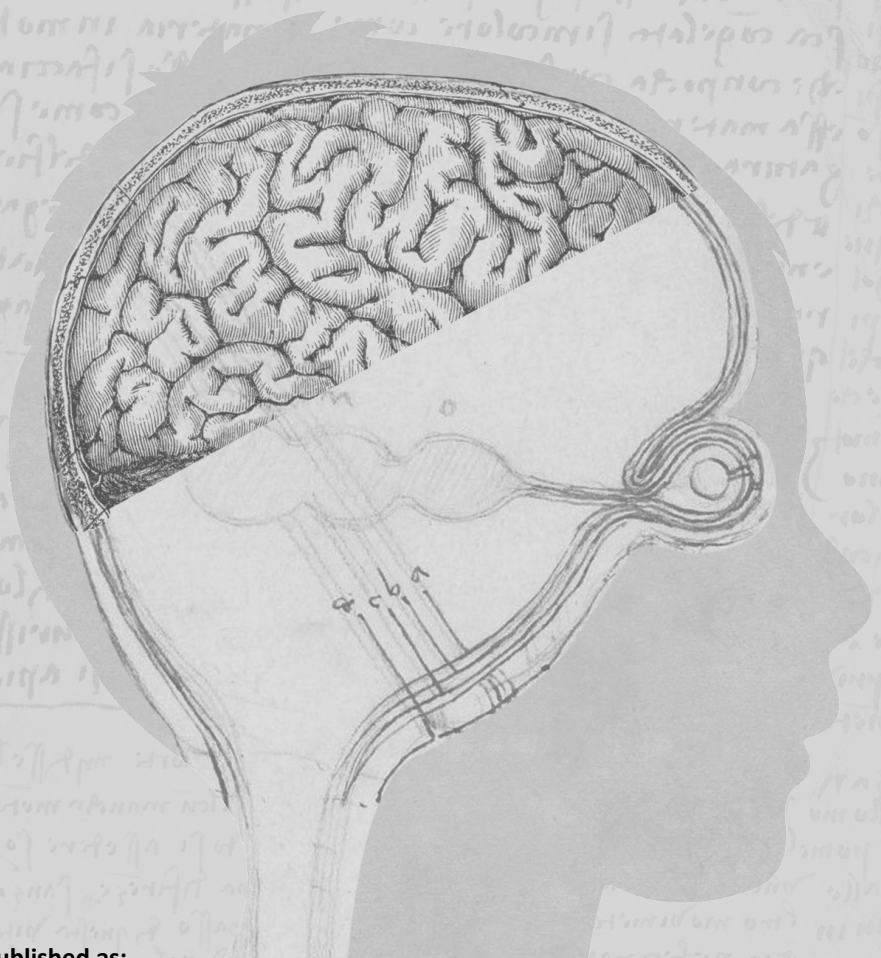
Chapter 2

Visual Perception And Visual-Motor Integration Invery Preterm and/or Very Low Birth Weightchildren: A Meta-Analysis



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ABSTRACT

A range of neurobehavioral impairments, including impaired visual perception and visual-motor integration, are found in very preterm born children, but reported findings show great variability. We aimed to aggregate the existing literature using meta-analysis, in order to provide robust estimates of the effect of very preterm birth on visual perceptive and visual-motor integration abilities. Very preterm born children showed deficits in visual-spatial abilities (medium to large effect sizes) but not in visual closure perception. Tests reporting broad visual perceptive indices showed inconclusive results. In addition, impaired visual-motor integration was found (medium effect size), particularly in boys compared to girls. The observed visual-spatial and visual-motor integration deficits may arise from affected occipital-parietal-frontal neural circuitries.

INTRODUCTION

Improved neonatal intensive care has increased survival rates of very preterm born (gestational age [GA] ≤ 32 weeks) and very low birth weight (VLBW; birth weight [BW] ≤ 1500 grams) children. The rate of major disabilities is fairly low,[1,2] but 50-75 % of VLBW children experience persisting mild to moderate deficits in multiple developmental domains of functioning,[2] including neurocognitive deficits,[3-5] motor impairments,[6] behavioral as well as emotional difficulties, and lower academic achievement.[5]

Deficits in the domain of visual perceptive functions may play an important role in the adverse outcomes of very preterm/VLBW children. Visual perceptive abilities and the ability to use visual information to guide motor behavior, referred to as visual-motor integration, substantially affect a wide range of adaptive abilities including motor skills[7] such as handwriting[8] as well as academic achievement.[9] Therefore, visual perceptive and visual-motor integration deficits may significantly interfere with adaptive functioning. The development of visual perceptive and visual-motor integration abilities in very preterm/VLBW children is considered to be at risk since an estimated 50-70 % of very preterm/VLBW children is reported to suffer from white matter abnormalities that affect neural connectivity.[10,11] Impairments in the neural connectivity, in turn, are associated with deficits in a range of neurocognitive functions.[12] Importantly, deficits in connectivity may hinder optimal signal conduction within the widespread network for visual information processing.[13]

Numerous studies have reported on impaired visual perceptive and/or visual-motor integration abilities in very preterm/VLBW children. However, the results reported show great variability and interpretation of results is hampered by the variety of methods used, small sample sizes and heterogeneous samples. The primary aim of our study was to provide a robust estimate of the effect of very preterm birth/VLBW on visual perceptive and visual-motor integration abilities, using techniques of meta-analysis. Therefore, aggregated effect sizes were calculated from studies that report results of motor-free tests for visual perception and the most widely used test of visual-motor integration: the Beery Developmental Test of Visual-Motor Integration (VMI).[14] The second aim was to study the effects of GA, BW, age at assessment, intelligence and year of birth on study outcome, in order to clarify heterogeneity in study outcomes.

METHODS

Study Selection

This meta-analysis was conducted in accordance with the guidelines proposed by Stroup et al.[15] The computerized databases Web of Science, PsycInfo and EMBASE (including Medline) were searched for relevant studies published before October 2010. Studies on visual perception were searched using the search terms preterm*, premature*, low birth weight, visu*percept*, visu*spatial and visu*cogniti*. Studies reporting on the VMI were retrieved using the search terms: preterm*, premature*, low birth weight, visual-motor integration and VMI. The reference lists of the studies retrieved were manually searched to identify other relevant studies.

Studies that reported outcomes on visual perceptive measures and/or the VMI were included if (1) a case-control design was used or results were reported for very preterm/VLBW children in terms of standardized normed scores; (2) the study included very preterm born (GA ≤ 32 weeks) and/or VLBW (BW ≤ 1500 grams) children; (3) the study included children without congenital or acquired malformations; (4) the study was published in an English language peer reviewed journal. If more than one study reported on the same sample, only the largest sample was incorporated into the analyses to prevent the use of correlated data that would inflate homogeneity of the meta-analytic findings. If a study stratified very preterm/VLBW children by different types of perinatal complications, only the very preterm/VLBW control group was included to minimize effects of additional complications on outcome measures. Data was extracted by the first author and authors of identified studies were contacted for additional data if necessary. To ensure stability of meta-analytic outcome, measures that were reported in fewer than three studies were not incorporated into the meta-analysis.

A total of 16 studies (1478 very preterm/VLBW children) reporting on visual perceptive abilities met inclusion criteria. The retrieved studies reported results on the Judgment of Line Orientation (JLO; n=3),[16] Gestalt Closure subtest of the Kaufman Assessment Battery for Children (K-ABC; n=3),[17] Motor-Free Visual Perception Test Revised (MVPT-R; n=4),[18] Arrow subtest of the Developmental Neuropsychological Assessment battery (NEPSY; n=3),[19] and Test of Visual Perceptual Skills Revised (TVPS-R; n=4).[20] Thirty-two studies (2132 very preterm/VLBW children) reporting on the VMI met inclusion criteria. A flow diagram describing the selection of studies and reasons for exclusion of studies is provided in Electronic Supplement I.

Visual Perceptive Tests

The JLO[16] is designed to measure deficits in the perception of line orientation. Stimuli are 30 items that each comprise an array of 11 differently oriented lines that are drawn at 18-degree intervals from a common point of origin. For each item, children are required to match two target lines, based on their orientation, to two lines within the array of 11 differently oriented lines. Correct responses are rewarded with one point each and summed across all items. Age means (SD) for the summed raw scores are provided in the manual.

The Gestalt Closure subtest of the K-ABC[17] aims to measure the ability to recognize incomplete silhouettes (visual closure). The examinee is required to name each of the 24 incomplete silhouettes of objects and visual scenes (alternative answers are not provided). Correct responses are assigned one point each. Testing is discontinued after 4 consecutive incorrect responses. Points are summed across all items and transformed into an one year interval age-adjusted norm score with a mean (SD) of 10 (3).[17]

The MVPT-R[18] aims to measure visual perception without motor involvement. The test comprises 40 items that assess recognition abilities regarding spatial relationships, visual discrimination, figure-ground perception (recognition of overlapping figures), visual closure and visual memory. The examinee is required to match the target shape to one of four alternatives. Correct responses are assigned one point each, summed across all items and transformed into a six months interval age-adjusted norm score with a mean (SD) of 100 (15).[18]

The Arrow subtest of the NEPSY[19] aims to measure the ability to judge line orientation. The task comprises 15 items that each show eight arrows and one target. The examinee is required to indicate the two arrows that point to the centre of the target and testing is discontinued after four consecutive failures. One point is assigned for each correctly indicated arrow. Points are summed across all items and transformed into a six months interval age-adjusted norm score with a mean (SD) of 10 (3).[19]

The TVPS-R[20] aims to measure visual perception without the involvement of motor ability. The test comprises 7 scales of 16 items each, measuring visual discrimination, visual memory, visual-spatial relationships, visual form-constancy, visual sequential memory, figure-ground perception and visual closure. The examinee is required to match target shapes to one of four or five alternatives. For each scale, correct responses are assigned one point each, added, and transformed into a three months interval age-adjusted norm score with a mean (SD) of 10 (3). The transformed scores on all scales are added and transformed into an overall quotient with a mean (SD) of 100 (15) measuring general visual perceptual ability.[20]

All visual perceptive outcome measures are paper and pencil tests for which adequate reliability and validity have been reported.[16-20] Tests that are discontinued after a specific number of consecutive incorrect responses, all comprise items of increasing difficulty. Norm scores for children between 4 and 13 years of age (JLO: 7 to 14 years) are provided in the manual of each test, are based on large and representative normative samples and higher scores indicate better performance.

Visual-Motor Integration

The VMI[14] is a paper and pencil test that aims to measure visual-motor integration. The test comprises 24 geometrical shapes of increasing difficulty and the examinee is required to copy these shapes. Detailed scoring-criteria are provided and testing is discontinued after three consecutive incorrect copies. Correct copies are assigned one point each and the sum of points is transformed into a six months interval age-adjusted norm score with a mean (SD) of 100 (15) or a mean (SD) of 10 (3) with higher scores indicating better performance. Adequate psychometric properties have been reported and norms are based on 2512 children aged 2 to 18 years.[14]

Quality Assessment

The quality of the included studies was independently assessed by two authors (C.J.A.G. and J.F. de K.) using the Newcastle-Ottawa Scale.[21] This scale rates the quality of observational studies in terms of the selection of subjects (4 criteria), comparability of study groups (1 criterion) and outcome assessment (3 criteria). Total rating scores may range from 1 to 9 points with higher scores indicating more favorable study quality. Differences in assessment scores were resolved by consensus. For none of the dependent measures a significant association was obtained between study quality and effect size (all *p*-values > .05; data available from the first author).

Statistical Analyses

The computer software Comprehensive Meta-Analysis (CMA) 2.2[22] was used to calculate the effect size (Cohen's *d*) of all individual studies for each of the dependent measures. Cohen's *d* depicts the difference between two means divided by the pooled SD for those means. Cohen's *d* was calculated using the mean and SD reported for very preterm/VLBW children and either (1) the reported mean and SD for term born controls in case-control studies or (2) the test's normative sample and assuming a sample size equal to the very preterm/VLBW group in uncontrolled studies. Comparability of these two methods was investigated by calculating the effect sizes of case-control studies using both methods and analyzing possible differences between the results generated by the two methods by means of *Q*-test statistics.

Results of studies that reported data on subgroups defined in terms of gender, BW or GA were pooled into overall weighted mean and SD scores. Subgroup means and SDs were weighed by their sample sizes, added, and divided by the sum of the total sample size. An overall combined effect size was computed by weighing the study specific effect sizes by the accompanying sample sizes.[23] Effect sizes of 0.20, 0.50 and 0.80 were considered small, medium and large, respectively.[24] To test heterogeneity of the obtained results, *Q*-tests were conducted.[25]

To analyze whether the observed effects are robust and to examine the possibility that the obtained results arise from publication bias, we calculated Rosenthal's fail-save *N* (FSN), defined as the number of studies with non-significant results that is needed to nullify the observed effect.[26] Results are considered robust when FSN exceeds 5*n* + 10 (*n* = number of studies in a meta-analysis). Furthermore, Egger's regression intercept[27] was calculated to investigate funnel plot asymmetry. In the presence of publication bias, Egger's regression intercept will deviate significantly from zero. Quality ratings were correlated with the study specific effect sizes in order to analyze the possible influence of study quality on study outcome.

Furthermore, moderating effects on VMI performance were investigated. The effect of gender on VMI performance was analyzed calculating and comparing effect sizes for studies that reported results for boys and girls separately. Mean GA, BW, age at assessment and full scale IQ (FSIQ) were extracted from the selected studies in order to identify moderating effects of these variables on VMI performance by means of standardized meta-regression analyses provided in CMA software.[22] Mean year of birth was extracted to examine if outcomes changed during a period of changes in neonatal intensive care practices. FSIQ scores were transformed into Cohen's *d* effect sizes.[24] The number of studies reporting on visual perceptive outcome was insufficient to study the effects of gender, GA, BW, age at assessment, FSIQ and year of birth. In all analyses, significance testing was two-sided and α set at .05.

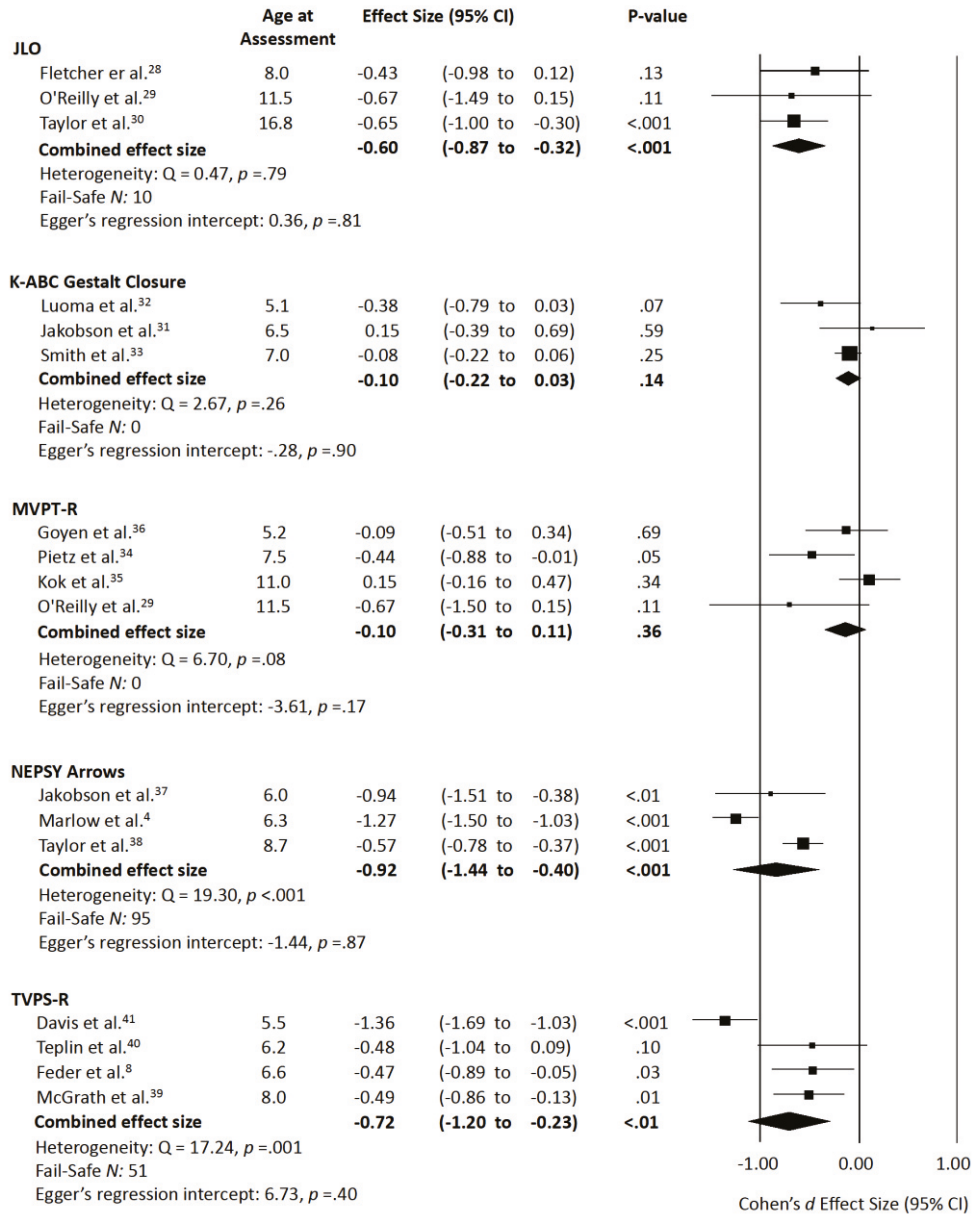


Figure 1 Effect sizes and 95% CIs for studies reporting on visual perceptive measures. Negative effect sizes indicate weaker performance of very preterm/VLBW children; CI = confidence interval.

RESULTS

Visual Perceptive Abilities

Details on studies reporting on visual perceptive measures are displayed in Electronic Supplement II. Figure 1 shows the study specific effect sizes and meta-analytic findings for each of the visual perceptive measures.

Three case-control studies[28-30] reported on the JLO test,[16] a test that requires examinees to match pairs of lines that have the same orientation. A significant medium combined effect size (d = -0.60, p < .001) from homogeneously distributed data was established, indicating weaker performance in very preterm/VLBW children. FSN indicated that results were not robust, but no evidence for publication bias was observed, as Egger's degree of funnel plot asymmetry was non-significant.

The K-ABC Gestalt Closure subtest[17] requires participants to recognize and name incomplete silhouettes and was used in two case-control studies[31,32] and one uncontrolled study that reported standardized normed scores for very preterm/VLBW children.[33] A non-significant combined effect size (d = -0.10, p = .14) was obtained with homogeneously distributed data, indicating that performance of very preterm/VLBW children was comparable to performance in term born controls. Egger's degree of funnel plot asymmetry revealed no evidence for publication bias.

The MVPT-R[18] requires examinees to match a sample shape to one of four alternatives and was used in two case-control studies[29,34] and two uncontrolled studies that reported standardized normed scores for very preterm/VLBW children.[35,36] A non-significant combined effect size (d = -0.10, p = .36) was found and data were distributed homogeneously, indicating similar performance for very preterm/VLBW children and term born peers. No significant degree of funnel plot asymmetry was observed, suggesting that there was no evidence for publication bias.

Three case-control studies[4,37,38] reported on the NEPSY Arrows subtest.[19] The NEPSY Arrows subtest requires examinees to indicate which arrows point exactly to the centre of a target. A significant and large combined effect size (d = -0.92, p < .001) was found, showing weaker performance in very preterm/VLBW children compared to term born controls. Data were distributed heterogeneously. FSN denoted that results were robust and Egger's non-significant degree of funnel plot asymmetry indicated no evidence for publication bias.

Results for the TVPS-R[20] were reported in three case-control studies[8,39,40] and one uncontrolled study that reported standardized normed scores for very preterm/VLBW children.[41] The TVPS-R requires participants to match a sample shape to one of four or five alternatives. The significant medium to large combined effect size (d = -0.72, p < .01) revealed weaker performance in very preterm/VLBW children compared to term born controls. Data were distributed heterogeneously, likely caused by the uncontrolled study by Davis et al.[41] that reported an effect size that greatly differed from the other studies included. After exclusion of this outlier, a significant medium effect size remained (d = -0.48, p < .001), with homogeneously distributed data (Q(2) = 0.01; p = .99). FSN denoted that results were robust and the non-significant degree of funnel plot asymmetry indicated no evidence for publication bias.

Summary of Results for Visual Perceptive Abilities

Summarizing the meta-analytic results for the visual perceptive tests, very preterm/VLBW children performed worse than controls on the two measures tapping into visual-spatial perceptive abilities: the JLO test and the NEPSY Arrows subtest. Comparison of the combined effect sizes obtained for the JLO test and NEPSY Arrows subtest revealed no meaningful difference (Q(1) = 1.18, p = .28). All studies that reported visual-spatial outcome used a case-control design. Studies spanned a wide age range encompassing 6 to 16 year old very preterm/VLBW children, suggesting that deficits in visual-spatial perceptive abilities persist throughout childhood and adolescence. Recognition of incomplete objects, also referred to as visual closure, as assessed by the K-ABC Gestalt Closure subtest, does not seem to be affected.

The two broad indices of visual perceptive abilities, the MVPT-R and the TVPS-R, revealed conflicting results. Comparison of the combined effect sizes obtained for both tests, revealed a larger combined effect size for the TVPS-R than for the MVPT-R (Q(1) = 3.21, p = .07), although this difference just escaped conventional levels of significance. After exclusion of the study of Davis et al.[41] that was regarded outlier, the difference between the combined effect sizes for MVPT-R and TVPS-R became non-significant (Q(1) = 2.09, p = .15). This discrepancy may also be related to differences in the populations studied. In general, studies reporting on the TVPS-R have included children with lower GA and BW as well younger age at assessment[8,40] than studies reporting on the MVPT-R.[34.35] Inspection of the MVPT-R and TVPS-R study specific effect sizes, suggests that all case-control studies report medium effect sizes, whereas the effect sizes of uncontrolled studies are either large or non-significant (please refer to Electronic Supplement II for details on study design). Studies included very preterm/VLBW children varying in age from 5 to 11 year old, suggesting that difficulties identified by broad indices of visual perceptive abilities persist throughout childhood.

Since results for the MVPT-R and TVPS-R were reported in terms of one aggregated score, it remains unknown whether specific aspects of visual perception, such as recognition abilities regarding spatial relationships, visual discrimination, figure-ground perception (recognition of overlapping figures), visual closure or visual memory account for the deficits observed or, alternatively, that results are based on global dysfunctions impacting multiple aspects of visual perception. Among the studies included, only two studies reported or additionally provided results for specific visual perceptive scales. Davis et al.[41] reported weak performance of very preterm children on all TVPS-R scales and Pietz et al.[34] found worse performance on the MVPT-R visual closure items in children with BW < 1500 grams compared to term born controls.

Visual-Motor Integration

Details of studies reporting on the VMI are provided in Electronic Supplement III. Figure 2 displays the study specific effect sizes and meta-analytic findings.

The VMI requires examinees to copy a series of geometrical shapes. Contrary to the motor-free visual perceptive tasks, the VMI taps into integration of visual-spatial perceptive abilities, fine motor abilities and motor planning. Results on VMI outcome were reported in 32 studies.[28-30,32,34-37,42-65] All studies consistently presented poorer VMI scores in very preterm/VLBW children compared to term born controls or the test's normative sample and were aggregated into a significant medium combined effect size (d = -0.69, p < .001). Data were distributed heterogeneously. Heterogeneity of results was examined using meta-regression. FSN indicated very robust results and no evidence for publication bias was observed since Egger's degree of funnel plot asymmetry was non-significant. Effect sizes for VMI performance were calculated using data reported for controls in case-control studies and normative data for uncontrolled studies. Comparability of the methods of effect size calculation for case-control and uncontrolled studies was investigated using the 18 case-control studies.[28,29,34,37,45-47,49-52,56,58,60,61,63-65] Results showed no significant difference between the combined effect size obtained using data of either term born controls or the test's normative data (Q(1) = 0.81, p = .37), thereby supporting comparability of both methods of effect sizes calculation.

Variables moderating VMI performance

To disentangle the heterogeneity of results for VMI performance, the possible moderating effects of gender, GA, BW, age at assessment, FSIQ and year of birth onto performance on the VMI were investigated. Four studies, including three case-control studies[45,51,53] and one uncontrolled study,[36] reported VMI results for boys and girls separately. A significant large combined effect size was found for boys (d = -0.94, p < .001), showing that very preterm/VLBW boys perform worse than term born boys. In contrast, a borderline significant small combined effect size was obtained for girls (d = -0.24, p = .06). For both

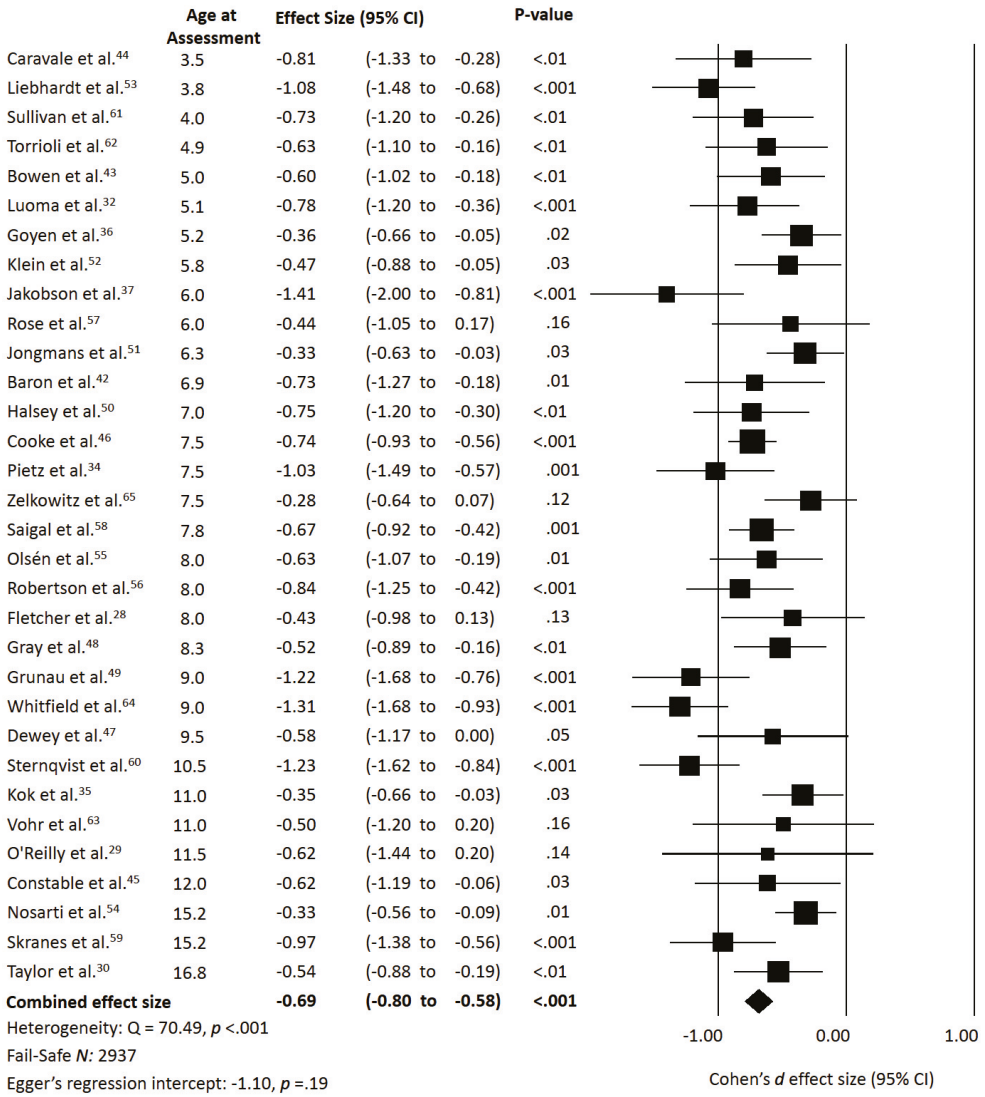


Figure 2 Effect sizes and 95% CIs for studies reporting on Beery VMI outcome. Negative effect sizes indicate weaker performance of very preterm/VLBW children; CI = confidence interval.

boys and girls, FSN denoted robust results and Egger's non-significant degree of funnel plot asymmetry revealed no evidence for publication bias. Interestingly, very preterm/VLBW girls were found to outperform boys born very preterm/VLBW ($Q(1) = 4.65$, $p = .03$).

The effect of GA (range: 26.0 to 32.8 weeks) on VMI performance was borderline significant (regression coefficient 0.06, 95% CI -0.002 to 0.12; p = .06). Accordingly, on average, VMI standardized scores decline with 0.9 points with each reduction of one week of gestation. In contrast, BW (range: 719 to 1755 grams) was not found to have a significant effect on VMI performance (p = .15). Similarly, age at assessment (range: 3.5 to 16.8 years) did not significantly affect VMI performance (p = .60). This finding suggests that visual-motor integration problems, as measured with the VMI, seem to persist from preschool years into adolescence. FSIQ was found to have a significant effect on VMI outcome (regression coefficient 0.41, 95% CI 0.19 to 0.64; p < .01), showing that lower FSIQ coincides with lower VMI performance in very preterm/VLBW children. The significant intercept (-0.43, 95% CI 0.09 to -0.59; p < .01), however, emphasizes that weaker VMI performance also occurs in the absence of FSIQ differences between very preterm/VLBW children and term born controls This finding suggests that VMI deficits may arise independently of intellectual deficits. Finally, no effect of year of birth (range: 1975 to 1999) was observed (p = .44), suggesting that advances in neonatal intensive care have not improved visual-motor integration ability for very preterm/VLBW children in the past decades.

Summary of Results for Visual-Motor Integration

Summarizing the meta-analytic findings for the VMI, the weaker performance of very preterm/VLBW children was seen particularly in boys as compared to girls. Further analyses on variables moderating VMI performance indicated a weak effect of GA with poorer performance in children with shorter GA, but no significant effect of BW. Age at assessment and year of birth had no significant effects, whereas FSIQ showed a strong interrelationship with VMI performance with worse performance in children with lower IQ.

Discussion

This meta-analysis shows that very preterm/VLBW children have deficits in the domains of visual perception and visual-motor integration. Our results seem to reveal specific rather than global deficits in visual perceptive abilities in very preterm/VLBW children. Results point out poorer visual-spatial perceptive abilities as measured by both the NEPSY Arrows subtest (d = -0.92) and the JLO test (d = -0.60). In contrast, the K-ABC Gestalt Closure test indicated no problems with respect to the perception of visual closure (d = -0.10). Furthermore, two measures providing broad indices for visual perceptive abilities revealed conflicting findings with the TVPS-R yielding evidence for poor visual perception in very preterm/VLBW children (d = -0.72), and the MPVT-R suggesting no general visual perception impairments (d = -0.10). Removal of one TVPS-R study that was regarded

outlier[41], decreased the effect size for the TVPS-R to -0.48 and eliminated the observed difference between the effects for the TVPS-R and MVPT-R. Although the study specific effect sizes for MVPT-R and TVPS-R studies showed great variability, all case-control studies using one of these measures reported medium-sized impaired performance in very preterm/VLBW children.

Our findings highlight the importance of more research into visual perceptive functions and the need to report results of subtests measuring specific visual perceptive functions instead of general indices, in order to elucidate the nature of the visual perceptive deficits observed in very preterm/VLBW children. Furthermore, most visual perceptive tests tap into a restricted set of visual perceptive functions[66] and mostly lack tasks measuring perception of objects, faces, facial expression, scenes and motion. Therefore, the range of visual perceptive tests should be extended and tests should be applied in studies with well-defined populations to obtain a complete view of visual perceptive abilities of very preterm/VLBW children. One study that contributes to further understanding of the visual perceptive problems in very preterm/VLBW children was designed to investigate perception of global form, global motion and biological motion.[67] In that study it was found that very preterm/VLBW children showed impaired perception for global motion and biological motion, but not for perception of global form.

Clear evidence was found for visual-motor integration problems as measured by the VMI, showing that very preterm/VLBW children on average lag -0.69 SD behind term born peers. Weaker VMI outcome was found for boys (d = -0.94) as compared to girls (d = -0.24). This finding adds to previous reports showing greater vulnerability for adverse neurodevelopmental outcome in very preterm/VLBW boys as compared to girls as well as the greater risk for adverse white matter development in very preterm/VLBW boys.[68] In addition, our meta-regression analysis suggests that lower GA is associated with weaker VMI performance. This relationship has also been described by Jongmans et al.[51] in a study of children born between 25 and 34 weeks of gestation. Effects of GA, however, were not found in other studies that compared VMI performance between groups with a specific GA range (Baron et al.:[42] 23 to 25 and 26 to 34 weeks of gestation; Goyen et al.:[36] <28 and >28 weeks of gestation), suggesting that the relationship between GA and VMI performance becomes only evident if a broad range of GA is studied. In our meta-analysis, BW was not associated with VMI outcome. Effects of BW on VMI performance have been obtained in studies that did not exclude very preterm/VLBW children with intracranial hemorrhages from their samples,[30,50] but were not found in studies that did exclude these children.[34,36] These findings suggest that the effects of BW on VMI performance reflect effects of accompanying brain abnormalities rather than growth as the explanatory factor for differences in VMI abilities. Alternatively, our finding that BW does not affect VMI performance might be related to the inclusion of children born small for gestational age

(SGA) in the studies in our meta-analysis, since studies have shown that SGA status does not impact on VMI outcome.[35,36,56,62]

The finding that age at assessment was not related to VMI performance suggests that visual-motor integration deficits persist from early childhood into adolescence, in turn suggesting that these deficits arise from early and persisting disruptions in neural connectivity. Our finding is supported by a longitudinal study,[30] showing decreasing VMI performance over time in children born < 750 grams as compared to children born with BW > 750 grams. The strong association between FSIQ and VMI outcome highlights the interrelation between visual-motor integration and intellectual functioning. Visual-motor integration deficits have been shown to coexist with or neurocognitive, behavioral and academic deficits in very preterm/VLBW children and to occur rarely in the absence of such associated impairments.[51] That finding suggests a common underlying neural circuit affected by decreased connectivity that may account for impaired VMI performance and neurocognitive, behavioral and academic deficits. Alternatively, impaired VMI may act as a moderator for FSIQ outcome.[69] Finally, since year of birth was not associated with VMI performance, outcome in terms of visual-motor integration does not seem to have received benefit from advances in neonatal intensive care practice.

It should be noted that the medium combined effect sizes obtained for both VMI outcome (*d* = -0.69) and visual-spatial perceptive abilities (*d* = -0.60 and *d* = -0.92) are of similar magnitude. This raises the possibility that the effect of very preterm birth/VLBW on VMI performance reflects a visual-spatial perceptive deficit and does not reflect problems in the integration of visual perceptual information into motor action. However, this interpretation seems unlikely as there are studies demonstrating motor impairments using tasks that do involve visual perceptual demands. For example, a meta-analysis by de Kieviet et al.[6] shows medium-sized impairments in manual dexterity skills in very preterm/VLBW children (effect size: -0.62). Furthermore, Van Braeckel et al.[70] reported less efficient elementary visual-motor processes (slower or less accurate pointing) in very preterm born children. Interestingly, integration of fine motor skills and visual-spatial perceptive abilities during VMI performance do not seem to add and result in a larger effect size for visual-motor integration.

Our meta-analytic results add to a growing body of literature indicating visual processing deficits in very preterm/VLBW children. Studies show delayed maturation of motion sensitivity,[71] impaired motion based recognition[37,67,72] and impaired perception of visual-spatial configuration.[73] Furthermore, altered activation of fronto-parietal-occipital networks during encoding of visual stimuli in very preterm/VLBW children is reported[74] and may be the underlying neural deficit. Atkinson and Braddick propose a theoretical model suggesting that a malfunctioning dorsal stream for visual information processing

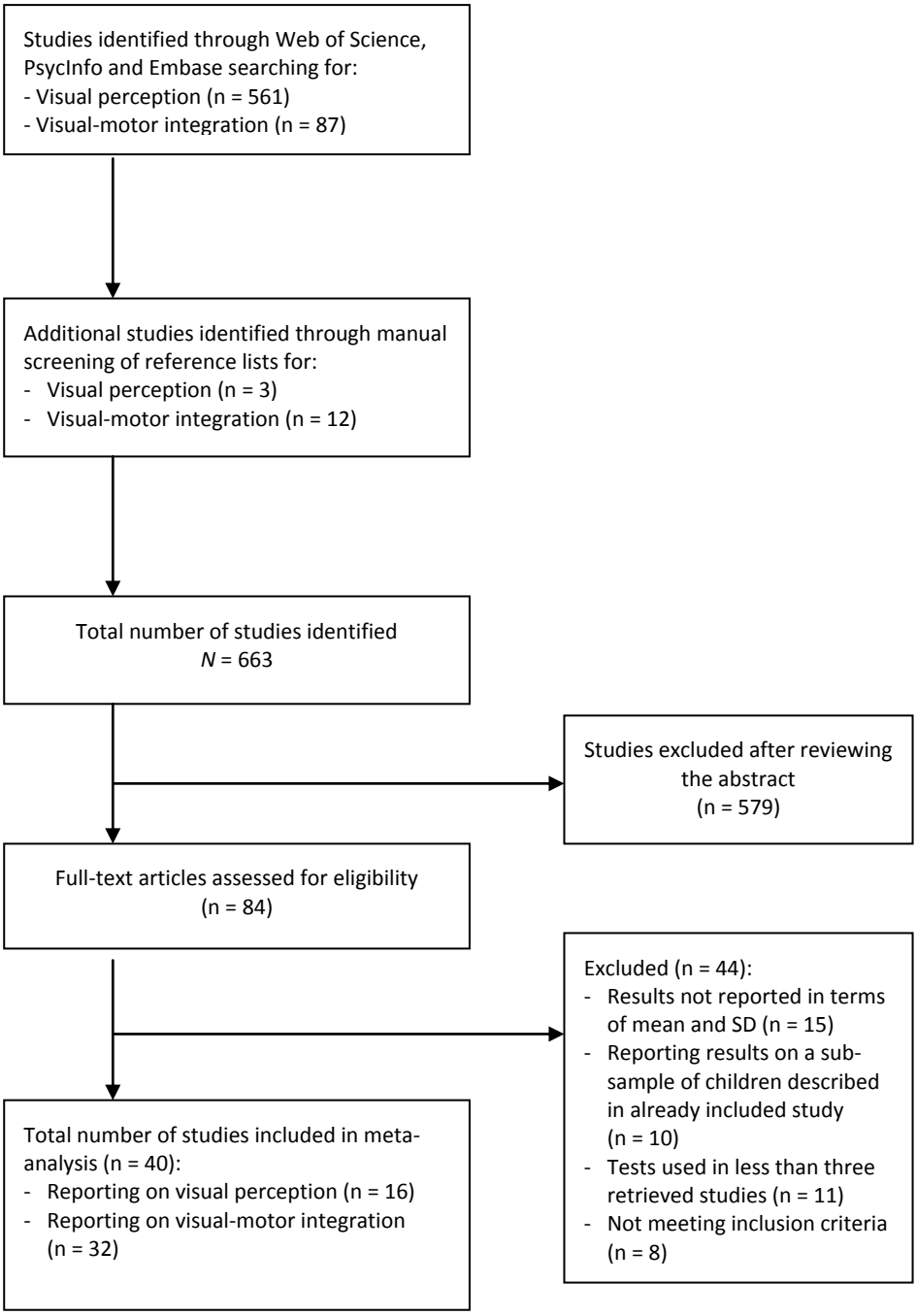
underlies the visual processing deficits observed in very preterm/VLBW children. Milner and Goodale[75] have emphasized the role of the dorsal visual stream in visual-spatial analysis and unconscious control for visual-motor action. Recently, evidence for subdivision of the dorsal stream has been reviewed by Kravitz, Saleem, Baker, & Mishkin.[76] These authors describe the occipital-parietal part of the dorsal stream to extend in neural projections to pre-motor-, prefrontal- and medial temporal lobe areas that are involved in automated visual-motor control, conscious visual-spatial control and visual navigation, respectively.[75,76] In contrast, the ventral stream, mainly involved in the perception of objects, faces and scenes,[75] is suggested to be unaffected in very preterm/VLBW children.[77] None of the studies included in our meta-analysis generated data to evaluate performance of very preterm/VLBW children on measures of perception of objects, faces and scenes. It should be noted that recognition of the incomplete silhouettes of the K-ABC Gestalt Closure test and the matching of geometrical shapes of the MVPT-R and TVPS-R tests require object perception among other visual perceptive abilities, but none of these tests purely assessed object perception. Ortibus et al.[66] reviewed four studies including heterogeneous samples of very preterm/VLBW children and found mixed evidence for impaired object recognition. All in all, the visual-spatial and visual-motor integration deficits demonstrated in our meta-analysis may result from impaired functioning of the occipital-parietal-prefrontal network, involved in both visual-spatial analysis and visual-spatial and visual-motor control. Affected neural connectivity emanating from disrupted growth of thalamo-cortical axons into the developing cortex after very preterm birth/VLBW[11] may be among the neural underpinnings for these deficits, since sensory information processing relies on the integrity of thalamo-cortical connections.[13]

Our meta-analysis demonstrates that there are no widely used visual perceptive tests and as a result, meta-analytic findings for visual perceptive measures are based on a small number of studies across a wide age range. Studies assessing perception of objects, faces, scenes and motion are few and could not be incorporated into our analyses. Future studies should fill this caveat in the literature. Furthermore, comparability of the results obtained in case-control and uncontrolled studies could not be investigated for visual perceptive measures. Effect sizes for uncontrolled studies, however, were calculated using large and representative normative samples. This meta-analysis included both very preterm as well as VLBW children causing heterogeneity in terms of BW and GA. Finally, general indices of visual perceptive abilities reported in literature, such as indices obtained from the MVPT-R and TVPS-R, hinder identification of specific visual perceptive deficits. Therefore, the exact nature of visual perceptive deficits in very preterm/VLBW children and consequences for other domains of functioning, remain to be studied in detail.

CONCLUSION

This meta-analysis aggregated studies into visual perceptive and visual-motor abilities in very preterm/VLBW children and provides evidence for medium to large-sized impairments in visual perceptive abilities, particularly in visual-spatial perception. In addition, medium-sized visual-motor integration deficits were observed that persist from early childhood into adolescence. Impairments in visual-motor integration were inversely related to GA and were more pronounced in boys than in girls. Our findings highlight the importance of extensive follow-up of visual perceptive and visual-motor abilities. Future studies should investigate whether visual perceptive and visual-motor integration dysfunctions are associated with, and possibly causal of other impairments observed in very preterm/VLBW children, including motor impairments,[6] cognitive deficits,[3,5,78] behavioral and emotional difficulties, and lower academic achievement.[5] Future research should elucidate underlying mechanisms and focus on prevention and possibilities for remediation.

Electronic Supplement I Flow Diagram of Study Identification and Selection



Electronic Supplement II Characteristics of Studies Reporting Visual Perceptive Outcome in Very Preterm/VLBW Children (Ordered by Test)

Study	Participants (N)	GA (weeks)	BW (grams)	Age (years)	Year of Birth	Full Scale IQ (Test)	Mean (SD)	Effect Size (*d*) [d]
JLO								
Fletcher et al. [28]	28 VPT	30.1 (1.8)	1338 (205)	8.0 (2.1)	1979-1988	> 69, WISC-R	93.5 (15.2) [b]	-0.43
	23 NC	39.7 (1.8)	3351 (682)			NA	100 (15) [b]	
O'Reilly et al. [29]	12 VPT	26.5 (1.3)	813.5 (132)	11.5 (0.7)	1992-1995	100 (16.2), WISC-III	19.3 (4.9) [c]	-0.67
	12 NC	NA	NA	11.2 (1.6)		117 (10.9), WISC-III	22.8 (5.5) [c]	
Taylor et al. [30]	95 VPT	27.6 (2.1)[a]	909 (142)[a]	16.8 (1.2)[a]	1982-1986	86.9 (19.3)[a], WISC/WAIS	18.7 (6.7) [c]	-0.65
	52 NC	> 37	3422 (591)	14.5 (1.3)		97.9 (16.2), WISC/WAIS	22.8 (5.6) [c]	
K-ABC Gestalt Closure								
Jakobson et al. [31]	31 EPT	26.9 (1.5)	844 (101)	6.5 (0.3)	1984-1987	NA	11.5 (2.7) [c]	0.15
	23 NC	40.3 (1.8)	3817 (533)	6.3 (0.2)		NA	11.1 (2.6) [c]	
Luoma et al. [32]	46 VPT	30.0 (1.9)	1422 (412)	5.1 (0.1)	1984-1986	115.8 (12.4), WPPSI-R	7.8 (3.8) [c]	-0.38
	46 NC	39.8 (1.4)	3443 (467)	5.1 (0.1)		123.0 (10.7), WPPSI-R	9.1 (3.0) [c]	
Smith et al. [33]	420 VLBW [a]	28.0 (2.4)[a]	1027 (255)[a]	6-8	1991-1993	96.1 (15.9)[a], K-ABC MP	9.76 (3.0)[a b]	-0.08
MVPT-R								
Goyen et al. [36]	43 VPT	< 32	< 1500	5.2 (0.2)	1986-1989	106.9 (11.8), SBIS	98.8 (12.7) [b]	-0.09
Kok et al. [35]	79 VPT	29.5 (1.9)	1362 (319)	11	1989	NA	102.3 (15.0) [b]	0.15
O'Reilly et al. [29]	12 VPT	26.5 (1.3)	813.5 (132)	11.5 (0.7)	1992-1995	100 (16.2), WISC-III	34.2 (1.9) [c]	-0.67
	12 NC	NA	NA	11.2 (1.6)		117 (10.9), WISC-III	35.2 (0.9) [c]	
Pietz et al. [34]	35 VPT	30.3 (2.2)[a]	1143 (113)[a]	7.5 (0.3)[a]	1986-1987	NA	106.1 (11.7)[a b]	-0.44
	50 NC	39.7 (1.2)	3360 (385)	7.5 (0.3)		NA	110.9 (10.4) [b]	

Electronic Supplement II (continued)

Study	Participants (N)	GA (weeks)	BW (grams)	Age (years)	Year of Birth	Full Scale IQ (Test)	Mean (SD)	Effect Size (*d*) [d]
NEPSY Arrows								
Jakobson et al. [37]	43 VPT	26.6 (1.7)	883 (173)	6 (0.5)	1993-1995	NA	10.2 (2.5) [b]	-0.94
	19 NC	37-41	2858-4366	6.2 (0.5)		NA	12.4 (1.9) [b]	
Marlow et al. [4]	182 EPT	24.5	NA	5.2-7.3	1995	78-99, K-ABC MP	7.0 (1.9) [b]	-1.27
	159 NC	NA	NA	5.1-7.2		99-113, K-ABC MP	9.6 (108) [b]	
Taylor et al. [38]	204 ELBW	26.4 (2)	810 (124)	8.7 (0.6)	1992-1995	90.2 (15.7), K-ABC	7.2 (2.9) [b]	-0.57
	176 NC	> 36	3300 (513)	9.2 (0.8)		99.8 (14.8), K-ABC	8.9 (3.1) [b]	
TVPS-R								
Davis et al. [41]	92 VLBW	27.8 (2.3)	1020 (258)	5.5 (0.5)	NA	100.6 (11.8), K-BIT MP	79.26 (15.6) [b]	-1.36
Feder et al. [8]	48 VPT	27.8 (2)	997.3 (175)	6.6 (0.3)	1992-1994	NA	109.8 (17.2) [b]	-0.47
	42 NC	> 37	NA	6.8 (0.3)		NA	117.3 (14.5) [b]	
McGrath et al. [39]	100 VPT	28.7 (2.1)	973.5 (231)	8 (0.2)	NA	93.9 (17.8), WISC-III	97.3 (20.6) [b]	-0.49
	37 NC	39.9 (0.9)	3399.8 (358)			103.9 (13.0), WISC-III	108.4 (18.7) [b]	
Teplin et al. [40]	26 ELBW	28 (1.5)	905 (86)	6.2 (0.3)	1980	87.8 (13.2), K-ABC	92.4 (20.5) [b]	-0.48
	24 NC	> 37	> 2500	6.0 (0.2)		97.8 (12.9), K-ABC	101.8 (19.0) [b]	

Note. Data displayed as mean (SD) or range. BW = Birth Weight, ELBW = Extremely Low Birth Weight, EPT = Extremely Preterm, GA = Gestational Age, JLO = Judgment of Line Orientation, K-ABC (MP) = Kaufmann Assessment Battery for Children (Mental Processing Composite), K-BIT MP = Kaufmann Brief Intelligence Test Mental Processing Composite, MVPT-R = Motor-free Visual Perception Test Revised, NC = Normal Control, NEPSY = A Developmental Neuropsychological Assessment, SBIS = Stanfort-Binet Intelligence Scale, TVPS-R = Test of Visual Perceptual Skills Revised, VLBW = Very Low Birth Weight, VPT = Very Preterm, WAIS = Wechsler Adult Intelligence Scale, WISC-R/III = Wechsler Intelligence Scale for Children Revised/Third Edition, WPPSI = Wechsler Preschool and Primary Scale of Intelligence.

[a] Calculated as weighted mean of the study's subgroups.

[b] Indicates age adjusted score: mean (SD) 100 (15) or mean (SD) 10 (3).

[c] Indicates raw score (age adjusted scores not available).

[d] Negative effect sizes indicate weaker performance of very preterm/VLBW children.

Electronic Supplement III Characteristics of Studies Reporting VMI Outcome in Very Preterm/VLBW Children (Ordered by Authors)

Study	Participants (N)	GA (weeks)	BW (grams)	Age (years)	Year of Birth	Full Scale IQ (Test)	Mean (SD)	Effect Size (*d*) [d]
Baron et al. [42]	49 ELBW	26.9 (1.8)[a]	796 (97)[a]	6.9 (0.9)[a]	1998-2000	101.4 (13.0)[a], DAS	91.7 (9.9)[a b]	-0.73
Bowen et al. [43]	45 ELBW	27.6 (2.3)	864 (90)	5	1985-1988	94.4 (11.2), SBIS	91.7 (12.7)[b]	-0.60
Caravale et al. [44]	30 VPT	30-34	910-2400	3-4	1998	110.8 (10.4), SBIS	42.6 (6.1)[c]	-0.81
	30 NC	NA	NA			121 (10.6), SBIS	47.4 (5.8)[c]	
Constable et al. [45]	29 VPT	28.4 (2.0)	974 (148)	12	1989-1992	88.9 (15.0)[a], WISC-III	84.6 (13.5)[a b]	-0.62
	22 NC	NA	NA	12		103.7 (15.7)[a], WISC-III	92.9 (12.9)[a b]	
Cooke et al. [46]	280 VPT	23-32	512-2860	6.8-8.4	1991-1992	89.4 (14.2), WISC-III	90.5 (9.2)[b]	-0.74
	210 NC	NA	NA	6.0-8.9		100.5 (13.7), WISC-III	96.9 (7.8)[b]	
Dewey et al. [47]	19 VLBW	28.1 (2)	1030 (119)	9.5 (3.1)	1979-1987	106.8 (10.9), WISC-III	98.5 (10.2)[b]	-0.58
	30 NC			9.1 (2.5)		108.1 (13.2), WISC-III	104.4 (13.4)[b]	
Fletcher et al. [28]	28 VPT	30.1 (1.8)	1338 (205)	8.0 (2.1)	1978-1988	> 69, WISC-R	89.0 (11.5)[b]	-0.43
	23 NC	39.7 (1.8)	3351 (682)			NA	93.9 (11.5)[b]	
Goyen et al. [36]	83 VLBW	28.5 (1.5)	1044 (243)	5.2 (0.2)	1986-1989	104.0 (11.3)[a], SBIS	95.1 (12.1)[a b]	-0.36
Gray et al. [48]	61 VPT	28.6 (1.3)	1077 (219)	8.3 (0.6)	1989-1990	93.5 (15.6), WISC-III	93.3 (10.1)[b]	-0.52
Grunau et al. [49]	74 ELBW	23-33	480-800	8.4-12.5	1982-1987	99.3 (10.9), WISC-R	94.0 (10.8)[b]	-1.22
	30 NC	38-40	2948-4706	9.0-10.0		117.3 (13.0), WISC-R	106.3 (8.0)[b]	
Halsey et al. [50]	76 VPT	NA	1292[a]	7	1984-1986	100.7 (17.4)[a], MSCA	91.7 (10.5)[a b]	-0.75
	27 NC	NA	3353	7		112.4 (19.6), MSCA	98.9 (6.5)[b]	
Jakobson et al. [37]	43 VPT	26.6 (1.7)	883 (173)	6 (0.5)	1993-1995	NA	90.2 (11.5)[b]	-1.41
	19 NC	37-41	2858-4366	5.3-6.8		NA	105.5 (9.3)[b]	
Jongmans et al. [51]	156 VPT	30 (2)	1306 (397)	6.1-7.8	1984-1986	106 (12.5)[a], BAS	8.45 (2.1)[a c]	-0.33
	60 NC	NA	NA			115.5 (13.5)[a], BAS	9.15 (2.25)[a b]	
Klein et al. [52]	46 VLBW	29.9 (2.4)	1216 (202)	5.8 (0.3)	1976	109.2 (14.0), SIT	8.5 (2.1)[b]	-0.47
	46 NC	> 37	3308 (534)	5.8 (0.3)		110.5 (17.0), SIT	9.5 (2.2)[b]	
Kok et al. [35]	79 VLBW	29.5 (1.9)	1362 (319)	11	1989	NA	94.5 (16.5)[b]	-0.35

Electronic Supplement III (continued)

Study	Participants (N)	GA (weeks)	BW (grams)	Age (years)	Year of Birth	Full Scale IQ (Test)	Mean (SD)	Effect Size (*d*) [d]
Liebhardt et al. [53]	40 VLBW	30.7 (2.4)	1367 (324)	3.8 (0.2)	1988-1989	NA	3.2 (1.3) [a c]	-1.08
	83 NC	NA	NA	3.8 (0.1)		NA	5.10 (1.9) [a c]	
Luoma et al. [32]	46 VPT	30.0 (1.9)	1422 (412)	5.1 (0.1)	1984-1986	115.8 (12.4), WPPSI-R	6.4 (2.5) [c]	-0.78
	46 NC	39.8 (1.4)	3443 (467)	5.1 (0.1)		123.0 (10.7), WPPSI-R	8.2 (2.1) [c]	
Nosarti et al. [54]	207 VPT	29.1 (2.2)	1276 (353.8)	15.2 (0.5)	1979-1982	NA	20.3 (4.0) [c]	-0.33
	104 NC	40.1 (1.3)	3358 (394.3)	15.0 (0.7)		NA	21.5 (3.0) [c]	
Olsén et al. [55]	42 VPT	31	1410	8	NA	97.5 (14.7), WISC-R	15.5 (3.0) [c]	-0.63
	42 NC	39	3323	8		103.5 (10.2), WISC-R	17.3 (2.7) [c]	
O'Reilly et al. [29]	12 VPT	26.5 (1.3)	813.5 (132)	11.5 (0.7)	1992-1995	100 (16.2), WISC-III	105 (18.2) [b]	-0.62
	12 NC	NA	NA	11.2 (1.6)		117 (10.9), WISC-III	114.8 (12.9) [b]	
Pietz et al. [34]	35 VPT	30.3 (2.2) [a]	1143 (113) [a]	7.5 (0.3) [a]	1986-1987	NA	95.2 (10.3) [a b]	-1.03
	50 NC	39.7 (1.2)	3360 (385)	7.5 (0.3)		NA	106.6 (11.6) [b]	
Robertson et al. [56]	72 VPT	31.4 (2.0)	1535 (339) [a]	8	1974-1979	102 (17) [a], WISC-R	7.2 (2.6) [a b]	-0.84
	36 NC	> 37	> 2500	8		112 (13), WISC-R	9.3 (2.3) [b]	
Rose et al. [57]	21 VPT	32.8 (2.2)	1614 (272)	6	1974-1976	100.7 (16.6), WISC-R	93.9 (12.5) [b]	-0.44
Saigal et al. [58]	113 ELBW	27.0 (2.1)	839 (124)	7.8 (0.4)	1977-1981	91.1 (16.3), WISC-R	6.0 (2.3) [b]	-0.67
	145 NC	> 37	3369 (495)	8.1 (0.5)		103.8 (12.3), WISC-R	7.5 (2.2) [b]	
Skranes et al. [59]	55 VLBW	29.3 (2.7)	1218 (229)	15.2 (0.7)	1986-1988	79.3 (21.9), WISC-III	19.3 (3.6) [c]	-0.97
	47 NC	39.5 (1.1)	3670 (439)	15.5 (0.5)		94.7 (16.3), WISC-III	22.5 (2.9) [c]	
Stjernqvist et al. [60]	61 EPT	27.1 (1.0)	1042 (242)	10.5 (0.6)	1985-1986	89.8 (15.1), WISC-R/III	93.3 (12.2) [b]	-1.23
	61 NC	40.1 (1.4)	3648 (533)	10.6 (0.6)		106.2 (15.0), WISC-R/III	109.6 (14.2) [b]	
Sullivan et al. [61]	41 VPT	31.2 (5.3)	1412 (338.8)	4 (0.17)	1985-1989	NA	8.7 (1.7) [b]	-0.73
	34 NC	40 (0.8)	3415 (357)			NA	10.2 (2.4) [b]	
Taylor et al. [30]	95 VPT	27.6 (2.1) [a]	909 (142) [a]	16.8 (1.2) [a]	1982-1986	86.9 (19.3) [a], WISC/WAIS	27.3 (10.7) [a c]	-0.54
	52 NC	> 37	3422 (591)	17.0 (1.3)		97.9 (16.2), WISC/WAIS	33.2 (11.1) [c]	

Electronic Supplement III (continued)

Study	Participants (N)	GA (weeks)	BW (grams)	Age (years)	Year of Birth	Full Scale IQ (Test)	Mean (SD)	Effect Size (*d*) [d]
Torrioli et al. [62]	36 VLBW	26-34	560-1500	4.9 (0.7)	1991-1993	99.6 (16), WPPSI	5.6 (3.0) [c]	-0.63
	36 NC	NA	NA			NA	7.5 (3.0) [c]	
Vohr et al. [63]	15 VLBW	30 (2)	1313 (354)	5	1975-1977	95 (16), MSCA	8 (2) [b]	-0.50
	15 NC	40 (1)	3359 (497)	5		112 (12), MSCA	9 (2) [b]	
Whitfield et al. [64]	90 ELBW	23-28	520-800	6.4-14.3	1974-1985	98.7 (12.6), WISC-R	92.5 (10.6) [b]	-1.31
	50 NC	38-42	2614-4706	6.5-12.1		111.6 (13.1), WISC-R	105.4 (8.4) [b]	
Zelkowitz et al. [65]	53 VLBW	29.7 (2.9)	1167 (236)	6-9	1980-1985	107.6 (13.7), WPPSI/WISC	99.8 (15.9) [b]	-0.28
	72 NC		3443 (462)			115.3 (13.1), WPPSI/WISC	104.0 (13.9) [b]	

Note. Data displayed as mean (SD) or range.BAS = British Ability Scales, BW = Birth Weight, DAS = Differential Ability Scales, ELBW = Extremely Low Birth Weight, EPT = Extremely Preterm, GA = Gestational Age, MSCA = McCarthy Scales of Children's Abilities, SBIS = Stanfort-Binet Intelligence Scale, SIT = Slosson Intelligence Test, VLBW = Very Low Birth Weight, VPT = Very Preterm, VMI = Developmental Test of Visual-Motor Integration, WAIS = Wechsler Adult Intelligence Scale, WISC-R/III = Wechsler Intelligence Scale for Children Revised/Third Edition, WPPSI-R = Wechsler Preschool and Primary Scale of Intelligence Revised.

[a] Calculated as weighted mean of the study's subgroups.

[b] Indicates age adjusted score: mean (SD) 100 (15) or mean (SD) 10 (3).

[c] Indicates raw score (age adjusted scores not available).

[d] Negative effect sizes indicate weaker performance of very preterm/VLBW children.

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