3½ years corrected age (CA). It also investigated the association between difficulties at 3½ years CA and educational provision at 5½ years CA in VLBW children. In this paper, ‘educational provision’ is used as a general term that encompasses school curriculum, school placement and/or the provided levels of learning support.

METHODS

This study utilised data from an earlier follow-up study of a multicentre randomised controlled trial (RCT) evaluating the effectiveness of an early neurobehavioral intervention program, the Infant Assessment and Intervention Program (IBAIP).

Participants

VLBW children, together with a comparison group of term-born children, were assessed at 44 months CA. This age was chosen in order to investigate the performance of the VLBW children across several developmental domains just before they started school. In the Netherlands, VLBW children enter school when they are 48 months old (uncorrected age). For readability, we use the...
term ‘3½ years CA’ instead of ‘44 months CA’. The RCT included 176 VLBW infants with a birth weight < 1500 g and/or a gestational age < 32 weeks. The VLBW infants were recruited at 7 hospitals in Amsterdam, the Netherlands. In the RCT, 86 VLBW children received the IBAIP 15 while 90 VLBW children received standard care. Briefly, the neurobehavioural intervention consisted of 6–8 interventions at home that were performed after hospital discharge up to 6 months CA. The infant’s neurobehavioural organisation and self-regulatory competence were assessed within the context of their home environment. The parents were shown how to adjust the environment to meet their infant’s needs and how to support the capacity for self-regulation. The VLBW children were assessed at 6, 12 and 24 months CA 15-17. Children with cerebral palsy (CP) often have multiple impairments and require special educational provisions 18; accordingly, children diagnosed with CP by a paediatrician or neurologist were excluded from this study.

The term-born children were recruited via Amsterdam’s Public Health Service. Invitation letters were sent to 200 parents a few months before their child would be 3½ years old. The inclusion criteria for the term group were as follows: born at 37 weeks of gestation or later; birth weight of at least 2500 g; and no referral to a psychologist, a paediatrician or another physician because of developmental or health problems. By a process of consecutive selection, the comparison group of term-born children and their parents were matched to the distribution of the VLBW group with respect to the following characteristics: male gender, maternal education ≤ 10 years and mother born abroad. The Medical Ethics Committee of the Academic Medical Centre in the Netherlands approved the follow-up study design.

**Procedure**

Parents who agreed to participate in the study were asked to complete questionnaires pertaining to their child’s behaviour and executive functioning. Home visits were organised, and the parents provided written informed consent for participation in the study. The child’s performance was assessed in the home environment by an occupational therapist who knew whether the child was a VLBW child. The children were assessed between August 2007 and February 2010 at 3½ years CA. The study aimed to assess the children approximately a few months before school entry, which in the Netherlands is at 4 years of (uncorrected) age.

The assessments were chosen for two reasons. First, they covered aspects of neurodevelopment in which VLBW children tend not to perform as well as their term-born peers; and second, the assessments included preschool activities that parents often do with their children. The activities included talking about the images in picture books, detecting differences in comparable pictures and drawing tasks. In the follow-up at 5½ years CA, information was collected about educational provisions for the VLBW children 19.
Measurements

Word comprehension

Word comprehension was assessed using the Peabody Picture Vocabulary Test–III-NL (PPVT)\textsuperscript{20}. The PPVT is a widely used norm-referenced test of receptive vocabulary for ages 2½ to 90 years and provides a Word Comprehension Quotient (WCQ). Standard WCQ scores have a mean of 100 and a SD of 15. The PPVT is validated for the Dutch population.

Visual Motor Integration, Visual perception, Motor coordination

The following tests were used: The Beery-Buktenica Developmental Tests of Visual-Motor Integration, including tests of Visual Motor Integration (VMI), Visual Perception (VP), and Motor Coordination (MC)\textsuperscript{21}. The VMI assesses the ability to copy increasingly complex geometric figures with pencil on paper. The VP assesses the ability to recognise the presented figure when it is presented with several comparable figures. As the VP assessment progresses, the number of comparable figures increases. For MC, the child is required to draw lines with a pencil on a printed form, join the dots and stay within the increasingly narrowing borders. The mean (SD) standard scores of the VMI, VP and MC are 100 (15).

Executive functioning

Parents completed a Dutch translation of the Behavior Rating Inventory of Executive Function–Preschool version (BRIEF-P)\textsuperscript{22,23}. This questionnaire assesses executive functioning at home and in a preschool environment. The Global Executive Composite (GEC) refers to the sum score of all items in the BRIEF-P. The raw score of the GEC was converted into a T score based on a gender- and age-related norm determined in American children. Higher scores indicate a higher degree of executive dysfunction. T scores > 62 (≥1 SD) represent difficulty in executive functioning\textsuperscript{22}.

Behaviour

The child’s behavioural and emotional functioning was assessed using the Child Behavior Checklist for ages 1½–5 years (CBCL)\textsuperscript{24}. The CBCL is a questionnaire that consists of 99 statements about the child’s behaviour. The Total Problems score was used. The raw score was converted into a T score using the American norm data, which are applicable to the Dutch population\textsuperscript{25}. A higher score indicates higher levels of behavioural problems. T scores >59 (≥1 SD) indicate a borderline clinical range\textsuperscript{24} and the presence of a behavioural or emotional functioning difficulty.
Educational provision at 5½ years CA

At 5½ years CA, parents were asked about their child’s educational provision, i.e. whether their child was receiving learning support (including whether the child was repeating a school year) and if this was provided in a mainstream or non-mainstream setting. Educational provision was dichotomised in receiving learning support versus following mainstream education.

Statistical analysis

Data were analysed using the Statistical Package for the Social Sciences (SPSS) 16.0 (SPSS Inc., Chicago, Illinois). Scores on the measures were calculated for the corrected age; age corrected for preterm birth. A score < 1 SD of the mean indicated a difficulty in the assessed domain. Missing values were considered ‘no difficulty’. Because the VLBW children were either part of the intervention group or the control group of the RCT, difficulties in the assessed domains of both VLBW groups were compared using chi-square tests or Fisher’s exact tests.

Chi-square tests or Fisher’s exact tests were used to compare the frequency of difficulty (scores < 1 SD) and of multiple (>1) developmental difficulties between the VLBW children and their term-born peers. The total number of difficulties in the VLBW preschoolers was compared with their term-born peers using the Mann-Whitney U test.

To explore the association between single and multiple difficulties in the VLBW children at 3½ years CA and educational provision at 5½ years CA, univariate and stepwise multiple logistic regression analyses were performed.

RESULTS

Participants

Just before school entry, at a mean (SD) corrected age of 44 (0.5) months (3½ years), 151 VLBW children (86% of the original cohort) were assessed, including 76 children in the intervention group and 75 in the control group. Reasons for non-participation were relocation to another country (6 children) and withdrawal from the study (11 children). Two children died and six children were untraceable. The perinatal characteristics and socio-demographic factors did not differ significantly between the 151 participants and the 25 non-participants. However, in children with a father born outside the Netherlands, participation was discontinued significantly more often ($p = .002$), and parents of first-born children continued to participate significantly more often ($p = .005$). Eight (5%) VLBW children were diagnosed with CP at 3½ years CA by a paediatrician or neurologist and were therefore excluded from the study. Thus, 143 VLBW children participated in the current study.
At 5½ years CA, 136 children were assessed in the follow-up of the RCT (77%). Data were available for 117 VLBW children at 3½ years CA as well as at 5½ years CA.

There were 57 parents of term-born children who were willing to participate in the study. To ensure a similar distribution with respect to maternal education in both groups, 16 term-born children from highly educated mothers who applied for participation were not selected for participation. The VLBW group and the term-born group \((n = 41)\) had the same mean age \((3½ \text{ years: } 44 \text{ months (SD 0.4)})\), and the same proportion of boys \((51\%)\), maternal education \(\leq 10 \text{ years (36\%)}\) and mothers born abroad \((39\%)\). The perinatal characteristics and the socio-demographic factors of the VLBW group \((n = 143)\) are shown in Table 1.

In the VLBW group, the following data were missing: WCQ \((n = 2)\), VP \((n = 1)\), GEC \((n = 1)\) and CBCL \((n = 1)\). In the term group, data were missing for the VMI \((n = 1)\) and MC \((n = 1)\).

### Table 1: Perinatal and socio-demographic characteristics of the VLBW sample \((n=143)\)

<table>
<thead>
<tr>
<th>Perinatal factors</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Weeks of gestation, mean (SD)</td>
<td>29.9 (2.1)</td>
<td></td>
</tr>
<tr>
<td>Gestation &lt; 28 weeks, n (%)</td>
<td>21 (15)</td>
<td></td>
</tr>
<tr>
<td>Birth weight in grams, mean (SD)</td>
<td>1284 (338)</td>
<td></td>
</tr>
<tr>
<td>Birth weight below 1000 grams, n (%)</td>
<td>36 (25)</td>
<td></td>
</tr>
<tr>
<td>Received oxygen therapy at 36 weeks postmenstrual age, n %</td>
<td>25 (18)</td>
<td></td>
</tr>
<tr>
<td>Abnormal cranial ultrasound(^a), n %</td>
<td>39 (27)</td>
<td></td>
</tr>
<tr>
<td>Septic periods before discharge, n (%)</td>
<td>68 (48)</td>
<td></td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>70 (49)</td>
<td></td>
</tr>
<tr>
<td>Part of twin or triplet, n (%)</td>
<td>35 (25)</td>
<td></td>
</tr>
<tr>
<td>First born child, n (%)</td>
<td>102 (71)</td>
<td></td>
</tr>
</tbody>
</table>

| At Discharge                          |          |          |
| Hospitalisation days, mean (SD)       | 53.0 (26)|          |
| Oxygen supply at discharge, n (%)     | 5 (4)    |          |
| Infant Behavioral Assessment and Intervention Program until 6 months CA, n (%) | 73 (51) |          |

| Social factors                        |          |          |
| Maternal education \(\leq 10 \text{ years, n (\%)}\) | 55 (39)  |          |
| Maternal education > 10 years, n (%)  | 88 (61)  |          |
| Maternal age in years, mean (SD)      | 32.2 (5.3)|          |
| Paternal age in years, mean (SD)      | 35.9 (7.1)|          |
| Mother born in the Netherlands, n (%) | 92 (61)  |          |
| Father born in the Netherlands, n (%) | 86 (60)  |          |
| Family status of 2 parents, n (%)     | 122 (85) |          |

\(^a\) abnormal ultrasound scan defined as; Intra ventricular haemorrhage (IVH), and/or periventricular leukomalacia (PVL) and/or ventricular dilatation

IVH was defined according to Papile \textit{et al}, 1983 \(^26\).

PVL was defined according to de Vries \textit{et al}, 1992 \(^27\).
Developmental difficulties

The VLBW children in the intervention group and the VLBW children in the control group showed no significant differences in the difficulty scores for any of the six assessments. Therefore, the outcomes of the VLBW intervention group and the VLBW control group were pooled.

Within the domain of motor coordination, the VLBW children had significantly more difficulties than their term-born peers (Table 2).

Table 2: Number (%) of difficulties (defined as a score <1 SD) on the six measures of development at 3½ years of age

<table>
<thead>
<tr>
<th>Assessments</th>
<th>VLBW (n=143)</th>
<th>Term (n=41)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Word Comprehension Quotient (WCQ)</td>
<td>26 (18)</td>
<td>4 (10)</td>
<td>.198a</td>
</tr>
<tr>
<td>Visual Motor Integration (VMI)</td>
<td>18 (13)</td>
<td>1 (2)</td>
<td>.079b</td>
</tr>
<tr>
<td>Visual Perception (VP)</td>
<td>34 (24)</td>
<td>6 (15)</td>
<td>.211a</td>
</tr>
<tr>
<td>Motor Coordination (MC)</td>
<td>37 (26)</td>
<td>4 (10)</td>
<td>.029a</td>
</tr>
<tr>
<td>Global Executive Composite (GEC)</td>
<td>16 (11)</td>
<td>1 (2)</td>
<td>.125b</td>
</tr>
<tr>
<td>CBCL total problems</td>
<td>18 (13)</td>
<td>2 (5)</td>
<td>.254b</td>
</tr>
<tr>
<td>Number (%) of children with multiple (&gt;1) developmental difficulties</td>
<td>39 (27)</td>
<td>4 (10)</td>
<td>.019a</td>
</tr>
</tbody>
</table>

p value: VLBW group compared with term-born group. 

* Pearson's chi-square test  

The median number of difficulties was significantly higher in the VLBW group compared to the term-born group: median (range) 1 (0–5) versus 0 (0–3), p = .002.

In the VLBW group, 65 (45%) children showed no difficulty on any of the six measures of development; in contrast, in the term-born group, 28 (68%) showed no difficulty on any of the six measures of development (p = .01). Multiple developmental difficulties (>1) were found significantly more often in VLBW children compared to their term-born peers: 39 (27%) versus 4 (10%), respectively, p = .019.

Associations with educational provision at 5½ years CA in the VLBW children

Assessment data were available at both 3½ years CA and at 5½ years CA for 117 VLBW children. Of these, 77 (66%) participated in mainstream education without any need for learning support, while 40 (34%) received learning support. Of the 40 that received learning support, 31 were required to repeat a school year, and 9 were referred for non-mainstream provision.

Univariate logistic regression analyses showed a significant association between the need for learning support at 5½ years CA and difficulty on each of the 4 measures performed by the children i.e. the PPVT-III, the VMI, the VP and the MC. (Table 3).
Table 3: Association between difficulty (score < 1 SD) at 3½ years CA and educational provision at 5½ years CA in very low birth weight children (n = 117)

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Exp(B)</th>
<th>95% CI for Exp(B)</th>
<th>p</th>
<th>R Square</th>
</tr>
</thead>
<tbody>
<tr>
<td>Word Comprehension Quotient (WCQ)</td>
<td>3.7</td>
<td>1.4-9.9</td>
<td>.008</td>
<td>.078</td>
</tr>
<tr>
<td>Visual Motor Integration (VMI)</td>
<td>4.4</td>
<td>1.5-12.8</td>
<td>.006</td>
<td>.086</td>
</tr>
<tr>
<td>Visual perception (VP)</td>
<td>2.8</td>
<td>1.2-6.5</td>
<td>.015</td>
<td>.065</td>
</tr>
<tr>
<td>Motor Coordination (MC)</td>
<td>4.4</td>
<td>2.0-10.1</td>
<td>&lt;.001</td>
<td>.139</td>
</tr>
<tr>
<td>Global Executive Composite (GEC)</td>
<td>.38</td>
<td>.55-1.6</td>
<td>.376</td>
<td>.009</td>
</tr>
<tr>
<td>CBCL Total problems</td>
<td>1.9</td>
<td>.67-5.3</td>
<td>.206</td>
<td>.018</td>
</tr>
<tr>
<td>Multiple (&gt;1) developmental difficulties</td>
<td>3.4</td>
<td>1.5-7.8</td>
<td>.004</td>
<td>.094</td>
</tr>
</tbody>
</table>

Univariate logistic regression analysis of difficulty on the six developmental tests and receiving educational provision. Educational provision was dichotomised in receiving learning support versus following mainstream education.

Stepwise multiple logistic regression analysis that included all 6 measures showed that difficulty in motor coordination alone was significantly associated with the need for learning support: Odds Ratio (OR) (95% CI) of 4.6 (1.9–11.0), p = .001; Nagelkerke R-Square, .14. The logistic regression analysis also showed a significant association between the need for learning support at 5½ years CA and the total number of difficulties as an independent variable (B of .56; p = .001; Table 4).

Table 4: Number of difficulties at age 3½ years and educational provision at age 5½ years in very low birth weight children (n = 117)

<table>
<thead>
<tr>
<th>Number of difficulties</th>
<th>Mainstream curriculum with no learning support (n = 77)</th>
<th>Learning support: repeating a school year, support in mainstream or non-mainstream (n = 40)</th>
<th>Learning support, excluding repeating a school year (n = 9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>45 (80%)</td>
<td>11 (20%)</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>17 (61%)</td>
<td>11 (39%)</td>
<td>2 (22%)</td>
</tr>
<tr>
<td>2</td>
<td>8 (57%)</td>
<td>6 (43%)</td>
<td>2 (22%)</td>
</tr>
<tr>
<td>3</td>
<td>5 (42%)</td>
<td>7 (58%)</td>
<td>2 (22%)</td>
</tr>
<tr>
<td>4</td>
<td>2 (50%)</td>
<td>2 (50%)</td>
<td>2 (22%)</td>
</tr>
<tr>
<td>5</td>
<td>0</td>
<td>3 (100%)</td>
<td>1 (11%)</td>
</tr>
<tr>
<td>Total</td>
<td>77 (66%)</td>
<td>40 (34%)</td>
<td></td>
</tr>
</tbody>
</table>

Having multiple developmental difficulties (> 1) at 3½ years CA was also significantly associated with the need for learning support at 5½ years CA; OR 3.4 (95% CI: 1.5–7.8), p = .004; Nagelkerke R-Square, .09 (Table 3).
DISCUSSION

VLBW children without CP had significantly more impaired motor coordination than their term-born peers at 3½ years CA. Difficulty in the other domains was up to 6 times more frequent in VLBW children compared to their term-born peers, but this was not significant. In addition, 27% of the VLBW children exhibited multiple developmental difficulties across a number of the assessed domains. Having impaired motor coordination and multiple developmental difficulties at 3½ years CA, before school entry, were each risk factors that could impact a child’s ability to reach his or her learning potential.

Developmental difficulties

In the current study, 27% of the preschool-age VLBW children had multiple developmental difficulties. Previous studies compared VLBW children with their term-born peers with respect to multiple developmental difficulties at higher ages 7-10. In older children, neurodevelopment is more advanced; thus, difficulties become easier to detect with increasing age. These studies differed from the current study with respect to the gestational age and birth weight of the participants, the number of outcome measures (≥ 8), the venue of the assessment and the assessments themselves. Nevertheless, these studies also found that VLBW children significantly more often had multiple difficulties compared to their term-born peers. In the current study, 44% of the VLBW children had no difficulty in the assessed domains at 3½ years CA. At 4 years of age, 38% of assessed VLBW children had no difficulties 10, while two studies reported that 25% 7 and 28% 8 had no difficulties at 5 years of age. These data indicate that in VLBW children, the number of difficulties can increase with increasing age. This was also found in the long-term follow-up of a cohort study of VLBW children assessed at 2, 5, 10 and 14 years of age 11.

Relationship of the presence of multiple difficulties to educational provision

In the Netherlands, 2.6% of Dutch children of primary school age (4–12 years) received learning support in either a mainstream or non-mainstream school in 2011 28. This 2.6% did not include children who repeated a school year. In our study, 7 (6%) of the 117 VLBW children with multiple difficulties required some level of learning support (not including repeating a school year). The need for learning support for VLBW children with multiple difficulties will almost certainly increase as they age 11 as the educational demands on a child increase. Coping with multiple difficulties therefore becomes more demanding with increasing age.

The findings of the current study show that developmental difficulties can be detected as early as 3½ years CA. The findings also suggest that detection of multiple difficulties in a VLBW child...
should not rely solely on the assessment of one or two domains or on an extremely abnormal score; rather, it should involve assessment across a number of domains and the detection of several mildly abnormal scores.

School readiness includes several areas: physical, cognitive and social competence as well as positive attitudes towards learning. The current study assessed only limited aspects of physical competence and cognition. It did not assess social competence or attitudes towards learning. This may be the cause of the limited variance with regard to educational provision as explained by having multiple difficulties, i.e. 9%. In addition, this might also explain why 22 of the 40 (55%) VLBW children who received learning support did not have multiple developmental difficulties.

Impaired motor coordination was the most common difficulty in VLBW children. In addition, impaired motor coordination was strongly associated with the need for learning support at 5½ years CA. The motor coordination assessment requires a child to accurately draw lines with pencil on a pre-printed form. This task demands several abilities: understanding the task, following instructions, maintaining a stable sitting posture, visual acuity for seeing the dots and borders on the form, the ability to hold and draw with a pencil, motor planning, sustained visual attention while drawing and persevering with a task even when it is difficult. The clear association between difficulty with motor coordination and the need for increased levels of learning support can be explained by the fact that 19% of the school curriculum for 5-year-old children requires the ability to take part in paper and pencil activities.

Relevance

Our findings suggest that the early identification (at 3½ years CA) of multiple difficulties in VLBW children is important and allows appropriate arrangements to be made for effective school entry. The multiple developmental difficulties that were assessed in the current study are relevant to common preschool activities and to activities that parents may be particularly willing to do with their child. Helping parents provide an environment/structure that supports their child's development and mitigates behavioural problems during routine preschool activities will almost certainly help prepare a child for school entry. Specifically, impaired motor coordination can be addressed using play/exercise books that require the use of fine motor skills. However, more research is needed to clarify which interventions best support school-readiness in VLBW children with multiple developmental difficulties.
Limitations

One limitation of this study is that the assessor was aware of whether a child was VLBW or term-born prior to the home assessment. However, the assessment protocols were strictly adhered to. Another limitation is that there were no educational data for 27 VLBW children and for the term-born peers.

Conclusions

Compared to their term-born peers, significantly more VLBW children, not diagnosed with CP, had multiple developmental difficulties at 3½ years CA just before they started school. In addition, impaired motor coordination or the presence of multiple developmental difficulties could impact a child’s ability to reach his or her learning potential.
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Chapter 7

General Discussion
Very low birth weight (VLBW) children are at risk of developmental problems (Chapter 1). The Infant Behavioral Assessment and Intervention Program (IBAIP)\(^1\) aims to prevent these problems by improving the self-regulation and the development of VLBW infants. The IBAIP sensitises parents to enhance their infant’s physical attempts to self-regulate him/her during interactions with the environment. These interactions comprise e.g. eye-contact and daily activities for example bathing, feeding and play. Self-regulation during the interactions requires adequate processing of sensory information. A randomised controlled trial (RCT) conducted by our departments showed positive effects on developmental outcomes at 6 and 24 months of corrected age (CA)\(^2\,^3\). This thesis comprises a follow-up study of this RCT that was designed to evaluate whether the IBAIP continued to be effective at the corrected age of 44 months. The corrected age of 44 months was chosen because this is shortly before children start school in the Netherlands at 4 years. The studies described in the previous chapters addressed two objectives of this thesis. The first objective was to evaluate the effect of the IBAIP at 44 months CA. The second objective was to compare outcomes of VLBW children with term born peers.

In this chapter the main results of the previous chapters will be discussed, followed by methodological considerations, clinical implications and suggestions for further research.

**MAIN FINDINGS**

**Effects of the IBAIP at 44 months CA**

The IBAIP improved mobility assessed with the Dutch version of the Pediatric Evaluation of Disability Inventory (PEDI-NL)\(^4\), and sensory processing with respect to endurance/tone and oral sensory processing as measured with the Dutch version of the Sensory Profile (SP-NL)\(^5\) at 44 months CA (Chapter 2).

The IBAIP did not improve self care and social functioning assessed with the PEDI-NL (Chapter 2), nor executive functioning as measured with the Dutch version of the Behavior Rating Inventory of Executive Function-Preschool version (BRIEF-P)\(^6\,^7\), the Visual attention task (VAT) of the Developmental Neuropsychological assessment (NEPSY)\(^8\) and the Gift delay task\(^9\) (Chapter 3). In addition, the IBAIP did not improve visual motor integration (VMI)\(^10\) nor word comprehension as measured with the Peabody Picture Vocabulary Test III-NL (PPVT)\(^11\) and cognition assessed by items of the Miller Assessment for Preschoolers (MAP)\(^12\) (Chapter 3). Further, the IBAIP did not impact on behaviour problems measured with the Dutch version of the Child Behavior Checklist (CBCL)\(^13\) (Chapter 3). At 6 months CA positive effects of the IBAIP were found with respect to motor, mental and behaviour outcomes\(^2\). We assume that the IBAIP stopped too early, at 6
months CA, to have long lasting effects on e.g. the mental development and behaviour because early improvements of early interventions may fade away if the interventions do not extend to the sensitive period during which for example cognition primarily develops 14.

However, subgroups of VLBW children namely children with bronchopulmonary dysplasia (BPD) 15, children born extremely preterm (EPT) at a gestation of less than 28 weeks, boys, children born to a low educated mother, and children with an abnormal ultrasound brain scan (US) profited significantly from the IBAIP compared to controls (Chapters 2 and 3). The domains of development for which positive effect of the IBIAP was found in these subgroups will be addressed in a separate paragraph.

In line with the improved developmental outcomes of the IBAIP at 6 and 24 months CA 2;3, better functional outcomes at 44 months CA were found for motor development. Apparently, the positive impact of the IBAIP on motor development at 6 and 24 months 2;3 sustained up to preschool age resulting in a higher level of independency in mobility.

We hypothesise that the parent’s adjustment of the environment to their infant’s neuro-behavioural needs combined with the physically co-regulatory support offered by the parents to their infants in the IBAIP group improved the infant’s sensory processing, which enhanced adequate sensory motor experiences and strengthened the bodily awareness. This hypothesis corroborates the theory of sensory integration 16. Previous studies have suggested that adolescents who continue to experience difficulties with processing and integrating sensory information exhibit difficulties in performing activities of daily living, education and work 17. We assume that the IBAIP by influencing the sensory processing is foundational for further motor development and results in better mobility during daily activities at preschool age.

Recent trials of two other post-discharge early interventions, the Victorian Infant Brain Study-Plus (VIBeS-Plus) and the Modified version of the Mother-Infant Transaction Program (MMITP), which also focus on sensitive parent-infant interactions and infant development, found different results at 3-4 years of age. The VIBeS-Plus did not influence motor development and cognition 18, but found a positive effect on behaviour at 4 years of age. The MMITP did not significantly improve motor development of the children at 3 years of CA, but significantly more children in the MMITP group had better cognitive outcomes 19. However, the difference was not significant when the cognitive outcomes were adjusted for maternal education 19.

Although the IBAIP, MMITP and VIBeS-Plus post-discharge early intervention programmes are comparable in that they address parent-infant interaction, there is variability with regard to the content of the interventions. The VIBeS-Plus and the MMITP primarily focus on the infant’s general development, while the IBAIP focuses on the infant’s physical self-regulatory strategies.
and on the infants' and parents' individual strengths instead of weaknesses.

Other differences between the interventions concern the frequency and the duration of the interventions, and the profession of the interventionists. Further, compared to the IBAIP the VIBeS-Plus was offered to infants with a lower gestational age whilst the MMITP was offered to infants born with higher birth weights.

We assume that the self regulatory support and the strengths based approach of the IBAIP are essential for improving motor development, and explain the sustained effects on motor functions at preschool age.

It would be interesting to identify which content and delivery components of these post-discharge early interventions are the active ingredients that make these interventions effective.

Effects of the IBAIP in most vulnerable VLBW children at 44 months CA

The positive impact on the development of the most vulnerable VLBW children found at 24 months 3 sustained at preschool age. For five subgroups of VLBW children, an extra positive effect of the IBAIP was found on several developmental domains (Chapters 2 and 3).

The first group concerned children with BPD (defined as receiving oxygen therapy at 36 weeks postmenstrual age) 15. Compared to BPD children in the control group, children with BPD in the IBAIP group showed better modulation relating to body position/movement measured with SP-NL (Chapter 2), better social functioning measured with PEDI-NL (Chapter 2) and less withdrawn behaviour measured with CBCL (Chapter 3). This was in line with the results of the IBAIP at 2 years of CA, where a positive impact of the IBAIP on mental and psychomotor development, in VLBW infants with BPD was found 3.

In addition to the overall effects of the intervention the children born extremely preterm (EPT), that is with a gestation of less than 28 weeks, in the IBAIP group had better executive functioning as measured with the BRIEF-P (Chapter 3), better modulation of visual input on emotions and activity level as measured with SP-NL (Chapter 2) and were less emotionally reactive as measured with the CBCL compared to the EPT children in the control group (Chapter 3).

Boys profited extra from the IBAIP in relation to self-care and social functioning as measured with the PEDI-NL (Chapter 2). Further, the VLBW children in the intervention group born to a low educated mother demonstrated better word comprehension according to the results of the PPVT (Chapter 3). The last subgroup for which significant intervention effects were found is the group of children with abnormal neonatal cerebral ultrasound findings. In these children, the IBAIP was found to be particularly effective with respect to modulation relating to body position/movement as measured with the SP-NL (Chapter 2).
The intervention effects in these subgroups of infants with BPD, EPT, male gender, being born to a low educated mother and having an abnormal US, who are known to be particularly at risk for developmental problems, demonstrate that the most vulnerable VLBW-infants gained most from the IBAIP intervention \textsuperscript{20-23}. This is in line with the studies on the MMITP, for which positive effects were seen on development in more vulnerable children with a birth weight below 2000 grams \textsuperscript{19}, but not for less vulnerable children with a GA between 30.0 and 36 weeks \textsuperscript{24}.

**Development of VLBW children compared with term born peers on daily activities, attention and multiple developmental difficulties at 44 months CA**

**Daily activities**

The total group of VLBW children performed significantly worse than their term born peers with regard to daily activities (Chapter 2). The VLBW children required significantly more assistance in self-care and social functioning and their mobility skills were significantly less well developed. Interestingly, the skills of VLBW children regarding self-care and social functioning and the assistance for mobility were more comparable to term born peers. This may indicate that VLBW children need more time to perform their daily activities and more scaffolding in their learning to perform daily activities independently.

The effective performance of daily activities enables a child to participate in family life and with their peers, and enhances health and wellbeing \textsuperscript{25-27}. The daily activities assessed in this thesis with the PEDI-NL (Chapter 2) are part of the definition of school readiness \textsuperscript{28}: a preparedness to learn to read, write, follow directions, interact socially, and function independently in routine, day-to-day activities. We found that 19\% of the VLBW children without CP, showed some level of disability in carrying out daily activities at school entry (Chapter 5). This implies that annually approximately 450 VLBW children at 4 years of age, have some degree of difficulty adjusting to school life in the Netherlands \textsuperscript{29,30}. Disabilities in daily activities cannot be sufficiently predicted via current standard procedures which are used in neonatal follow up: the Bayley Scale of Infant Development- II (BSID-II)\textsuperscript{31} (Chapter 5). Therefore, the assessment of daily activities prior to school entry is required to identify those VLBW children who have limited levels of independence. These children might profit from interventions addressing their functional skills in order to improve their school readiness.
**Attention**

Attention comprises the child’s ability to orientate to, shift between and remain focussed on events, objects, tasks, and problems in the external world. To measure this broad spectrum of abilities comprehensively and from different perspectives at preschool age, attention was explored from the perspective of the child, the parents and the investigator (Chapter 3). VLBW children had significantly lower outcomes on 5 of the 6 evaluation instruments that were applied compared to their term born peers. They had significantly more abnormal scores on the CBCL’s Attention Problems syndrome scale (CBCL-AP) and Miller assessment for preschoolers’ Behavior During Testing Attention Domain (BDT-AD) which measure parent’s perspective on attention during daily life and the investigator’s perspective on attention during testing, respectively.

Attention problems can hinder academic achievement. Therefore, the association between attention problems and educational provision was evaluated. This evaluation showed that the observed problems with attention during testing (BDT-AD) and being distracted by auditory stimuli as measured by the Inattention/distractibility scale of SP-NL were associated with worse educational provision at 5.5 years. Based on the items in the BDT-AD, VLBW children need more support to completely finish a task.

The SP-NL’s Inattention/distractibility scale specifically addresses auditory attention/distraction. Chapter 4 showed that there was no significant difference between VLBW children and their term born peers with respect to this aspect of attention at 44 months CA. This is in line with a study which concludes that no difference between VLBW and term born peers, of 9-10 years of age, existed in sustained attention requiring auditory discrimination. Thus VLBW children are at risk of attention problems, but not all aspects of attention are at an increased risk.

**Multiple developmental difficulties**

VLBW children exhibit several developmental difficulties during their school period which in concert, might hinder their academic achievements. Therefore, detection of multiple developmental difficulties prior to school entry is necessary in order to address these difficulties at an early age to support the VLBW children in utilizing their learning potential.

At preschool age, 27% of the VLBW children without CP had multiple difficulties; significantly more often compared to their term born peers (10%) (Chapter 6). It can be hypothesised that children who have multiple relatively mild problems will experience more difficulty with complex tasks or situations that require the collaborative use of several functions. This was confirmed by our finding that children with multiple developmental difficulties have a three fold increase of the need for learning support (including repeating a school year). This finding supports the assumption that multiple developmental difficulties hinder academic achievement.
METHODOLOGICAL CONSIDERATIONS

The assessments

Since long term effects of the IBAIP were not known, the impact of the IBAIP was evaluated three years afterwards with instruments covering a broad spectrum of developmental domains including the perspectives of the parents.

Two criteria influenced the selection of assessments. First, according to the limited perseverance of a 44 months old child to perform a series of tasks, it was arbitrary decided that the assessments by the children had to be completed within one hour. Second, to avoid stress in the VLBW children and their parents and to facilitate study participation the assessments were done at the children's homes.

It is known that VLBW children are at risk of having multiple difficulties in several areas of development at school age, but this has not been evaluated at preschool age. Therefore, we composed a comprehensive assessment to evaluate the children at preschool age. We included an assessment on daily activities to gain insight into whether the levels of independency in daily activities in VLBW children of 44 months CA, are appropriate for a successful start in school. Executive functions (EF) were assessed because VLBW children are known to have problems with EF (including attention) at school age which hinder their academically achievements. The IBAIP is aimed at improving self-regulation during interaction. It is assumed that a better self regulation might translate in improved sensory processing and less behaviour problems. Therefore, parents completed questionnaires on sensory processing (SP-NL) and behaviour problems (CBCL).

It could be argued that the assessments performed by the children are only validated for the use in a health care institution. However, for the studies described in this thesis we compared three groups of children; VLBW children of the IBAIP group, VLBW children in the control group and a matched group of term-born children. The children from all groups performed the assessments at home. Therefore, the comparisons of results between groups as presented in this thesis were not biased by the venue of the assessments.

The assessments performed by the children mainly covered activities performed seated in a chair, and related to activities children of preschool age perform spontaneously or with their parents. Assessments covering gross motor skills and intelligent quotient were not included because (1) they are difficult to perform in the home environment and (2) are time-consuming. Thus, precise information on cognition and gross motor functions e.g. balance, jumping, ball skills is missing. However, the PEDI-NL and SP-NL contain domains on aspects of gross motor performance, and aspects of cognition were assessed by items of the Miller Assessment for Preschoolers (MAP) and the PPVT.
Other studies evaluated multiple developmental difficulties in VLBW children at school age including gross motor tests and IQ assessments. This limits the comparison of the results presented in chapter 6 with the studies assessing VLBW children at school age.

The MMITP positively influenced cognition, measured with the BSID at 3 years of age. The BSID was not part of our evaluation at 44 months CA and it remains unknown whether comparable results would have been detected.

A problem for analysing the data was the absence of Dutch norms for the BRIEF-P, VAT, VMI, VP, MC and MAP. To evaluate the performance of Dutch children on these assessments, we composed a group of healthy term born peers. This group was matched with the VLBW groups with respect to age of the children, gender, level of education of the mother, and mother born abroad. It can be argued that this matched group doesn’t precisely reflect the performance of a Dutch child of 44 months because we excluded children with known developmental or health problems.

In addition, we based the cut off value for abnormal scores on the USA norm (Chapters 4 and 6). These norms may not be applicable for Dutch children. However, in the assessed sample 39% of the children were born to a mother born abroad. Therefore, the USA norms of these assessments are arguably acceptable because these norms are based on a comparable number of non-native participants as the assessed sample of our study.

In several assessments, scores for both the corrected and uncorrected age of the VLBW children were applied. Differences were larger between VLBW and their term born peers when using the uncorrected age. No significant difference was found for word comprehension, when calculated for the corrected age (Chapter 3). These findings are important with respect to the school readiness of VLBW children. Given that certain areas such as word comprehension develop rapidly at preschool age, it would seem appropriate to use the corrected age when judging the performance of VLBW children against the norms of their peers at school entry.

We used a conservative level of significance .01 instead of .05 to correct for multiple testing in the comparison of the assessment results of the VLBW groups and term born group (Chapters 2 and 3). Therefore, some outcomes were not considered significant although these were below .05. However, we can be confident about the findings that were significant.

**Study design**

Although the VLBW children were randomised at the start of the RCT, significant differences in perinatal characteristics between the groups of this RCT were found: more children in the IBAIP group were born at < 28 weeks gestation than in the control group, more children in the IBAIP group were oxygen dependent for a period of > 28 days, had septic periods before discharge,
received surfactant, and received indomethacin. As these perinatal characteristics are known to influence development, the outcomes were corrected for these differences (Chapters 2 and 3). Only after these corrections, positive intervention effects were detected. This corroborates the assumption that extra vulnerable infants are at a higher risk of an impaired development.

At 44 months CA 86% of the children included in the RCT participated. This is notable for a cohort in which 36% of the mothers were low educated. The assessed children did not differ from the non-participants, except for only two aspects: firstborn children more often continued to participate and children with a father born abroad more often discontinued. Therefore, we assume that the results of the assessed sample are representative for the total cohort of VLBW children at preschool age.

Although the assessor was blinded for the IBAIP intervention, this was not the case for the investigated child being term born or VLBW. However, the assessor strictly adhered to the assessment instructions to limit bias. Further, parents assessed the performance of their VLBW children not systematically worse compared to the parents of the term born peers on the domains assessed by the SP-NL and CBCL. Therefore it can be assumed that the awareness of parents that their child was born very preterm, did not bias their answers on the questionnaires.

**CLINICAL IMPLICATIONS**

**Effects of the IBAIP at 44 months CA**

In the studies described in the previous chapters, the benefits of the IBAIP for the development of VLBW children was further confirmed as sustained effects on motor development and interaction effects in subgroups of extra vulnerable VLBW children were found at preschool age (Chapters 2 and 3). However, the IBAIP did not improve self care, social functioning, executive functioning, cognition and behaviour at preschool age. The IBAIP was provided up to 6 months CA. Self-care, social functioning, executive functioning and cognition mainly develop when children are older than 6 months. Possibly, early neurodevelopmental improvements of post discharge intervention may fade away if they do not extend to the sensitive period during which the behavioural and mental domain primarily develop 14. Therefore, currently an early intervention program is provided up to 12 months CA, of which the outcomes on development will be evaluated 44.

Interventions that support early development do not just aim for short-term benefits but need to create sustained effects over time 30. However, intervention effects may diminish after cessation of the intervention. Earlier research 45 showed that a second, age-specific intervention “dose” has better results than early intervention alone. In line with this finding, a pilot study is in
progress assessing the additive effect on development of a second intervention at 18-22 months CA in VLBW infants after receiving an early post-discharge intervention up to 12 months CA. To stimulate development in all domains, preventive intervention may be extended across early childhood, aimed at the developmental issues for that specific age.

**Functioning of VLBW children at 44 months CA**

The studies described in the previous chapters demonstrated that VLBW children with a disability in daily activities that hamper their participation in family life and with peers can be identified already at preschool age. In addition, attention problems and having multiple difficulties can be identified before school entry. Possibly, combinations of these problems occur. Unfortunately, we did not evaluate how many VLBW children do have combinations of these three developmental problems. Nevertheless, the early identification of these individual problems is the first step in order to be able to intervene timely in order to support these VLBW children in achieving higher levels of independency in daily activities, improve their attention and preschool skills, and prepare them for school entry.

Allied health professionals (physical, speech and occupational therapists) can offer intervention to VLBW children before they start school. Physical therapy can address the physical condition and mobility skills. Speech therapy can address the speech and language skills. Occupational therapy can help to promote effective participation in daily activities, a child's social-emotional development, the motor coordination of the hands, the visual-motor development and the early cognitive development. In chapter 3 it is described that 44 VLBW children (29%) had received intervention from an allied health professional during the last two years at the age of 44 months. It would be interesting to know to what extent the children had profited from these interventions and how this may have affected outcome.

The results in chapter 4 demonstrated that attention difficulties could be identified before children start school. This is important because the identification of attention problems before school entry provides the opportunity to intervene in order to diminish the negative impact on academic achievements. It is suggested in order to identify attention problems to evaluate specifically whether a VLBW child of preschool age is able to maintain attention during task-directed behaviour, as this ability is associated with later educational provision (Chapter 4).

Multiple developmental difficulties with respect to visual motor integration (including visual perception and motor coordination), word comprehension, executive functioning and behaviour hindered the development and were also detectable already at preschool age (Chapter 6) and increased the need for learning support three fold. Therefore, we recommend to assess VLBW children at preschool age with a comprehensive assessment covering motor development...
(including motor coordination of the hands), cognition and behaviour problems to identify the children with multiple mildly abnormalities. These children might profit from intervention (physical, speech and occupational therapy) aimed at improving their skills levels and to prepare them better for school entry.

Earlier, in the methodological considerations, is described that certain areas such as word comprehension develop rapidly at preschool age. Therefore, it should be considered that VLBW children start school at the corrected age of 4 years rather than at the uncorrected age of 4 years.

FURTHER RESEARCH

Studies evaluating the extended early intervention up to 12 months CA and the additive effect on development of a second intervention at 18-22 months CA in VLBW infants after receiving the extended early post-discharge intervention up to 12 months CA are in progress.

Positive results of the IBAIP were found particularly for VLBW children with BPD and in the EPT born children. However, the number of VLBW children with BPD and EPT included in our study was rather small. Therefore, a study to evaluate the effects of early intervention in these particular vulnerable children is recommended, focussing specifically on social functioning and executive functioning, respectively.

VLBW children at preschool age were shown to have lower levels of independency in daily activities (Chapters 2 and 5), less well developed executive functioning (Chapter 3), more attention problems (Chapter 4) and more multiple developmental difficulties (Chapter 6) compared to term born peers. Therefore, complementary support to improve daily activities, executive functioning (including attention) and preschool skills in VLBW children needs to be developed and evaluated to determine their effectiveness.

In order to ensure school readiness in VLBW children with developmental delay(s) it is proposed to evaluate whether, prior to school entry, occupational therapy, physical therapy and speech therapy positively influence the academic achievements of the VLBW children with developmental delays.

It is proposed to collaborate with the teachers of preschool programmes. Preschool programmes aim specifically to increase school readiness, but are specifically beneficial for children with social risk factors. Research is needed to evaluate the effects of these programmes on the development of VLBW children with developmental delay(s).

The BDT-AD appeared to be suitable to detect attention problems in VLBW children. Attention problems detected with the BDT-AD were associated with educational provision at 5.5 years. However, the reliability and validity of the BDT-AD in VLBW children need to be established.
CONCLUSION

The IBAIP improved motor development in VLBW infants up to 44 months CA. Subgroups of extra vulnerable VLBW infants profited especially from the IBAIP. The impact of VLBW at 44 months CA is: a lower level of independency in daily activities, less favourable executive functioning, less well developed attention and more multiple developmental difficulties. The results in this thesis may indicate that VLBW children need more time to perform their daily activities and more scaffolding in their learning to perform activities independently.

It is proposed to extend the preventive intervention across early childhood, aimed at the developmental issues for that specific age. With respect to attention, it is suggested to observe especially the ability to maintain attention during task-directed behaviour, as this ability is associated with later educational provision. We recommend for the follow up of VLBW children at preschool age a comprehensive assessment with a focus on multiple mildly abnormalities. It is proposed to consider starting school at the corrected age of 4 years rather than at the uncorrected age of 4 years.

To conclude, complementary support to improve daily activities, executive functioning (including attention) and preschool skills in VLBW children needs to be developed and evaluated to determine the effectiveness.
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Summary / Samenvatting
List of Abbreviations
Dankwoord
Curriculum vitae / Portfolio
SUMMARY

This thesis aims to contribute to improvements in the care of children born preterm with a gestation of less than 32 weeks and/or a birth weight below 1500 grams (VLBW). In this thesis, the effects of the Infant Behavioral Assessment and Intervention Program (IBAIP) in VLBW infants, 3 years after the end of the intervention, are presented. In addition, the VLBW children are compared with their term born peers with regard to several aspects of development at 44 months of corrected age (CA).

In the introduction (Chapter 1) is described that VLBW infants are at risk of developmental problems. Several risk factors play a role in the origin of developmental problems. However, also protective factors, like responsive parenting, have been described and may be essential for intervention. Several post-discharge early intervention programmes for preterm infants are developed which focus on parent-infant interaction and aim to improve infant development. One of these programmes is the IBAIP. The IBAIP aims to support an infant's self-regulatory competence and developmental functions via responsive parent-infant interactions. The IBAIP utilises the strengths of the infants and parents. The IBAIP interventionist sensitises parents to interpret their infant's neuro-behavioural expressions in order to securely support their infant's interactions with the environment. The IBAIP interventionist helps parents to adjust the intensity, complexity and timing of the sensory information from the environment to their infant's neuro-behavioural needs and to offer co-regulatory support when interacting with their infant. The co-regulatory support involves, for example, help for bringing the hands together when the infant tries to decrease his/her movements in order to focus his/her attention.

A multicentre RCT was undertaken in 2004 in Amsterdam, the Netherlands. Seven hospitals participated and 176 VLBW infants were randomised; 86 infants received the IBAIP and 90 infants in the control group received standard care. Positive effects of the IBAIP were found for motor, cognitive and behavioural outcomes at 6 months of corrected age (CA). The IBAIP was also found to improve motor development at 24 months CA, and positively influenced cognition in VLBW infants with bronchopulmonary dysplasia (BPD), and VLBW infants with a combination of low maternal education and abnormal cranial ultrasound and/or BPD at 24 months CA. In order to evaluate whether the positive effects of the IBAIP were sustainable, this cohort was reassessed at 44 months. A comprehensive assessment was collated which could be completed at home. In order to compare the performance of the VLBW children of the RCT with term born children, a comparison group of term born children was formed. The comparison group matched the VLBW group with respect to gender, having a low educated mother, and a mother of non-Dutch origin.
Chapter 2 evaluates the effects of the IBAIP in VLBW children at 44 months CA with regard to sensory processing and daily activities. In the follow-up study of the RCT at 44 months CA, the Sensory Profile-Dutch version (SP-NL) and the Pediatric Evaluation of Disability Inventory-Dutch version (PEDI-NL) were administered. At 44 months CA 76 children (88%) of the IBAIP group and 75 children of the control group (83%) participated. In addition, parents of a comparison group of 41 term born peers completed the SP-NL. This group of term born peers was matched with the VLBW groups with respect to the following criteria: male gender (50%), low maternal education (36%) and mother of non-Dutch origin (39%).

After adjustments for pre-randomisation differences in perinatal characteristics, the IBAIP group outperformed the control group significantly on two SP-NL domains (oral sensory processing and sensory processing related to endurance/tone) and on the mobility domains of PEDI-NL.

The following subgroups of VLBW infants profited especially from the intervention: infants with BPD, infants with a gestation < 28 weeks, infants with an abnormal cranial ultrasound scan, and boys.

The term-born group outperformed only the control group, on only one domain of SP-NL: sensory processing related to endurance/tone. The control group scored lower on 5 domains and the IBAIP group on 3 domains compared to the PEDI-NL norm.

These results show, 3 years after the end of intervention, that the IBAIP has a sustained effect on motor development: independency in mobility in daily activities was improved.

In Chapter 3 the IBAIP’s effect on executive functioning, behaviour and cognitive skills at 44 months CA is examined. In addition, the VLBW children are compared with their term born peers.

The Visual Attention Task (VAT), Gift delay, Peabody Picture Vocabulary Test-III-NL (PPVT), Visual motor integration tests and 8 items of the Miller assessment for preschoolers were administered. Parents completed the Behavior Rating Inventory of Executive Function-Preschool (BRIEF-P) and the Child Behavior Checklist (CBCL).

At preschool age, 76 (88%) children of the intervention group, 75 (83%) children of the control group and the 41 children of the term comparison group participated. There were no significant differences between the intervention and control group. However, positive effects of the IBAIP were found on the CBCL, CBCL and BRIEF-P, and PPVT in subgroups of VLBW children: VLBW children with BPD, VLBW children with a gestation < 28 weeks and VLBW children born to a low educated mother, respectively. The VLBW children performed significantly worse than their term born peers with respect to executive functioning, visual attention, attention problems and figure-ground perception.
To conclude, the IBAIP did not effect executive functioning, behaviour and cognition in VLBW children at 44 months CA. However, the most vulnerable children had a clinical relevant profit from the IBAIP. VLBW children performed less well than the term born children.

In Chapter 4 VLBW children are compared with their term born peers on measures of attention at the age of school entry (44 months CA). In addition, the association with educational provision at 5.5 years is explored.

One hundred and fifty-one VLBW children of 44 months CA and 41 healthy term born peers were assessed. Attention was explored using six measures. The children performed the Visual Attention Task of the Developmental neuropsychological assessment and the Gift delay test. The parents completed the Attention problems domain of the Child Behavior Checklist (CBCL-AP), the Inhibit domain of the Behavior Rating Inventory of Executive Function (BRIEF-preschool version), and the Inattention/Distractibility scale of the Dutch Sensory Profile (SP-ID). The assessor completed the attention domain within the Behavior During Testing (BDT-AD) of the Miller assessment for preschoolers. Mean scores and abnormal scores were calculated.

VLBW children performed significantly worse than their term born peers on all attention measures except for the SP-ID. Significantly more abnormal scores were found in the VLBW group than in the term group on the CBCL-AP and the BDT-AD. Abnormal scores on the BDT-AD and the SP-ID were significantly associated with lower levels of participation in the curricula of mainstream education at 5.5 years CA.

The results presented in this chapter confirm that VLBW children perform less well on attention measures than their term born peers at 44 months CA. The results of the BDT-AD are associated with later functioning in school. This may therefore be a valuable tool for identifying children in need of intervention at preschool age. Further studies on this attention measurement are suggested.

Chapter 5 presents the results of an evaluation of the levels of independence in VLBW children in daily activities at the age of school entry. In addition, risk factors for disability in daily activities are explored.

The Dutch Pediatric Evaluation of Disability Inventory (PEDI-NL) was used to detect disability in daily activities in 143 VLBW children without cerebral palsy (CP) at 44 months CA. Disability in daily activity was defined as a score below 2 SD on a domain of the PEDI-NL.

Data was utilised from the psychomotor-developmental index (PDI) and the mental developmental index (MDI) of the Bayley Scales of Infant Development II (BSID II) at 24 months CA, together with data relating to perinatal and socio-economic status.
Disability in daily activities was found in 27 (19%) VLBW children without CP. High frequencies of disability were found on the mobility domain (in 19 (13%) children) and on the social functioning domain (in 12 (8%) children). The multiple logistic regression analyses showed that low BSID II outcomes (< 2SD) were risk factors for disability in the mobility domain, but not for disability in the social functioning domain. The predictive value of the BSID II outcomes is moderate, 46% of the VLBW children with a low PDI and 44% with a low MDI developed a disability in the mobility domain.

This study found a higher frequency of disability in daily activities in VLBW preschoolers compared to their term born peers at the age of school entry. Prediction of disability in daily activity is limited. Therefore, an assessment of a VLBW child’s performance of daily activities is recommended before school entry.

In Chapter 6 the frequency of multiple developmental difficulties between VLBW children and those born full term is examined. In VLBW children the association between multiple developmental difficulties assessed at 44 months CA and educational provision, at 5.5 years CA, was also investigated. ‘Educational provision’ refers to the curriculum, school placement and the level of learning support.

There were 143 VLBW children, without cerebral palsy (CP), and 41 term-born peers assessed at 44 months CA. The assessment included 6 measures of development: word comprehension, visual motor integration, visual perception, motor co-ordination, executive functioning and behaviour. Educational provision was determined at 5.5 years CA. A mildly abnormal score (score <1 SD) was considered to indicate developmental difficulty. Scores from the six measures of development were analysed to determine the difficulty frequency and the presence of multiple difficulties (>1 difficulty score) in each child. This study found that at 44 months CA, VLBW children had significantly more difficulty with motor co-ordination than their term-born peers: 26% versus 10% (p=.029). In addition, 27% of the VLBW children had multiple difficulties compared to 10% in the term-born group (p=.01). Multiple logistic regression analyses showed that of the difficulties, impaired motor co-ordination was most strongly associated with the requirement for learning support two years later. Regression analyses showed that the presence of multiple difficulties was significantly associated with the need for learning support (Odds Ratio of 3.4 (95% CI 1.5–7.8). These results show that the presence of multiple difficulties in a VLBW child of preschool age can impact the child’s educational provision two years later.
Chapter 7 presents a general discussion of the main findings, the strengths and limitations of the studies, suggestions for clinical practice and suggestions for further research.

The IBAIP improved motor development in VLBW infants up to 44 months CA. However, the IBAIP did not improve executive functioning, behaviour and cognitive skills. Subgroups of extra vulnerable VLBW infants profited especially from the IBAIP.

Being of VLBW, at 44 months CA, results in lower levels of independence in daily activities, less favourable executive functioning, attention difficulties and, more often, multiple developmental difficulties.

The following clinical implications of the results presented in this thesis were formulated. In order to stimulate development in all domains, preventive intervention may be extended across early childhood, aimed at the developmental issues for that specific age.

It is recommended to assess daily activities in VLBW children before they enter school.

With respect to attention, it is suggested to observe systematically the attention during testing as these observations are associated with later educational provision. We recommend for the follow-up of VLBW children at preschool age a comprehensive assessment with a focus on multiple mildly abnormal scores. Given that certain areas such as word comprehension develop rapidly at preschool age, it would seem appropriate to consider starting school at the corrected age of 4 years rather than at the uncorrected age of 4 years.

Several suggestions for further study are formulated. Complementary support to improve daily activities, executive functioning, attention and level of preschool skills in VLBW children needs to be developed and evaluated to determine the effectiveness. It is suggested to further research the effect of the early intervention in VLBW infants with BPD and infants with a gestation < 28 weeks. Establishing the reliability and validity of the BDT-AD in VLBW children seems valuable. It is proposed to study the benefits of allied health interventions for the VLBW children with developmental difficulties. In addition, it is suggested to evaluate the effects of preschool programmes in VLBW children with developmental delay(s).
SAMENVATTING

Dit proefschrift heeft als doel de zorg voor prematuur geboren kinderen te verbeteren. Het gaat in dit proefschrift om kinderen die geboren zijn na een zwangerschapsduur van minder dan 32 weken en/of met een geboortegewicht van minder dan 1500 gram. Het proefschrift beschrijft het effect van het Infant Behavioural Assessment and Intervention Programma (IBAIP), 3 jaar na het afsluiten van het IBAIP, wanneer de prematuur geboren kinderen de gecorrigeerde leeftijd van 44 maanden bereikt hebben. Ook worden de prematuur geboren kinderen met hun op tijd geboren leeftijdgenootjes vergeleken op diverse domeinen van de ontwikkeling.

Introductie (hoofdstuk 1):

Prematuur geboren kinderen hebben een verhoogd risico op problemen in hun ontwikkeling. Er zijn verschillende risicofactoren die een rol spelen in het ontstaan van de problemen. Daarnaast zijn er ook beschermende factoren, bijvoorbeeld een sensitieve en responsieve ouder-kind interactie, die een belangrijke rol kunnen spelen in de interventie voor prematuur geboren kinderen. Er zijn diverse interventies ontwikkeld voor prematuur geboren kinderen die gericht zijn op het verbeteren van een sensitieve en responsieve ouder-kind interactie. Die interventies worden thuis gegeven nadat het kind ontslagen is uit het ziekenhuis. Eén van deze interventies is het Infant Behavioural Assessment and Intervention Programma (IBAIP).

Het doel van het IBAIP is responsieve en positieve interacties tussen ouder en kind te ondersteunen, waardoor de zelfregulatie en de geïntegreerde ontwikkeling van het kind wordt bevorderd. Daarbij wordt uitgegaan van de mogelijkheden van de baby en de ouders. De IBAIP gecertificeerde kinderfysiotherapeut helpt de ouders om bewust naar de gedragsuitingen van hun baby te kijken en om het gedrag van hun baby te interpreteren, zodat zij hun baby veiligheid kunnen bieden en kunnen ondersteunen bij zijn interacties met de omgeving. De ondersteuning door ouders bestaat uit het aanpassen (van de intensiteit, de complexiteit of de timing) van zintuiglijke omgevingsprikkels en/of uit het ondersteunen van de fysieke pogingen die de baby doet om zichzelf te reguleren. Ondersteuning bij zelfregulatie bestaat bijvoorbeeld uit hulp geven voor het bij elkaar brengen van de handjes wanneer de baby pogingen doet zijn bewegingen te verstillen bij het richten van zijn aandacht.

Een gerandomiseerde gecontroleerde effect studie (RCT) naar het effect van het IBAIP werd in 2004 opgezet waaraan zeven Amsterdamse ziekenhuizen meededen. In totaal namen 176 prematuur geboren kinderen deel; 86 kregen IBAIP en 90 kregen de standaard nazorg.

Positieve effecten van het IBAIP werden gevonden voor de motoriek, de cognitie en het gedrag van de kinderen op de gecorrigeerde leeftijd van 6 maanden. Later, op de gecorrigeerde leeftijd
van 24 maanden, werd een positief effect gevonden van het IBAIP op de motoriek. Ook werden positieve significante interacties gevonden tussen IBAIP en (a) kinderen met bronchopulmonale dysplasie (BPD; zuurstof afhankelijkheid ≥ 36 weken post menstruele leeftijd), en (b) kinderen met een combinatie van biologische en sociale risicofactoren (een combinatie van de factor laag opgeleide moeder, afwijkingen op de neonatale hersenscan en/of BPD). Daarom werd besloten om te onderzoeken of er nog effect van het IBAIP was, drie jaar na het stoppen van de interventie, op de corrigeerde leeftijd van 44 maanden. Er werd een uitgebreide testbatterij samengesteld, die afgenomen kon worden in de thuissituatie. Daarnaast werden de prematuur geboren vergeleken met op tijd geboren op diverse aspecten van de ontwikkeling. Daarvoor werd er een groep op tijd geboren geformeerd die vergelijkbaar was voor wat betreft het percentage jongens, het percentage laag opgeleide moeders en het percentages moeders die buiten Nederland zijn geboren.

In hoofdstuk 2 is het effect van het IBAIP beschreven, op de gecorrigeerde leeftijd van 44 maanden, met betrekking tot sensorische informatieverwerking (gemeten met de Nederlandse Sensory Profile (SP-NL)) en alledaagse vaardigheden (gemeten met de Nederlandse Pediatric Evaluation of Disability Inventory (PEDI-NL)). In totaal participeerden 151 kinderen (86%): 76 (88%) van de IBAIP groep en 75 (83%) van de controle groep. De SP-NL werd ook afgenomen bij een groep van 41 op tijd geboren gezonde kinderen die overeenkwam met de groep prematuur geboren, voor wat betreft percentages jongens (50%), laag opgeleide moeders (36%) en in het buitenland geboren moeders (39%). Na correcties voor de verschillen in de perinatale karakteristieken, die er waren tussen de IBAIP groep en de controle groep ondanks de randomisatie, bleken de kinderen in de IBAIP groep significant te verschillen ten opzichte van de kinderen in de controle groep op 3 domeinen van ontwikkeling. Het IBAIP heeft, 3 jaar na het stoppen van de interventie, nog effect en resulteert in (1) een betere sensorische prikkelverwerking met betrekking tot uithoudingsvermogen/tonus, (2) een betere orale sensorische prikkelverwerking en (3) een betere ontwikkeling van dagelijkse activiteiten die een beroep doen op voortbewegen en het maken van transfers (de ambulantie).

Positieve interactie effecten van het IBAIP werden gevonden voor de volgende subgroepen prematuur geboren kinderen: kinderen met BPD, kinderen geboren na een zwangerschapsduur van minder dan 28 weken, kinderen met een abnormale neonatale hersenscan en jongens. De op tijd geboren presteerden beter op 1 domein van de SP-NL en alleen ten opzichte van de prematuur geboren die geen interventie hebben gehad: Sensorische prikkelverwerking met betrekking tot uithoudingsvermogen/tonus. De kinderen in de IBAIP groep presteerden minder t.o.v. de normgroep op 3 van de 6 PEDI-NL domeinen en de kinderen in de controle groep op 5 van de 6 PEDI-NL domeinen.
De resultaten laten zien dat er 3 jaar na het stoppen van de interventie een blijvend effect is van het IBAIP op de motorische ontwikkeling, er is een verbetering van de dagelijkse vaardigheden die een beroep doen op de ambulantie, zoals lopen, transfers en fietsen.

In hoofdstuk 3 is het effect van het IBAIP beschreven op executieve functies, gedrag en cognitieve vaardigheden gemeten tijdens de follow-up op de gecorrigeerde leeftijd van 44 maanden. Kinderen (151 prematuur geboren en 41 op tijd geboren) voerden de volgende testen uit: Visual Attention Task (VAT), Gift delay, Peabody Picture Vocabulary Test-III-NL (PPVT), Visual motor integration tests en 8 items van de Miler assessment for preschooers. De ouders vulden de Nederlandse versies in van de Behavior Rating Inventory of Executive Function-Preschool version (BRIEF-P) en de Child Behavior Checklist (CBCL). In totaal participeerden 151 prematuur geboren kinderen: 76 (88%) van de IBAIP groep en 75 (83%) van de controle groep. Er waren geen significante verschillen tussen de IBAIP groep en de controlegroep. Er werden echter wel positieve significante interactie effecten van het IBAIP gevonden voor subgroepen van prematuur geboren kinderen op respectievelijk de CBCL voor prematuur geboren kinderen met BPD, op de CBCL en de BRIEF-P voor kinderen geboren na een zwangerschapsduur van minder dan 28 weken, en op de PPVT voor kinderen met een laag opgeleide moeder.

De prematuur geboren kinderen presteerden significant minder dan de op tijd geborenen op het gebied van executieve functies, visuele aandacht, figuur achtergrond discriminatie en de prematuur geborenen hadden significant vaker aandachtsproblemen.

De conclusie is dat het IBAIP geen effect heeft op executieve functies, gedragsproblemen en cognitieve vaardigheden op de gecorrigeerde leeftijd van 44 maanden, maar de meest kwetsbare prematuur geborenen hadden wel een klinisch relevant profijt van het IBAIP. De prematuur geborenen presteerden minder goed dan de op tijd geborenen.

In hoofdstuk 4 werden de prematuur geboren kinderen vergeleken met hun op tijd geboren leeftijdsgenootjes met betrekking tot 6 meetinstrumenten die aandacht meten. Dit onderzoek werd gedaan net voordat ze naar de basisschool zullen gaan, op de gecorrigeerde leeftijd van 44 maanden. De samenhang van aandachtsproblemen en de gegeven hulp voor het kunnen volgen van het onderwijs op 5½ jaar, werd onderzocht voor de prematuur geborenen. De kinderen (151 prematuur geboren en 41 op tijd geboren) voerden 2 aandachtstakjes uit namelijk de Visual Attention Task (VAT) en Gift delay. Ouders vulden drie vragenlijsten in waarvan de aandachtsdomeinen werden gebruikt: het Attention problems domein van de CBCL, het Inhibitie domein van de (BRIEF-P) en de Onoplettendheid/ Afleidbaarheid schaal van de SP-NL: SP-ID. De onderzoeker (GV) observeerde de aandacht van de kinderen tijdens het afnemen van alle testen met
behulp van de aandachtsschaal van de Behavior During Testing (BDT-AD) van de Miller assessment for preschoolers. Gemiddelde scores en afwijkende scores werden berekend en vergeleken. De prematuur geboren kinderen presenteerden significant minder op alle meetinstrumenten, behalve op de SP-ID. Significant vaker werden afwijkende scores behaald door de prematuur geboren op 2 van de 6 meetinstrumenten: de BDT-AD en Attention problems van de CBCL.

Kinderen met een afwijkende score op de SP-ID of op de observatiemeting van de onderzoeker (BDT-AD) bleken vaker speciaal onderwijs te volgen of een klas over te doen dan de kinderen die een goede score behaalden.

De resultaten bevestigen dat prematuur geboren minder goed presteren met betrekking tot aandacht, kort voordat ze voor het eerst naar de basisschool zullen gaan. De observaties van de onderzoeker met de BDT-AD hebben een significant verband met de latere schoolprestaties. Dit zou een geschikt instrument kunnen zijn om kinderen te identificeren die behoefte hebben aan interventie voordat ze naar school gaan. Verder onderzoek om de betrouwbaarheid en de validiteit van deze observaties te onderzoeken wordt gesuggereerd.

In hoofdstuk 5 is onderzocht hoeveel prematuur geboren kinderen een beperking hebben in dagelijkse activiteiten en wat de risico factoren voor een beperking in dagelijkse activiteiten zijn.

De Nederlandse Pediatric Evaluation of Disability Inventory (PEDI-NL) werd hiervoor gebruikt bij 143 prematuur geboren kinderen, zonder de diagnose cerebrale paresis, op de gecorrigeerde leeftijd van 44 maanden. Een score onder de 2 SD op een domein van de PEDI-NL werd beschouwd als een beperking in dagelijkse activiteiten. Perinatale karakteristieken van de kinderen, sociaal demografische gegevens en de op 24 maanden afgenomen psychomotor-developmental index (PDI) en mental developmental index (MDI) van de Bayley Scales of Infant Development II (BSID II) werden gebruikt.

Een beperking in zelfstandigheid van alledaagse activiteiten kwam voor bij 27 (19 %) van de prematuur geboren. Hoge percentages van beperking in zelfstandigheid werden gevonden voor de ambulantie vaardigheden (19 (13%)) en voor de hulp bij het sociaal functioneren (12 (8%). Uit de multiple logistische regressie analyses bleek dat lage BSID II uitkomsten (< 2SD) risicofactoren zijn voor een beperking in de ambulantie maar niet voor een beperking in het sociaal functioneren. De voorspellende waarde van de BSID II uitkomsten is matig want slechts 46% van de prematuren met een lage PDI en 44% met een lage MDI hadden een beperking in de ambulantie.

De studie vond dat meer prematuur geboren beperkingen met betrekking tot dagelijkse activiteiten hebben dan op tijd geboren leeftijdgenoten, kort voordat ze voor het eerst naar de basisschool zullen gaan. Een beperking in dagelijkse activiteiten is echter niet goed te voorspellen.
Daarom wordt aanbevolen om de dagelijkse activiteiten van prematuur geborenen te evalueren voordat ze voor het eerst naar de basisschool zullen gaan.

In hoofdstuk 6 werd onderzocht of prematuur geboren kinderen, van 44 maanden oud en zonder cerebrale parese, net zo vaak ontwikkelingsproblemen hebben op meerdere domeinen als op tijd geboren leeftijdgenootjes. Ook werd onderzocht of er een verband is tussen het hebben van meerdere ontwikkelingsproblemen, en het wel of geen hulp nodig hebben voor het kunnen volgen van het onderwijs op 5½ jaar. De vergelijking werd gemaakt voor de volgende 6 ontwikkelingsdomeinen: woordbegrip, visuele motorische integratie, visuele perceptie, motorische coördinatie van de handen, executieve functies en gedragsproblemen. Een score lager dan 1 SD werd beschouwd als een ontwikkelingsprobleem.

Gegevens van 143 prematuur geborenen, zonder CP, en 41 op tijd geborenen werden geanalyseerd.

De prematuur geboren hadden significant vaker een ontwikkelingsprobleem m.b.t. de motorische coördinatie van de handen dan de op tijd geboren: 26% versus 10% p = .029. Ontwikkelingsproblemen op meerdere domeinen werden significant vaker gevonden in de prematuur geborenen (27%) dan in de groep op tijd geboren (10%) p = .01. De multiple regressie analyse liet zien dat een probleem met de motorische coördinatie van de handen van alle onderzochte ontwikkelingsdomeinen het sterkst samenhangt met extra hulp voor het kunnen volgen van het curriculum op school op de leeftijd van 5½ jaar. Ontwikkelingsproblemen op meerdere domeinen bleken significant samen te hangen met extra hulp voor het kunnen volgen van het curriculum op school, 2 jaar later (Odds Ratio is 3.4 (95% CI 1.5–7.8). Deze resultaten laten zien dat op meerdere domeinen ontwikkelingsproblemen hebben een negatief effect kan hebben op de school prestaties 2 jaar later.

In hoofdstuk 7 worden de belangrijkste bevindingen van de studies en enkele methodologische overwegingen besproken. Het hoofdstuk sluit af met suggesties voor het verbeteren van de zorg voor de prematuur geboren kinderen en suggesties voor onderzoek.

Het IBAIP heeft een positief effect op de motorische ontwikkeling van prematuur geboren kinderen, 3 jaar na het stoppen van de interventie. Er werden geen positieve effecten van het IBAIP gevonden voor executieve functies, gedrag en cognitieve vaardigheden. Extra kwetsbare prematuur geboren kinderen profiteerden het meest van het IBAIP.

De premature geboorte heeft op de gecorrigeerde leeftijd van 44 maanden een negatief effect op zelfstandigheid in dagelijkse activiteiten, executieve functies en aandacht. Daarnaast vergroot de premature geboorte de kans op het hebben van problemen op meerdere domeinen van de ontwikkeling.
De volgende klinische implicaties van de resultaten werden geformuleerd. Om te zorgen dat de interventie effect heeft op alle ontwikkelingsdomeinen zou de interventie verlengd moeten worden, bijvoorbeeld tot en met de kleutertijd. De verlengde interventie dient gericht te zijn op de aspecten van ontwikkeling die op die bepaalde leeftijd vooral tot ontwikkeling komen. Het wordt aanbevolen om bij te vroeg geboren kinderen de zelfstandigheid met betrekking tot het uitvoeren van dagelijkse activiteiten te evalueren voordat ze voor het eerst naar de basisschool zullen gaan.

Er is gesuggereerd dat het systematisch in kaart brengen van de aandachtsvaardigheden van het kind tijdens het afnemen van testen bij de follow-up belangrijk is omdat van alle aandachtswaardigheden deze observaties een significante relatie hebben met schoolprestaties op 5½ jaar. Er wordt aanbevolen om bij de follow-up op de peuterleeftijd te identificeren of er sprake is van het hebben van ontwikkelingsproblemen op meerdere domeinen.

Gezien het feit dat bepaalde domeinen op de peuterleeftijd snel ontwikkelen, stellen we voor om te overwegen of het prematuur geboren kind op de gecorrigeerde leeftijd in plaats van op de ongecorrigeerde leeftijd, van 4 jaar, voor het eerst naar de basisschool zou moeten gaan.

De volgende suggesties voor onderzoek zijn gedaan.

Onderzoek naar wat het niveau van dagelijks activiteiten, executieve functies, aandacht en peutervoordelen van prematuur geboren kinderen zou kunnen verbeteren.

Onderzoek naar het effect van de vroege preventieve interventie in kinderen met BPD en kinderen met een extreme vroege geboorte.

Vaststellen wat de betrouwbaarheid en validiteit is van de BDT-AD bij prematuur geborenen.

Onderzoek naar het effect van ergotherapie, fysiotherapie en logopedie bij prematuur geborenen met problemen in hun ontwikkeling.

Onderzoek naar het effect van de voorschool op prematuur geborenen met problemen in hun ontwikkeling.
### List of Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>BDT-AD</td>
<td>Miller Assessment for Preschoolers’ Behaviour During Testing Attention Domain</td>
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<tr>
<td>BPD</td>
<td>Bronchopulmonary Dysplasia</td>
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<tr>
<td>BRIEF-P</td>
<td>Behavior Rating Inventory of Executive Function - Preschool version</td>
</tr>
<tr>
<td>BSID-II</td>
<td>Bayley Scales of Infant Development - II</td>
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<tr>
<td>CA</td>
<td>Corrected Age</td>
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<tr>
<td>CBCL</td>
<td>Child Behavior Check List</td>
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<tr>
<td>CP</td>
<td>Cerebral Palsy</td>
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<td>EF</td>
<td>Executive Functioning</td>
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<tr>
<td>ELBW</td>
<td>Extremely Low Birth Weight (birth weight &lt; 1000 grams)</td>
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<tr>
<td>EPT</td>
<td>Extremely PreTerm born (GA &lt; 28 weeks)</td>
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<td>GA</td>
<td>Gestational Age</td>
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<tr>
<td>IBA©</td>
<td>Infant Behavioral Assessment</td>
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<tr>
<td>IBAIP©</td>
<td>Infant Behavioral Assessment and Intervention Program</td>
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<tr>
<td>ICC</td>
<td>Intra class correlation coefficient</td>
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<tr>
<td>ICF-CY</td>
<td>International Classification of Functioning, disability and health, Children and Youth version</td>
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<tr>
<td>MAP</td>
<td>Miller Assessment for Preschoolers</td>
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<tr>
<td>MC</td>
<td>Motor Coordination test</td>
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<td>MMITP</td>
<td>Modified version of the Mother-Infant Transaction Program</td>
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<td>NICU</td>
<td>Neonatal Intensive Care Unit</td>
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<td>NEPSY</td>
<td>NEuroPSYchological Assessment</td>
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<tr>
<td>NIDCAP</td>
<td>Newborn Individualized Developmental Care and Assessment Program</td>
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<tr>
<td>PEDINL</td>
<td>The Dutch version of the Pediatric Evaluation of Disability Inventory</td>
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<tr>
<td>PPVT</td>
<td>Peabody Picture Vocabulary Test.</td>
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<td>RCT</td>
<td>Randomised Controlled Trail</td>
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<td>SD</td>
<td>Standard Deviation</td>
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<td>SP-ID</td>
<td>Inattention / distractibility scale of SP-NL</td>
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<td>SP-NL</td>
<td>The Dutch version of the Sensory Profile</td>
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<tr>
<td>US</td>
<td>Ultrasound Scanning</td>
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<tr>
<td>VAT</td>
<td>Visual Attention task of NEPSY</td>
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<tr>
<td>VIBeS-Plus</td>
<td>Victorian Infant Brain Studies Plus</td>
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<tr>
<td>VLBW</td>
<td>Very Low Birth Weight</td>
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<tr>
<td>VMI</td>
<td>Visual Motor Integration test</td>
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<tr>
<td>VP</td>
<td>Visual Perception test</td>
</tr>
<tr>
<td>WCQ</td>
<td>Word Comprehension Quotient</td>
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</table>
DANKWOORD

Veel mensen hebben bijgedragen aan dit proefschrift. De promotoren Frans Nollet en Joke Kok, de copromotor Martine Jeukens-Visser, de medeauteurs Aleid van Wassenaer, Karen Koldewijn en Bregje Houtzager, vormden met mij de studie groep voor de studies die beschreven zijn in dit proefschrift. De leden van de studiegroep hebben telkens weer constructief commentaar geleverd op de versies van elk hoofdstuk. Er zijn vele versies van elk hoofdstuk gemaakt voordat ze uiteindelijk publicatie waardig waren. Beste Martine, hartelijk dank, ik kreeg van jou vaak echt super snel een reactie en vrijwel elke keer als ik met een vraag bij je kwam kreeg ik direct antwoord. Ik heb dit ervaren als een grote steun. Door alle individuele bijdrages van de leden van de studiegroep ontstond er steeds meer inzicht in de betekenis van de verzamelde data. In de loop van de tijd heeft dit geleid tot de 5 publicaties! Beste Frans, Joke, Martine, Aleid, Bregje en Karen hartelijk dank! Voor de hoofdstukken 5 en 6 mocht ik gebruik maken van de data die Janeline van Hus verzamelde. Janeline bedankt hiervoor en ook voor onze overlegmomenten “tussendoor”. Ik bedank ook Marie Jeanne Wolf. Samen met Marie Jeanne en later ook met Bregje, zijn we begonnen met creëren van het onderzoek “STIPP 3.8”, waarvan het resultaat beschreven is in dit proefschrift. Ook wil ik graag de collega’s bedanken, speciaal Annoek Louwers die mij vaak heeft geholpen bij het ontwerpen van de posters en power points en ook Marielle de Ridder, die een luisterend oor bood en het afmaken van het proefschrift faciliteerde.

Ik bedank ook de ouders van de prematuur geboren kinderen, die ik mocht behandelen in de polikliniek van de revalidatie afdeling van het AMC. Door hen te behandelen zag ik daadwerkelijk wat de wetenschappelijke publicaties over de premature geboorte betekende voor het kind en zijn/haar ouders. Deze kinderen daagden me uit om oplossingen te zoeken voor de problemen die zij en hun ouders ondervonden. Deze behandelingen inspireerden me om door te gaan met het maken van de publicaties van het onderzoek, waarin ik de behandelde kinderen herkende. Hartelijk bedankt: Lucas, Jente, Boi, Issa, Estreya, Oumaima, Florian, Ferry, Romy, Rachel, Flint, Daen, Sara, Jasna, Lauren, Simon, Oumaima, Sara, Livia en Ramiel!

Van Richard van Seenus BV kregen we de stoel waarin de kinderen getest zijn. Hartelijk dank daarvoor.

Zonder de medewerking van de GGD Amsterdam hadden we geen gegevens van op tijd geboren leeftijdgenootjes kunnen verzamelen. Hartelijk dank Marcel van der Wal (Hoofd Productgroep Jeugd Cluster Epidemiologie, Documentatie en Gezondheidsbevordering) van GGD Amsterdam voor de hulp!
Prof. Dr. van Baar, Prof. Dr. Becher, Prof Dr. Van Goudoever, Prof Dr. Grootenhuis, Dr. Meester, Prof Dr. Nijhuis-van der Sanden bedank ik voor hun welwillendheid om zitting te nemen in de promotiecommissie.

Warsito Suyatiman, Susan Verkerk, andere familieleden, Manon Kruse en de paranimfen (Anita van Kerkwijk en Gerry van der Hulst) stimuleerden mij om niet te stoppen maar door te gaan en het proefschrift af te maken; allen bedankt! Vele uren heb ik met Susan aan de keukentafel gezeten om het Engels te verbeteren. Dit heeft vast bijgedragen aan de snelle acceptatie van hoofdstukken 5 en 6 door het tijdschrift Research in Developmental Disabilities.
CURRICULUM VITAE

Gijs Verkerk is geboren op 3-6-1959 in Leeuwarden. Hij volgde het VWO aan het St Antoniuscollege in Gouda. In 1983 behaalde hij het diploma Ergotherapeut aan de opleiding Ergotherapie in Weesp. Al op de opleiding Ergotherapie was Gijs gefascineerd door de ontwikkeling van jonge kinderen. Hij studeerde af met een onderzoek naar het gebruik van rola’s en schommels in de kinderergotherapie.


In de periode 1984-1985 was hij mede initiatiefnemer van, en parttime groepsleider in, een nieuw opgezet kinderdagverblijf voor Arabischtalige en Nederlandstalige kinderen in de Indische buurt in Amsterdam. Daarnaast werkte hij van 1986-1988 als groepsleider in het Janna-huis, een instelling met dag- en nachttopvang voor 0-7 jarige kinderen met psycho-sociale problemen in Amsterdam.

In deze periode leerde hij de babyverzorging en zag hij hoe gezonde kinderen zich spontaan als het ware “als vanzelf” ontwikkelen.


In 1991 stapte hij over naar het Revalidatie centrum Amsterdam waar hij werkte met volwassenen.

Van 1987 tot 1996 werkte hij, part-time, als ergotherapeut in het multidisciplinaire team van de Stichting Dysfatische Ontwikkeling. Binnen deze stichting leverde hij een bijdrage aan:

-Het verbeteren de ergotherapie diagnostiek van ontwikkelingsdyspraxie.
-Het opzetten van een groepsbehandeling voor kinderen met dysfatische ontwikkeling.
-Het geven van ergotherapie aan kinderen met dysfatische ontwikkeling en ontwikkelingsdyspraxie op de school die voor deze kinderen is opgezet.
-Het ontwikkelen van de cursus voor de diagnostiek en behandeling van kinderen met dysfatische ontwikkeling en ontwikkelingsdyspraxie.

In 1992 trad hij in dienst van de revalidatie afdeling van het AMC. In eerste instantie leverde hij een bijdrage aan het ontwikkelen en verbeteren van de ergotherapeutische zorg aan zowel volwassenen als kinderen in de kliniek en polikliniek. Hij introduceerde diverse meetinstrumenten binnen de ergotherapiebehandeling.

Onderwijs

Gijs Verkerk ontwikkelde diverse onderwijs modules:
In 1995 ontwikkelde hij 2 modules voor paramedici in Estland over de ergotherapie behandeling van kinderen met cerebrale parese. Beide modules doceerde hij in Tartu (Estland). In 1996 paste hij deze modules aan en doceerde de aangepaste versie binnen de opleiding ergotherapie in Praag.
In 1997-1998 werkte hij part-time bij de Hogeschool van Amsterdam als docent ergotherapie. Hij gaf de modules kinderergotherapie aan 2e jaars studenten ergotherapie.
In 1998 maakte Gijs, voor de Transfer groep Rotterdam en Omstreken (TRO), een opzet voor de Post-HBO opleiding Kinderergotherapie. Deze opzet werd in 1999 gebruikt door de TRO.

Gijs hoopt in de toekomst een bijdrage te kunnen leveren aan het verder onderbouwen van: de zorg voor prematuren, de kinderrevalidatie en de kinderergotherapie.
Publicaties:

In wetenschappelijke tijdschriften


In niet-wetenschappelijke tijdschriften / boek.


Verkerk G., Onderzoek naar de bruikbaarheid van de Canadian Occupational Performance Measure (COPM) bij ouders van kinderen met beperkingen, *BOSK Magazine*, 2006;Nr.5:36.


# Portfolio

PhD student: G.J.Q. Verkerk  
PhD period: Februari 2007 – January 2014  
PhD supervisor: Prof. dr. F. Nollet

<table>
<thead>
<tr>
<th>1. PhD training</th>
<th>Year</th>
<th>Workload (Hours/ECTS)</th>
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<tbody>
<tr>
<td><strong>Specific courses</strong></td>
<td></td>
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<tr>
<td>- “How to practice evidence based Health Care”. The Dutch Cochrane Centre in AMC.</td>
<td>1998</td>
<td>32 / 1.1</td>
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<tr>
<td>- Module “Praktische Biostatistiek”. Afdeling Klinische Epidemiologie en Biostatistiek, AMC.</td>
<td>2001</td>
<td>30 / 1.1</td>
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<td>- Reference Manager basis. Stafgroep Automatiseringsopleidingen AMC.</td>
<td>2005</td>
<td>3 / 0.1</td>
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<td>- ICH GCP Training Course. PROFESS® Medical Consultancy B.V.</td>
<td>2006</td>
<td>16 / 0.6</td>
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<tr>
<td>- Training in de “Sensory Profile”, Harcourt, Amsterdam.</td>
<td>20-2-2007</td>
<td>4 / 0.2</td>
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<tr>
<td>- Clinical Epidemiology- The essentials. AMC Graduate School for Medical Sciences.</td>
<td>2009</td>
<td>12 / 0.4</td>
</tr>
<tr>
<td>- Congres Executieve functies, Hogrefe, Utrecht.</td>
<td>11-6-2009</td>
<td>4 / 0.2</td>
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<td>- Introductie van “Infant Behavioral Assessment and Intervention Program” AMC, Amsterdam.</td>
<td>22-6 t/m 25-6-2009</td>
<td>32 / 1.2</td>
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<tr>
<td>- Practical Biostatistics. AMC Graduate School for Medical Sciences.</td>
<td>2011</td>
<td>33 / 1.2</td>
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<td>- Attending “Infant Behavioral Assessment and Intervention Program” course.</td>
<td>29-11-2011</td>
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**Subtotal courses**: 170 / 6.3
Presentations

- Oral presentation: Frame work for the follow up study STIPP at 3.8 years. Bi-weekly research presentations at Rehabilitation Department, AMC, Amsterdam. 
  1-11-2007  14 / 0.5

- Oral presentation: Discussing lack of Dutch norms for the follow up study STIPP at 3.8 years. Bi-weekly research presentations at Rehabilitation Department, AMC, Amsterdam. 
  10-11-2008  14 / 0.5

- Oral presentation: Results of the follow up study STIPP at 3.8 years. Bi-weekly research presentations at Rehabilitation Department, AMC, Amsterdam. 
  19-4-2010  14 / 0.5

- Oral presentation “The Infant Behavioral Assessment and Intervention Program in very low birth weight infants improves functional motor activities at preschool age” op derde Symposium Landelijke Werkgroep Neonatale Follow up, Amsterdam. 
  10-3-2011  14 / 0.5

- Poster presentation “The Infant Behavioral Assessment and Intervention Program improves functional skills in infants born preterm at the age of 44 months” op16th International WCPT Congress, World Physical Therapy 2011, Amsterdam, The Netherlands. 
  23-6-2011  14 / 0.5

- Oral presentation “Te vroeg geboren peuters en het meten van aandacht” op 2e jaarcongres Ergotherapie Nederland, te, Utrecht. 
  24-11-2011  14 / 0.5

- Oral presentation “Prematuur geboren kinderen hebben beperkingen in de dagelijkse vaardigheden op de peuterleeftijd. Bi-weekly research presentations at the Rehabilitation department, AMC Amsterdam. 
  2-4-2012  14 / 0.5

- Oral presentation “Prematuur geboren kinderen hebben beperkingen in de dagelijkse vaardigheden op de peuterleeftijd”. Bi-weekly research presentation at the Neonatology department, AMC Amsterdam. 
  19-4-2012  14 / 0.5
Presentations (continued)
- Oral presentation “Prematuur geboren kinderen hebben beperkingen in de dagelijkse vaardigheden op de peuterleeftijd”. Presentatie op: Onderzoekers Netwerk Ergotherapie (ONE) regio Amsterdam.
- Oral presentations: “Attention problems in VLBW preschoolers” en “VLBW preschoolers’ disabilities in daily activities” op het 4e Symposium Landelijke Werkgroep Neonale Follow up, Amsterdam.
- Poster presentation: “Preterm born preschoolers’ disabilities in daily activities” op 4th congress of the European Academy of Paediatric Societies (EAPS), Istanbul, Turkey.
- Oral presentation “Attention problems in very low birth weight preschoolers” op 4th congress of the European Academy of Paediatric Societies (EAPS), Istanbul, Turkey.
- Oral presentation “Attention problems in very low birth weight preschoolers” op 4th congress of the European Academy of Paediatric Societies (EAPS), Istanbul, Turkey.
- Oral presentation “Multiple problems bij prematures” follow-up of de STIPP studie op 3.8 years. Bi-weekly research presentations at the Rehabilitation department, AMC Amsterdam.
- Oral presentation “Ergotherapie behandeling van een ernstig te vroeg geboren kleuter”. Monthly Evidence Based Practice meetings at the Rehabilitation Department, AMC Amsterdam.

<table>
<thead>
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<th>Date</th>
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<td>25-9-2012</td>
<td>28 / 1</td>
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<td>21-1-2013</td>
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<td>7-10-2013</td>
<td>14 / 0.5</td>
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Attendance (Inter)national conferences
- Congress Impact of intervention “Can we affect typical and atypical development of the human brain?”, Groningen, the Netherlands.
- Derde Symposium Landelijke Werkgroep Neonale follow up, Amsterdam.
- 2e jaarcongres Ergotherapie Nederland, te, Utrecht.
- 4th Congress of the European Academy of Paediatric Societies (EAPS), Istanbul.
- 4e Symposium Landelijke Werkgroep Neonale Follow up, Amsterdam.

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<th>Subtotal conferences</th>
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<tr>
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<td>20 t/m 23-6-2011</td>
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<td>5 t/m 9-10-2012</td>
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<td>25-9-2012</td>
<td>8 / 0.25</td>
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2. Teaching

<table>
<thead>
<tr>
<th>Year</th>
<th>Workload (Hours/ECTS)</th>
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<tr>
<td>2008</td>
<td>56 / 2</td>
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**Running the course** (organizing, lecturing and mentoring):
"De ergotherapie behandeling van kinderen met ontwikkelingsdyspraxie".

**Subtotal teaching**  
56 / 2

3. Other activities

<table>
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<th>Workload (Hours)</th>
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<td>2012</td>
<td>8 / 0.25</td>
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<tr>
<td>2013</td>
<td>8 / 0.25</td>
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Deelname “Onderzoekers Netwerk Ergotherapie (ONE) regio Amsterdam”.


Attending “Infant Behavioral Assessment and Intervention Porgram class “.

**Subtotal other activities**  
40 / 1.4

**Total**  
610 / 21.7
Functioning of very preterm born children at preschool age
Follow-up of an early intervention programme

Gijs Verkerk

Uitnodiging

Voor het bijwonen van de openbare verdediging van het proefschrift:

Functioning of very preterm born children at preschool age
Follow-up of an early intervention programme

Door Gijs Verkerk

Op vrijdag 10-1-2014 om 14.00 uur.
In de Agrieten kapel
Oudezijds Voorburgwal 231
1012 EZ Amsterdam

Na afloop bent u van harte welkom op de receptie aldaar

Paranimfen
Gerry van der Hulst
gerryvanderhulst@yahoo.com

Anita van Kerkwijk
hajstol@zonnet.nl