

The main aims of this thesis were to extend insight into visual functioning of very preterm/very low birth weight (VP/VLBW) children, including oculomotor, visual sensory and visual perceptive functioning. In addition, we aimed to study associations between deficits in these visual functions and behavioral and motor functioning. To meet these aims, studies were undertaken 1) to clarify previous heterogeneous findings on visual perceptive and visual-motor integration dysfunctions in very preterm born children, 2) to establish a comprehensive profile of visual functioning in VP/VLBW children using a wide range of measures of oculomotor, visual sensory as well as visual perceptive functioning, 3) to extend the profile of visual functioning with measures of visual attention and visual-motor integration performance, 4) to define cerebral visual impairment (CVI) using clear cut empirical criteria derived from the visual assessment outcomes, and evaluate its validity against measures of intellectual and behavioral functioning, and 5) to investigate the visual correlates of motor performance of VP/VLBW children. The main results are summarized in Table 1.

SUMMARY OF MAIN FINDINGS

In a systematic review using meta-analytic techniques, evidence was found for substantial dysfunctions in visual perceptive as well as visual-motor integration functioning in VP/VLBW children (**chapter 2**). Results were derived from 16 studies covering a total sample of 1478 VP/VLBW children, indicating selective rather than global effects of VP birth/VLBW on visual perceptive functioning. Specifically, visual-spatial perception was found most affected, as indicated by medium to large-sized differences between VP/VLBW and term born children on the Judgment of Line Orientation ($d = 0.60$) and NEPSY Arrows tests ($d = 0.92$), respectively. Measures reporting a composite score consisting of multiple visual perceptive abilities provided inconsistent findings (Motor-free Visual Perception Test $d = 0.10$, Test of Visual Perceptual Skills Revised $d = 0.72$). Since these meta-analytic results are based on a small number of studies for each of the tests, the findings should be cautiously interpreted and await replication in future studies. In addition, the measures eligible for meta-analysis only tapped into few visual perceptive abilities, highlighting the need to extend the range of measures employed to further unravel visual perceptive problems in VP/VLBW children. Furthermore, our meta-analytic results provided clear evidence for medium-sized visual-motor integration problems ($d = 0.69$), i.e. the ability to copy geometrical shapes, in a sample of 2132 VP/VLBW children derived from 32 studies using the Beery Visual-Motor Integration test. Visual-motor integration deficits were particularly present in boys as compared to girls, were positively associated with gestational age and intelligence, and persisted from childhood into adolescence.

Visual functioning of five-year-old VP/VLBW children was thoroughly investigated, including measures of oculomotor, visual sensory and visual perceptive functioning (**chapter 3**). This extensive examination revealed medium-sized dysfunctions in visual sensory functioning, as well as small to medium-sized dysfunctions in visual perceptive functioning. Specific visual dysfunctions were found in VP/VLBW children, including worse visual sensory functioning than term controls in terms of visual acuity, stereovision and the inferior visual field, and weaker visual perceptive functioning in terms of decreased sensitivity to visual coherence and visual-spatial perceptive dysfunctions. Visual sensory deficits were associated with a history of severe cranial ultrasound abnormalities and retinopathy of prematurity (ROP), but visual perceptive deficits were not associated with any of these neonatal morbidities. Notably, visual sensory and perceptive deficits were only weakly associated with each other, highlighting the fact that most VP/VLBW children with visual perceptive deficits remain unnoticed in routine screening of visual sensory functioning.¹

In addition to visual functioning, we investigated visual attention abilities of VP/VLBW children using newly developed and adapted measures of visual search and attention network functioning that minimized involvement of motor responses (**chapter 4**). Our visual search test minimized fine motor demands using a touchscreen. The systematic manipulation of task conditions in the attention network test (ANT) enabled us to control demands on non-relevant (motor) skills while obtaining indices of attention network efficiency. We found that, compared to term born children, VP/VLBW children showed small and medium-sized decreases in visual search performance and executive attention (i.e. processing conflicting information), respectively. VP/VLBW children showed longer search times and increased error rates during visual search, especially under high stimulus density conditions.

Taken together, the outcomes of the studies described in chapters 2 to 4 confirm the presence of visual sensory, visual perceptive, visual attention and visual-motor integration dysfunctions in VP/VLBW children. Specifically, our findings indicate mostly mild dysfunctions in visual acuity, visual field, binocularity, visual-spatial analysis, recognition under high stimulus density conditions and when processing conflicting information. Visual-motor integration deficits persist throughout childhood and into adolescence, consistent with difficulties in motor development.²

Based on the visual deficits that were found in the study described in chapter 3, a functional and empirically driven classification of CVI was investigated (**chapter 5**). Using this classification, CVI was almost four times more prevalent in VP/VLBW children than in controls. The concurrent validity of the CVI classification was confirmed by medium to large-sized increases in parent reported vision-related problems in children meeting

Table 1 Summary of the main findings of this thesis

Chapter	Participants	Measures	Main findings
2	Meta-analytic sample of 1478 children on visual perceptible functioning and 2132 children on visual-motor integration functioning.	Meta-analytic results of 16 studies on visual perceptible functioning (JLO, K-ABC Gestalt Closure, MVPT, NEPSY Arrows, TVPS-R) and 32 studies on visual-motor integration functioning (Beery VMI)	<ul style="list-style-type: none"> • Particularly visual-spatial perceptible dysfunction in VP/VLBW children • No effect of VP/VLBW on gestalt-closure • Inconsistent findings for visual perceptible measures providing composite scores • Consistent evidence for visual-motor integration dysfunction in VP/VLBW children • Visual-motor integration dysfunction is negatively associated with gestational age and is not associated with age at assessment
3	116 VP/VLBW children 73 term born children	<i>Oculomotor</i> : eye position, motility, convergence, nystagmus, torticollis; <i>Visual sensory</i> : visual acuity, visual field, contrast, stereovision, color vision; <i>Visual perceptible</i> : DTVP-2, face recognition, static and moving coherence;	<ul style="list-style-type: none"> • Visual sensory deficits of VP/VLBW children include visual acuity, inferior visual field and stereovision • Visual perceptible deficits of VP/VLBW children include static visual coherence and visual-spatial perception • No association between visual sensory and perceptible deficits • Moderately positive association between visual perceptible abilities and performance IQ
4	108 VP/VLBW children 72 term born children	Refractive status, WISC-III ANT, WISC-III, newly developed visual search test	<ul style="list-style-type: none"> • Worse visual search speed and accuracy in VP/VLBW children • Group by stimulus density interaction indicating specifically impaired visual search under high stimulus density conditions • Worse executive attention functioning in VP/VLBW children • No effect of VP/VLBW on alerting and orienting attention • Weak and positive association between attention abilities and full scale IQ

Table 1 (continued)

Chapter	Participants	Measures	Main findings
5	105 VP/VLBW children 67 term born children	Oculomotor, visual sensory, visual perceptible measures (detailed above, chapter 3), visual attention measures (detailed above, chapter 4); CSBQ, SDQ, WISC-III, CVI questionnaire	<ul style="list-style-type: none"> • Empirical CVI classification is almost four times more prevalent in VP/VLBW children (24%) than in term controls (7%) • CVI-status positively associated with vision-related problems as indicated by CVI questionnaire • CVI-status positively associated with behavioral and social difficulties as indicated by SDQ and CSBQ • No effects of VP/VLBW without CVI on CVI questionnaire, SDQ and CSBQ • Stepwise effect of CVI and VP/VLBW on performance IQ: VP/VLBW with CVI < VP/VLBW without CVI < term control • No effect of CVI-status on use of therapeutic services or visual rehabilitation
6	106 VP/VLBW children	Oculomotor, visual sensory, visual perceptible measures (detailed above, chapter 3), visual attention measures (detailed above, chapter 4); Beery VMI, M-ABC, neurological examination according to Touwen	<ul style="list-style-type: none"> • Impaired motor functioning in 23-36% of VP/VLBW children • Weak negatively association between oculomotor and visual-motor integration deficits on motor functioning • Moderate negatively association between abnormal neurological status on motor functioning

Note. CVI: cerebral visual impairment CSBQ: Children's Social Behavior Questionnaire; DTVP-2: Developmental Test of Visual Perception, 2nd edition; JLO: Judgment of Line Orientation; K-ABC: Kaufman Assessment Battery for Children; M-ABC: Movement Assessment Battery for Children; MVPT: Motor-free Visual Perception Test; SDQ: Strengths and Difficulties Questionnaire; TVPS-R: Test of Visual Perceptual Skills Revised; VMI: Visual-Motor Integration; VP/VLBW: very preterm/very low birth weight; WISC-III: Wechsler Intelligence Scale for Children, 3rd edition.



criteria for our definition of CVI. No differences in vision-related problems were found between VP/VLBW and term born children without CVI. In addition, analyses of attention and intellectual functioning indicated worse selective attention and performance IQ in VP/VLBW children with CVI. Similar to parent reported vision-related problems, medium to large-sized behavioral and social difficulties were also specifically present in VP/VLBW children with CVI. Interestingly, the difficulties associated with CVI-status did not translate to referrals to therapeutic services or visual rehabilitation.

Visual deficits potentially underlying motor functioning of VP/VLBW children were investigated by analyzing the predictive value of oculomotor, visual sensory and visual perceptive deficits, as well as deficits in visual attention and visual-motor integration functioning on motor performance (**chapter 6**). We confirmed motor problems in VP/VLBW children. Oculomotor and visual-motor integration deficits were weakly predictive of motor functioning. Visual perceptive deficits were weakly associated with aiming and catching ability. In contrast to the weak associations between these visual deficits and motor functioning, abnormal neurological status was moderately associated with motor performance, suggesting that abnormalities in brain development may be more fundamental for the difficulties in motor performance of VP/VLBW children, than abnormalities in visual functioning.

Taken together, the findings described in and chapter 5 and chapter 6 suggest that visual deficits in VP/VLBW children are differentially associated with intellectual, behavioral and motor functioning. Whereas visual deficits, particularly those covered by the CVI classification, were substantially associated with lower performance IQ and difficulties in social and behavioral functioning, visual deficits were not or only weakly related to motor performance of VP/VLBW children. In addition, the CVI classification study (chapter 5) shows that CVI is associated with vision-related as well as non-visual behavioral difficulties in VP/VLBW children, thereby highlighting the possibility that CVI acts as a sensitive indicator of these behavioral difficulties and that the questionnaires for vision-related problems, and social and behavioral functioning cover overlapping aspects of the behavioral outcome of VP/VLBW children.