

Early Motor Function of Children With Autism Spectrum Disorder: A Systematic Review

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abstract

CONTEXT: Early motor impairments have been reported in children with neurodevelopmental disorders (NDD), but it is not clear if early detection of motor impairments can identify children at risk for NDD or how early such impairments might be detected.

OBJECTIVE: To characterize early motor function in children later diagnosed with NDD relative to typically developing children or normative data.

DATA SOURCES: The Cumulative Index to Nursing and Allied Health Literature, Embase, Medline, PsycINFO, and Scopus electronic databases were searched.

STUDY SELECTION: Eligible studies were required to include an examination of motor function in children (0–24 months) with later diagnosis of NDD by using standardized assessment tools.

DATA EXTRACTION: Data were extracted by 4 independent researchers. The quality of the studies was assessed by using the Standard Quality Assessment Criteria for Evaluating Primary Research Papers from a Variety of Fields checklist.

RESULTS: Twenty-five studies were included in this review; in most of the studies, the authors examined children with later autism spectrum disorder (ASD). Early motor impairments were detected in children later diagnosed with ASD. The meta-analysis results indicated that differences in fine, gross, and generalized motor functions between the later ASD and typically developing groups increased with age. Motor function across different NDD groups was found to be mixed.

LIMITATIONS: Results may not be applicable to children with different types of NDD not reported in this review.

CONCLUSIONS: Early motor impairments are evident in children later diagnosed with ASD. More research is needed to ascertain the clinical utility of motor impairment detection as an early transdiagnostic marker of NDD risk.



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Neurodevelopmental disorders (NDD) result from a deviation in the development of the brain early in life.¹ According to the *International Classification of Diseases, 11th Revision (ICD-11)*,² NDD include intellectual disability, language or speech disorder, autism spectrum disorder (ASD), learning disorder, developmental coordination disorder (DCD), attention-deficit/hyperactivity disorder (ADHD), and neurodevelopmental syndrome due to prenatal alcohol exposure (a condition also classified under fetal alcohol syndrome in the *ICD-11* and grouped elsewhere under the umbrella term of fetal alcohol spectrum disorder [FASD]).² Although these disorders have different etiologies (ie, FASD is clearly linked to alcohol exposure in utero, whereas the origins of the other disorders are less clear), they have substantial comorbidity and overlapping symptoms. For example, individuals with NDD experience significant impairments in an array of neurodevelopmental domains, including cognition, social, and motor functioning. These impairments can have a profound and lifelong impact on health outcomes and quality of life.³⁻⁶

Early identification of children with NDD facilitates the delivery of support to prevent or minimize later functional impairments.⁷ In several studies,^{8,9} researchers have discussed the benefits of early intervention (ie, from birth) to capitalize on heightened neuroplasticity and potentially alter developmental outcomes for children at risk.¹⁰⁻¹² However, many children miss the opportunity for any early intervention because a formal diagnosis is not obtained until they reach school age.¹³⁻¹⁵ This is partly because NDD diagnosis is frequently contingent on evidence of clinically significant behaviors that typically appear at an older age.^{16,17} There is a need to identify early markers of NDD risk that can be used to support

referral for preemptive intervention (ie, intervention administered before the full clinical presentation of a disorder).

One early behavioral marker that may serve to identify those who are likely to be later diagnosed with NDD is motor impairment. Although impaired motor development has been investigated primarily and extensively in preterm infants and those at risk for cerebral palsy,^{18,19} there is evidence to indicate that early motor impairments may represent a transdiagnostic marker of neurodevelopmental vulnerability. For example, in a recent review, authors reported a high occurrence of abnormal general movements (ie, spontaneous movements present in the first few months of life) in infants later diagnosed with ASD.²⁰ In another study, it was found that 70% (21 of 30) of children who demonstrated motor delays before 2 years of age fulfilled the diagnostic criteria for NDD at follow-up (between 9 and 98 months).²¹ These studies suggest that early motor impairments may prove useful in detecting children at risk for NDD beyond those disorders in which motor dysfunction is a core symptom.

The transdiagnostic or cross-syndrome approach to NDD is focused on the identification of shared characteristics and mechanisms across NDD and interventions that are pertinent across disorders.¹⁶ Although evidence of motor impairments among school-aged children with different NDD is reported elsewhere,^{22,23} there has been no synthesis of early motor function across studies of children later diagnosed with different NDD between the ages of 0 and 24 months. Accordingly, our aim for this systematic review was to synthesize studies describing early motor function of children (0-24 months) later diagnosed with NDD by using a transdiagnostic approach. We sought to include studies of children

later diagnosed with intellectual disability, language or speech disorder, ASD, learning disorder, DCD, ADHD, and FASD. FASD is an umbrella term that encompasses neurodevelopmental syndrome due to prenatal alcohol exposure (*ICD-11*) and is used in this review because of current and historical inconsistencies in diagnostic terms for NDD associated with prenatal alcohol exposure.

METHODS

In this systematic review, we follow the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines,²⁴ and the study protocol was registered with PROSPERO (registration number: CRD42019131708).

Eligibility Criteria

Articles were included in the systematic review if (1) the cohort of interest was children with NDD, as identified in the *ICD-11*²; (2) they included a comparator group, including typically developing (TD) children or normative data; (3) children were tested for motor function between 0 and 24 months of age; (4) motor functions were assessed by using standardized assessments; and (5) they were published in English peer-reviewed journals. Articles were excluded if the cohort included children at risk for NDD without a later formal diagnosis.

Information Sources

The article search was performed systematically in the Cumulative Index to Nursing and Allied Health Literature, Embase, Medline, PsycINFO, and Scopus electronic databases. A combination of key terms, as well as free-text words, was included in the systematic search: "infant," "toddler," "intellectual developmental disorder," "developmental speech sound disorder," "autism spectrum disorder," "developmental learning disorder,"

“developmental coordination disorder,” “attention deficit hyperactivity disorder,” “stereotyped movement disorder,” “fetal alcohol spectrum disorder,” “sensory integration disorder,” “motor impairment,” and “motor delay.” Search results were dated from the earliest record to the first week of June 2019. Reference lists from relevant articles were hand searched for eligible studies. The Medline search strategy is displayed in Supplemental Table 3.

Study Selection

One reviewer (Y.H.L.) screened all the search results, and 3 independent reviewers (M.L., A.F.-J., and J.D.) each screened one-third of the search results by applying the eligibility criteria on the title and abstract of identified articles and then conducting a full-text screening. Disagreements were resolved through discussion to achieve a final consensus on included articles.

Data Extraction and Quality Assessment

Four reviewers (Y.H.L., M.L., J.D., and A.F.-J.) independently extracted data from the eligible studies using standardized forms. Data included country of study, study design, participant characteristics, motor function assessment tool, outcome measure, results, and quality appraisal of the study. The methodologic quality of the studies was assessed by using the Standard Quality Assessment Criteria for Evaluating Primary Research Papers from a Variety of Fields checklist²⁵ (Supplemental Table 4). Study quality was classified on the basis of the calculated score percentages²⁶: strong (>80%), good (70%–80%), adequate (50%–69%), or limited (<50%). Studies rated as limited quality were excluded from analysis.

Data Synthesis and Analysis

Narrative synthesis was used to synthesize data across all studies.

Motor functions were categorized on the basis of the domains of the outcome measures: fine motor, gross motor, generalized motor, and general movement functions. Generalized motor function was derived from outcome measures that provided composite scores for fine and gross motor functions. In addition, a meta-analysis was used to synthesize data from studies involving children with later ASD because both mean and SD values of motor function outcomes were reported in most of those studies, whereas they were not reported in studies involving other children with later NDD. Data used in the meta-analysis were analyzed by age group (0–6, 7–12, 13–18, and 19–24 months). When SD values were not available, they were estimated from available confidence interval (CI) data, SEs, or other methods recommended by the Cochrane Collaboration.²⁷ Data represented in figures and graphical representations were extracted by using the WebPlotDigitizer software.²³ Standardized mean difference and 95% CI values for each motor outcome were calculated and presented in forest plots by using the Review Manager software version 5.3.²⁸ Random-effects models were used to calculate the pooled estimates and their CI. Statistical significance was assumed when the *P* value was <.05. The *I*² value was used to interpret the degree of heterogeneity.²⁷ The magnitude of the effect size, the standardized mean difference, was interpreted as follows: small, 0.20 to <0.50; medium, 0.50 to <0.80; and large, ≥0.80.²⁹

RESULTS

Study Selection

In the search, we identified 7689 studies from across 5 databases. After eligibility screening, 25 studies were included in the systematic review, and 13 of these were included in the

meta-analysis (Fig 1). In total, 1028 children had later NDD, and 74 861 were TD children. In 2 of the included studies, normative data were used as a comparator.

Study Characteristics

The main characteristics of the included studies are summarized in Table 1. Participants ranged between 0 and 24 months old at the time of motor function assessment. Later diagnoses of NDD included ADHD (2 studies), ASD (21 studies), DCD (1 study), FASD (2 studies), and pervasive developmental disorder not otherwise specified (PDD-NOS) (1 study). The motor function assessment tools used included the Ages and Stages Questionnaire, Second Edition³⁰ (ASQ-2), Bayley Scales of Infant Development, Second Edition³¹ (BSID-II), Bayley Short Form Research Edition³² (BSFR), Denver Developmental Screening Test³³ (DDST), General Movements Assessment³⁴ (GMA), Griffiths Mental Developmental Scales–Extended Revised³⁵ (GMDS-ER), Kyoto Scale of Psychological Development³⁶ (KSPD), Mullen Scales of Early Learning³⁷ (MSEL), Peabody Developmental Motor Scales, Second Edition³⁸ (PDMS-2), and Vineland Adaptive Behavior Scales, Second Edition³⁹ (VABS-II). Of these, the MSEL was the most frequently used motor function assessment tool.

In Table 2, we describe the motor outcomes reported in each study across the 4 age ranges. In one study,⁴⁰ both the MSEL and VABS-II were used to assess fine and gross motor functions; data from both motor assessment tools were displayed in forest plots, but only data from the MSEL were used in the calculation of the effect size.

Methodologic Quality of Included Studies

Classification of the quality of the included studies revealed that 12 studies were of strong quality, 4 were

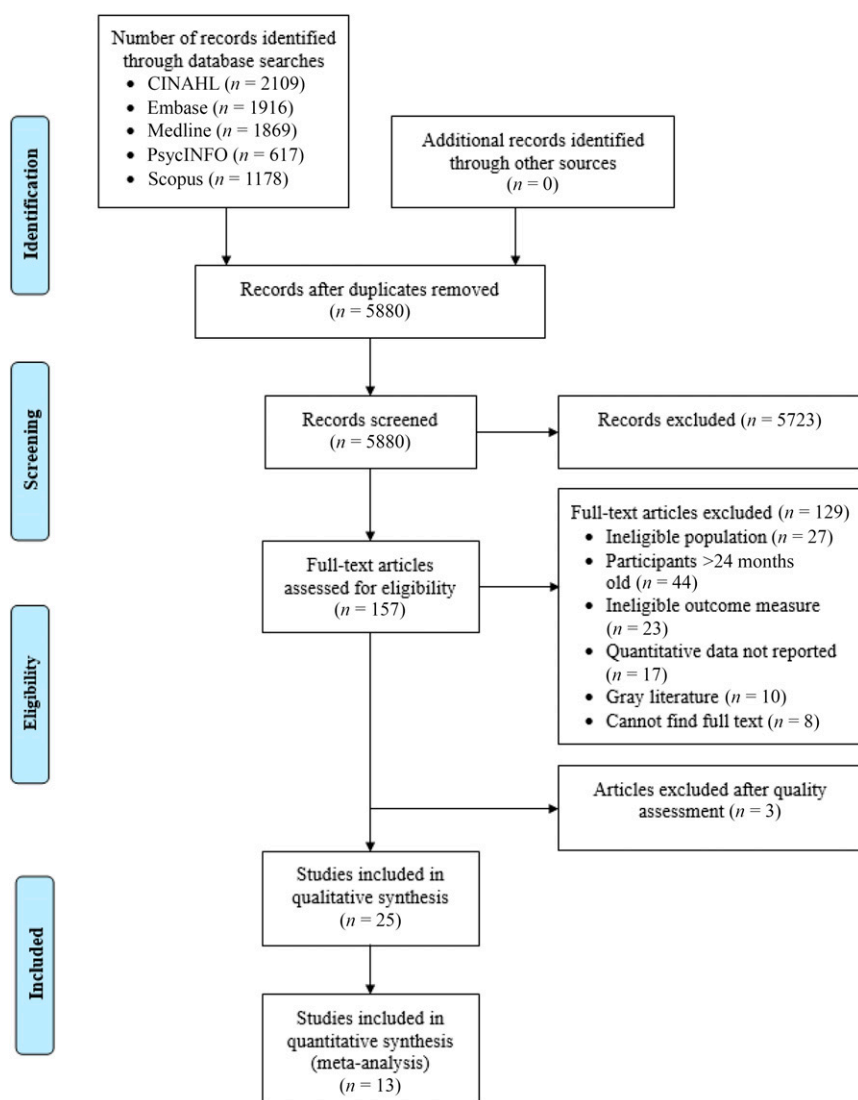


FIGURE 1
Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram of the included studies. CINAHL, Cumulative Index to Nursing and Allied Health Literature.

of good quality, and 9 were of adequate quality (Supplemental Table 5). Three studies identified as being of limited quality were excluded from analysis.

Early Motor Function at 0 to 6 Months

Fine Motor

Fine motor function of children with later ASD was examined in 8 studies by using the DDST, MSEL, and PDMS-2. In 5 studies,^{41–45} the authors reported no difference in fine motor

function between the later ASD and TD groups (mean age: 6 months). In contrast, the authors of 3 studies^{44,46,47} found that children with later ASD (mean age: 6 months) demonstrated poorer fine motor function in relation to TD children.

A meta-analysis of 6 studies involving children with later ASD and TD children revealed an overall small effect size of 0.40 (95% CI –0.57 to –0.23; $P < .001$) (Fig 2A), indicating poorer fine motor function in the

later ASD group. There was evidence of insignificant heterogeneity of the effect size ($I^2 = 0\%$).

Gross Motor

Gross motor function of children with later ADHD and ASD was examined in 7 studies by using the DDST, KSPD, MSEL, and PDMS-2. In 4 studies,^{43,44,46,47} the authors reported no difference in gross motor function between the later ASD and TD groups (mean age: 6 months). In contrast, the authors of 3 studies^{42,48,49} reported that children with later ADHD and ASD (ADHD, 1 study; ASD, 2 studies; age range: 3–6 months) showed poorer gross motor function compared with TD children.

A meta-analysis of 5 studies involving children with later ASD and TD children revealed an overall small effect size of 0.24 (95% CI –0.46 to –0.03; $P = .03$) (Fig 2B), indicating poorer gross motor function in the later ASD group. There was evidence of insignificant heterogeneity of the effect size ($I^2 = 20\%$).

Generalized Motor Function

Generalized motor function of children with later ASD and FASD was examined in 2 studies by using the BSID-II and VABS-II. In both studies,^{42,50} the authors reported that children with later ASD and FASD (ASD, 1 study; FASD, 1 study; mean age: 6 months) showed poorer generalized motor function when compared with TD group. A meta-analysis was not performed because of the availability of only one study in which generalized motor function in children with later ASD was reported.

General Movements

General movements of children with later ADHD, ASD, DCD, and PDD-NOS was examined in 3 studies by using the GMA. In one prospective study,⁵¹ the authors assessed GMA in 5 children with 3 different NDD (ADHD, $n = 1$; DCD, $n = 3$; PDD-NOS, $n = 1$) and 23 TD children (age range: 3–5

TABLE 1 Study Characteristics

Study	Design	Participants (Sample Size, Age, Location, Age at Diagnosis)	Assessment Tools and Outcomes	Major Findings	Quality Appraisal
Choi et al ⁴¹	Prospective cohort	Children with ASD (<i>n</i> = 30; 27 boys), high-risk children without ASD diagnosis (<i>n</i> = 71; 33 boys), and TD children (<i>n</i> = 69; 38 boys); age range: 6–24 mo; United States; ASD diagnosed at 18–36 mo	MSEL; fine motor subscale	Fine motor, 6 mo: no group difference between ASD, high-risk without ASD diagnosis, and TD groups (<i>P</i> = .20); fine motor, 12 mo: ASD group (mean = 16.5, SD = 2.08) showed poorer motor function compared with high-risk without ASD diagnosis group (mean = 17.27, SD = 1.80) (<i>P</i> = .015); fine motor, 18 mo: ASD group (mean = 20.36, SD = 1.66) showed poorer motor function compared with TD group (mean = 20.96, SD = 1.54) (<i>P</i> = .02); no group difference between ASD and high-risk without ASD diagnosis groups; fine motor, 24 mo: ASD group (mean = 24.12, SD = 2.42) showed poorer motor function compared with high-risk without ASD diagnosis (mean = 25.13, SD = 2.12) and TD groups (mean = 25.56, SD = 2.59) (<i>P</i> = .04)	Strong: 19 of 22 (86%)
Davies et al ⁵⁷	Prospective cohort	Children with FASD (<i>n</i> = 29; 11 boys) and TD children (<i>n</i> = 35; 13 boys); age range: 7–12 mo; South Africa; FASD diagnosed at 5 y	GMDS-ER; eye-hand coordination and locomotion subscales	Eye-hand coordination, 7–12 mo: no group difference between FASD and TD groups (<i>P</i> = .13); locomotion, 7–12 mo: FASD group showed poorer motor function (mean = 88.9) compared with TD group (mean = 97.3) (<i>P</i> = .034)	Strong: 18 of 22 (82%)
Emerson et al ⁶⁴	Prospective cohort	Children with ASD (<i>n</i> = 11; 11 boys) and high-risk children without ASD diagnosis (<i>n</i> = 48; 30 boys); mean age: 24 mo; United States; ASD diagnosed at 24 mo	MSEL; fine and gross motor subscales	Fine motor, 24 mo: group difference was not reported (ASD: mean = 24.08, SD = 1.0; high-risk without ASD diagnosis: mean = 23.84, SD = 0.3); gross motor, 24 mo: group difference was not reported (ASD: mean = 24.64, SD = 0.5; high-risk without ASD diagnosis: mean = 25.79, SD = 0.4)	Adequate: 11 of 22 (50%)
Estes et al ⁴²	Prospective cohort	High-risk children with ASD (<i>n</i> = 31; 26 boys), moderate-risk children with ASD (<i>n</i> = 18; 15 boys), high-risk children without ASD diagnosis (<i>n</i> = 161; 88 boys), and TD children (<i>n</i> = 98; 55 boys); age range: 6–24 mo; United States; ASD diagnosed at 24 mo	MSEL; fine and gross motor subscales	Fine motor, 6 mo: no group difference between high-risk ASD, moderate-risk ASD, high-risk without ASD diagnosis, and TD groups (<i>P</i> = .54); gross motor, 6 mo: high-risk ASD group (LSM = 43.7, SE = 1.5) showed poorer motor function compared with TD group (LSM = 50.8, SE = 0.9) (<i>P</i> = .014); fine motor, 12 mo: high-risk ASD group (LSM = 53.9, SE = 1.7) showed poorer motor function compared with TD group (LSM = 59.6, SE = 0.7) (<i>P</i> < .001); gross motor, 12 mo: high-risk ASD group (LSM = 42.7, SE = 2.2) showed poorer motor function compared with TD group (LSM = 50.4, SE = 1.2) (<i>P</i> < .001); fine motor, 24 mo: high-risk ASD group (LSM = 39.9, SE =	Strong: 22 of 22 (100%)

TABLE 1 Continued

Study	Design	Participants (Sample Size, Age, Location, Age at Diagnosis)	Assessment Tools and Outcomes	Major Findings	Quality Appraisal
Estes et al ⁴²	Prospective cohort	High-risk children with ASD ($n = 31$; 26 boys), moderate-risk children with ASD ($n = 18$; 15 boys), high-risk children without ASD diagnosis ($n = 161$; 88 boys), and TD children ($n = 98$; 55 boys); age range: 6–24 mo; United States; ASD diagnosed at 24 mo	VABS-II; motor subscale	1.7) showed poorer motor function compared with moderate-risk ASD (LSM = 42.9, SE = 2.3) and TD groups (LSM = 54.6, SE = 1.0) ($P < .001$); gross motor; 24 mo: high-risk ASD group (LSM = 38.4, SE = 1.6) showed poorer motor function compared with moderate-risk ASD (LSM = 43.9, SE = 2.1) and TD groups (LSM = 52.0, SE = 0.9) ($P < .001$) Generalized motor, 6 mo: high-risk ASD group (LSM = 84.3, SE = 2.3) showed poorer motor function compared with TD group (LSM = 95.5, SE = 1.3) ($P < .005$); generalized motor, 12 mo: high-risk ASD group (LSM = 94.1, SE = 1.9) showed poorer motor function compared with TD group (LSM = 103.3, SE = 1.0) ($P < .01$); generalized motor, 24 mo: high-risk ASD group (LSM = 92.9, SE = 1.7) showed poorer motor function compared with TD group (LSM = 102.8, SE = 0.9) ($P < .001$)	Strong: 22 of 22 (100%)
Gurevitz et al ⁴⁸	Prospective cohort	Children with ADHD ($n = 58$; 40 boys) and TD children ($n = 58$; 38 boys); ages: 3, 9, and 18 mo; Israel; ADHD diagnosed at 8 y	DDST; fine and gross motor subscales	Gross motor, 3 mo: 44.8% of ADHD group showed poorer motor function compared with 19% of TD group ($P = .002$); fine motor, 9 mo: no group difference between ADHD and TD groups ($P = .122$); gross motor, 9 mo: 34.5% of ADHD group showed poorer motor function compared with 13.8% of TD group ($P = .008$); fine motor, 18 mo: no group difference between ADHD and TD groups ($P = .219$); gross motor, 18 mo: 12.1% of ADHD group showed poorer motor function compared with 1.7% of TD group ($P = .03$) Motor scores of children with ASD were not reported.	Strong: 19 of 22 (86%)
Heathcock et al ⁷⁶	Case-control	Children with ASD ($n = 5$), high-risk children without ASD diagnosis ($n = 18$), and TD children ($n = 14$); mean age: 6 mo; United States; ASD diagnosed at 24–48 mo	AIMS		Limited: 10 of 22 (46%)
Iverson et al ⁴⁶	Prospective cohort	Children with ASD ($n = 69$; 49 boys) and TD children ($n = 188$; 107 boys); mean age: 6 mo; United States; ASD diagnosed at 3 y	MSEL; fine and gross motor subscales	Fine motor, 6 mo: ASD group showed poorer motor function (mean = 45.9, SD = 9.1) compared with TD group (mean = 50.1, SD = 7.9) ($P = .004$); gross motor, 6 mo: no group difference between ASD and TD groups	Strong: 18 of 22 (82%)
Jeans et al ⁵⁸	Prospective cohort	Children with ASD ($n = 100$; 70 boys) and TD children ($n = 7700$; 3773 boys); age range: 9–24 mo; United States; ASD diagnosed at 4 y	BSFR; motor index	Generalized motor, 9 mo: no group difference between ASD and TD groups ($P = .982$); generalized motor, 24 mo: ASD group (mean	Strong: 21 of 22 (96%)

TABLE 1 Continued

Study	Design	Participants (Sample Size, Age, Location, Age at Diagnosis)	Assessment Tools and Outcomes	Major Findings	Quality Appraisal
Kihara and Nakamura ⁴⁹	Prospective cohort	Children with ASD (<i>n</i> = 35; 22 boys) and TD children (<i>n</i> = 169; 63 boys); age range: 6–18 mo; Japan; ASD diagnosed at 3–6 y	KSPD; postural motor	<p>= 74.69, SD = 5.78) showed poorer motor function compared with TD group (mean = 81.74, SD = 4.78) (<i>P</i> < .001)</p> <p>Gross motor; postural motor; 6 mo: ASD group (mean = 84) showed poorer motor function compared with TD group (mean = 93) (<i>P</i> < .01); gross motor; postural motor; 18 mo: ASD group (mean = 90) showed poorer motor function compared with TD group (mean = 98) (<i>P</i> < .05)</p>	Good: 16 of 22 (73%)
Landa and Garrett-Mayer ⁴³	Prospective cohort	Children with ASD (<i>n</i> = 24) and TD children (<i>n</i> = 52); ages: 6, 14, and 24 mo; United States; ASD diagnosed at 2 y	MSEL; fine and gross motor subscales	<p>Fine motor; 6 mo: no group difference between ASD and TD groups; gross motor; 6 mo: no group difference between ASD and TD groups; fine motor; 14 mo: ASD group showed poorer motor function (mean = 50.42, SD = 10.21) compared with TD group (mean = 57.38, SD = 7.35) (<i>P</i> = .01); gross motor; 14 mo: children with ASD showed poorer motor function (mean = 47.46, SD = 12.36) compared with TD children (mean = 58.00, SD = 10.48) (<i>P</i> < .001); fine motor; 24 mo: ASD group showed poorer motor function (mean = 36.71, SD = 14.23) compared with TD group (mean = 52.58, SD = 11.07) (<i>P</i> < .001); gross motor; 24 mo: ASD group showed poorer motor function (mean = 36.21, SD = 9.31) compared with TD group (mean = 51.94, SD = 11.02) (<i>P</i> < .001)</p> <p>Motor scores of children with ASD cannot be identified.</p>	Good: 16 of 22 (73%)
Landa et al ⁷⁷	Prospective cohort	Children with ASD (<i>n</i> = 52; 43 boys) and TD children (<i>n</i> = 121; 53 boys); age range: 14–24 mo; United States; ASD diagnosed at 30–36 mo	MSEL; fine and gross motor subscales	Motor scores of children with ASD cannot be identified.	Limited: 11 of 22 (46%)
Landa et al ⁵⁹	Prospective cohort	Children with early ASD (<i>n</i> = 28; 22 boys), children with later ASD (<i>n</i> = 26; 22 boys), and TD children (<i>n</i> = 181; 84 boys); age range: 14 and 24 mo; United States; ASD diagnosed at 30–36 mo	MSEL; fine motor subscale	Fine motor; 14 mo: no group difference between early ASD and TD groups, later ASD group (mean = 16.9) showed poorer motor function compared with TD children (mean = 18.1) (<i>P</i> = .008); fine motor; 24 mo: no group difference between early ASD, later ASD, and TD groups	Adequate: 13 of 22 (59%)
LeBarton and Iverson ⁶²	Prospective cohort	Children with ASD (<i>n</i> = 7; 4 boys), high-risk children without ASD diagnosis (<i>n</i> = 27; 13 boys), and TD children (<i>n</i> = 25; 10 boys); mean age: 24 mo; United States; ASD diagnosed at 3 y	MSEL; fine motor subscale	Fine motor; 24 mo: ASD group (mean = 18.29, SD = 3.15) showed poorer motor function compared with high-risk without ASD diagnosis group (mean = 24, SD = 1.89) (<i>P</i> < .01); fine motor data for TD group was not reported	Adequate: 15 of 22 (68%)

TABLE 1 Continued

Study	Design	Participants (Sample Size, Age, Location, Age at Diagnosis)	Assessment Tools and Outcomes	Major Findings	Quality Appraisal
LeBarton and Landa ⁴⁴	Prospective cohort	Children with ASD (<i>n</i> = 20; 12 boys), high-risk children without ASD diagnosis (<i>n</i> = 69; 40 boys), and TD children (<i>n</i> = 51; 27 boys); mean age: 6 mo; United States; ASD diagnosed at 24–36 mo	PDMS-2; grasping, visual-motor integration, and stationary subscales	Fine motor, grasping, 6 mo: no group difference between ASD, high-risk without ASD diagnosis, and TD groups; fine motor, visual-motor integration, 6 mo: ASD group (mean = 31.05, SE = 1.59) showed poorer motor function compared with TD group (mean = 33.24, SE = 0.83) (<i>P</i> = .032), no group difference between ASD and high-risk without ASD diagnosis groups (<i>P</i> = .171); gross motor, stationary, 6 mo: no group difference between ASD, high-risk without ASD diagnosis, and TD groups (<i>P</i> = .069)	Strong: 19 of 22 (86%)
Leonard et al ⁴⁰	Prospective cohort	Children with ASD (<i>n</i> = 17; 11 boys), high-risk children without ASD diagnosis (<i>n</i> = 24; 7 boys), and TD children (<i>n</i> = 50; 21 boys); ages: 7, 14, and 24 mo; United Kingdom; ASD diagnosed at 36 mo	MSEL; fine and gross motor subscales	Fine motor, 7 mo: ASD (mean = 49.81, SD = 11.08) and high-risk without ASD diagnosis groups (mean = 53.54, SD = 11.11) showed poorer motor function compared with TD group (mean = 57.79, SD = 9.49) (<i>P</i> = .01); gross motor, 7 mo: ASD (mean = 46.06, SD = 12.58) and high-risk without ASD diagnosis groups (mean = 45.17, SD = 8.39) showed poorer motor function compared with TD group (mean = 50.17, SD = 8.98) (<i>P</i> = .01); fine motor, 14 mo: ASD (mean = 51.18, SD = 12.91) and high-risk without ASD diagnosis groups (mean = 56.74, SD = 12.45) showed poorer motor function compared with TD group (mean = 61.28, SD = 9.23) (<i>P</i> = .01); gross motor, 14 mo: no group difference between ASD, high-risk without ASD diagnosis, and TD groups; fine motor, 24 mo: no group difference between ASD, high-risk without ASD diagnosis, and TD groups; gross motor, 24 mo: ASD (mean = 44.00, SD = 13.21) and high-risk without ASD diagnosis groups (mean = 44.59, SD = 11.35) showed poorer motor function compared with TD group (mean = 59.89, SD = 8.08) (<i>P</i> < .001)	Adequate: 14 of 22 (64%)
Leonard et al ⁴⁰	Prospective cohort	Children with ASD (<i>n</i> = 17; 11 boys), high-risk children without ASD diagnosis (<i>n</i> = 24; 7 boys), and TD children (<i>n</i> = 50; 21 boys); ages: 7, 14, and 24 mo; United Kingdom; ASD diagnosed at 36 mo	VABS-II; fine and gross motor subscales	Fine motor, 7 mo: ASD (mean = 13.53, SD = 2.13) and high-risk without ASD diagnosis groups (mean = 14.26, SD = 3.36) showed poorer motor function compared with TD group (mean = 15.53, SD = 2.56) (<i>P</i> = .001); gross motor, 7 mo: ASD (mean = 12.82, SD = 3.47) and high-risk without ASD diagnosis groups (mean = 13.04, SD = 3.31) showed poorer	Adequate: 14 of 22 (64%)

TABLE 1 Continued

Study	Design	Participants (Sample Size, Age, Location, Age at Diagnosis)	Assessment Tools and Outcomes	Major Findings	Quality Appraisal
Leonard et al ⁵⁶	Prospective cohort	Children with ASD ($n = 17$; 11 boys), high-risk children without ASD diagnosis ($n = 36$; 10 boys), and TD children ($n = 48$; 17 boys); mean age: 7 mo; United Kingdom; ASD diagnosed at 36 mo	MSEL; fine and gross motor subscales	motor function compared with TD group (mean = 14.60, SD = 2.62) ($P = .001$); fine motor, 14 mo: ASD (mean = 15.71, SD = 3.06) and high-risk without ASD diagnosis groups (mean = 15.24, SD = 2.10) showed poorer motor function compared with TD group (mean = 17.27 = 2.18) ($P = .001$); gross motor, 14 mo: no group difference between ASD, high-risk without ASD diagnosis, and TD groups; fine motor, 24 mo: no group difference between ASD, high-risk without ASD diagnosis, and TD groups ($P = .05$)	Adequate: 14 of 22 (64%)
Libertus et al ⁴⁷	Prospective cohort study	Children with ASD ($n = 22$; 9 boys), high-risk children without ASD diagnosis ($n = 57$; 24 boys), and TD children ($n = 22$; 17 boys); mean age: 6 mo; United States; ASD diagnosed at 36 mo	MSEL; fine and gross motor subscales	Fine motor, 6 mo: ASD (mean = 44.18, SD = 9.90) and high-risk without ASD diagnosis groups (mean = 45.53, SD = 10.02) showed poorer motor function compared with TD group (mean = 51.23, SD = 8.11) ($P < .05$); gross motor, 6 mo: no group difference between ASD, high-risk without ASD diagnosis, and TD groups	Strong: 19 of 22 (86%)
Lloyd et al ⁶⁵	Retrospective cohort	Children with ASD ($n = 34$; 28 boys), mean age: 20 mo old; United States	VABS-II; fine and gross motor subscales	Fine motor, 14–24 mo: motor function of ASD group (mean age equivalent = 16.88 mo, SD = 5.06) was shown to be 3.9 mo behind normative data (mean age equivalent = 16.50 mo, SD = 2.86); gross motor, 14–24 mo: motor function of ASD group (mean age equivalent = 18.45 mo, SD = 3.43) was shown to be 3.5 mo behind normative data (mean age equivalent = 17.47 mo, SD = 3.18)	Strong: 18 of 20 (90%)
Øien et al ⁶⁰	Prospective cohort	Children with ASD (false-negative) ($n = 216$; 193 boys) and TD children (true-negative) ($n = 65$ 394; 33 163 boys); mean age: 18 mo; Norway; ASD diagnosed at ≥ 40 mo	ASQ-2; fine and gross motor subscales	Fine motor, 18 mo: boys with ASD showed poorer motor function (mean = 8.76, SD = 1.78) compared with TD boys (mean = 9.39, SD = 1.27) ($P < .001$), girls with ASD showed	Strong: 18 of 22 (82%)

TABLE 1 Continued

Study	Design	Participants (Sample Size, Age, Location, Age at Diagnosis)	Assessment Tools and Outcomes	Major Findings	Quality Appraisal
Ozonoff et al ⁴⁵	Prospective cohort	Children with ASD (<i>n</i> = 51; 43 boys), high-risk children without ASD diagnosis (<i>n</i> = 160; 70 boys), and TD children (<i>n</i> = 116; 63 boys); ages: 6, 12, and 24 mo; United States; ASD diagnosed at 36 mo	MSEL; fine motor subscale	poorer motor function (mean = 8.28, SD = 2.34) compared with TD girls (mean = 9.28, SD = 1.37) (<i>P</i> < .001); gross motor, 18 mo: boys with ASD showed poorer motor function (mean = 8.83, SD = 2.29) compared with TD boys (mean = 9.49, SD = 1.49) (<i>P</i> < .001), girls with ASD showed poorer motor function (mean = 6.36, SD = 3.85) compared with TD girls (mean = 9.46, SD = 1.49) (<i>P</i> < .001)	Good: 16 of 22 (73%)
Ozonoff et al ⁶¹	Prospective cohort	Children with ASD (true-positives) (<i>n</i> = 38) and TD children (true-negatives) (<i>n</i> = 293); age range: 18–24 mo; United States; ASD diagnosed at 36 mo	MSEL; fine motor subscale	Fine motor, 18 mo: group difference was not reported (ASD: mean = 44.3 [95% CI 41.6 to 47.1]; TD: mean = 52.8 [95% CI 51.3 to 54.4]); fine motor, 24 mo: group difference was not reported (ASD: mean = 39.4 [95% CI 36.8 to 42.0]; TD: mean = 51.0 [95% CI 49.6 to 52.4])	Strong: 20 of 22 (91%)
Phagava et al ⁵²	Case-control	Children with ASD (<i>n</i> = 20; 17 boys) and TD children (<i>n</i> = 20; 10 boys); age range: 6–21 wk; Georgia	GMA; general movements optimality score	General movements, 1–3 mo: ASD group (mean = 16.9) showed poorer motor function compared with TD group (mean = 23.9) (<i>P</i> < .001)	Adequate: 11 of 22 (50%)
Serdarevic et al ⁷⁸	Prospective cohort	Children with ASD (<i>n</i> = 30); age range: 2–5 mo; Netherlands; ASD diagnosed at 6 y	Touwen's Neurodevelopmental Examination; muscle tone	Motor scores of children with ASD cannot be identified.	Limited: 9 of 20 (45%)
Sowell et al ³⁰	Case-control	Children with FASD (<i>n</i> = 90; 47 boys) and TD children (<i>n</i> = 47; 25 boys); age range: 6–12 mo; Ukraine	BSID-II; psychomotor development index	Generalized motor, 6 mo: FASD group (mean = 79.79, SE = 1.32) showed poorer motor function compared with TD group (mean = 96.07, SE = 1.06) (<i>P</i> < .05); generalized motor, 12 mo: FASD group (mean = 87.05, SE = 1.72) showed poorer motor function compared with TD group (mean = 101.94, SE = 1.32) (<i>P</i> < .05)	Good: 16 of 22 (73%)
St John et al ⁵⁵	Prospective cohort	Children with ASD (<i>n</i> = 23; 17 boys), high-risk children without ASD diagnosis (<i>n</i> = 101; 57 boys), and TD children (<i>n</i> = 50; 29 boys); mean age: 12 mo; United States; ASD	MSEL; fine and gross motor subscales	Fine motor, 12 mo: ASD group (mean = 54.35, SD = 9.00) showed poorer motor function compared with high-risk without ASD diagnosis (mean = 58.18, SD = 8.58) and TD	Strong: 20 of 22 (91%)

TABLE 1 Continued

Study	Design	Participants (Sample Size, Age, Location, Age at Diagnosis)	Assessment Tools and Outcomes	Major Findings	Quality Appraisal
Young et al ⁵⁴	Prospective cohort	Children with ASD (<i>n</i> = 24; 21 boys) and TD children (<i>n</i> = 75; 42 boys); age range: 12–24 mo; United States; ASD diagnosed at 3 y	MSEL; fine motor subscale	Fine motor; 12 mo: no group difference between ASD and TD groups; fine motor; 18 mo: no group difference between ASD and TD groups; fine motor; 24 mo: no group difference between ASD and TD groups	Adequate: 15 of 22 (68%)
Yuge et al ⁵¹	Prospective cohort	Children with DCD (<i>n</i> = 3; 1 boy), children with PDD-NOS (<i>n</i> = 1; 0 boys), children with ADHD (<i>n</i> = 1; 1 boy), and TD children (<i>n</i> = 23; 12 boys); age range: 3–5 mo; Japan; NDD diagnosed at 5 y	GMA; general movements optimality score	General movements, 3–5 mo: group difference was not reported (ADHD: mean = 26; DCD: mean = 22; PDD-NOS: mean = 26; TD: median = 24 [IQR 22–26])	Adequate: 12 of 22 (55%)
Zappella et al ⁵³	Retrospective cohort	Children with ASD (<i>n</i> = 10; 10 boys) and without ASD (<i>n</i> = 8; 8 boys); age range: 1–6 mo; Italy; ASD diagnosed at 3–7 y	GMA; general movements	General movements, 1–6 mo: 87.5% (7 of 8) of ASD group showed abnormal general movements; inadequate information on 2 infants with later ASD	Adequate: 14 of 22 (64%)

AMS, Alberta Infant Motor Scale; IQR, interquartile range; LSM, least square mean.

TABLE 2 Summary of the Domains of Motor Function Examined in the Included Studies

Study	Fine Motor	Gross Motor	Generalized Motor Function	General Movements
0–6 mo				
Choi et al ⁴¹	X	—	—	—
Estes et al ⁴²	X	X	X	—
Gurevitz et al ⁴⁸	—	X	—	—
Iverson et al ⁴⁶	X	X	—	—
Kihara and Nakamura ⁴⁹	—	X	—	—
Landa and Garrett-Mayer ⁴³	X	X	—	—
LeBarton and Landa ⁴⁴	X	X	—	—
Libertus et al ⁴⁷	X	X	—	—
Ozonoff et al ⁴⁵	X	—	—	—
Phagava et al ⁵²	—	—	—	X
Sowell et al ⁵⁰	—	—	X	—
Yuge et al ⁵¹	—	—	—	X
Zappella et al ⁵³	—	—	—	X
13–18 mo				
Choi et al ⁴¹	X	—	—	—
Gurevitz et al ⁴⁸	X	X	—	—
Kihara and Nakamura ⁴⁹	—	X	—	—
Landa and Garrett-Mayer ⁴³	X	X	—	—
Landa et al ⁵⁹	X	—	—	—
Leonard et al ⁴⁰	X	X	—	—
Øien et al ⁶⁰	X	X	—	—
Ozonoff et al ⁶¹	X	—	—	—
Young et al ⁵⁴	X	—	—	—
7–12 mo				
Choi et al ⁴¹	X	—	—	—
Davies et al ⁵⁷	X	X	—	—
Estes et al ⁴²	X	X	X	—
Gurevitz et al ⁴⁸	X	X	—	—
Jeans et al ⁵⁸	—	—	X	—
Leonard et al ⁴⁰	X	X	—	—
Leonard et al ⁵⁶	X	X	—	—
Ozonoff et al ⁴⁵	X	—	—	—
Sowell et al ⁵⁰	—	—	X	—
St John et al ⁵⁵	X	X	—	—
Young et al ⁵⁴	X	—	—	—
19–24 mo				
Choi et al ⁴¹	X	—	—	—
Emerson et al ⁶⁴	X	X	—	—
Estes et al ⁴²	X	X	X	—
Jeans et al ⁵⁸	—	—	X	—
Landa and Garrett-Mayer ⁴³	X	X	—	—
Landa et al ⁵⁹	X	—	—	—
LeBarton and Iverson ⁶²	X	—	—	—
Leonard et al ⁴⁰	X	X	—	—
Lloyd et al ⁶³	X	X	—	—
Ozonoff et al ⁴⁵	X	—	—	—
Ozonoff et al ⁶¹	X	—	—	—
St John et al ⁵⁵	X	X	—	—
Young et al ⁵⁴	X	—	—	—

Total number of outcomes assessed: fine motor = 37; gross motor = 24; generalized motor function = 7; general movements = 3. X, specified domain of motor function examined in the study; —, not applicable.

months) and found that the general movement optimality scores of children with later-diagnosed ADHD, DCD, and PDD-NOS were in the normal range of those of TD children. It is important to note that the

findings by Yuge et al⁵¹ are limited by a small sample size and included insufficient quantitative data to compare general movement function between different groups with later-diagnosed NDD and the TD group. In

contrast, the authors of one retrospective study⁵² compared the general movement optimality scores between 20 children with later ASD (age range: 1–3 months) and 20 TD children and found that those with

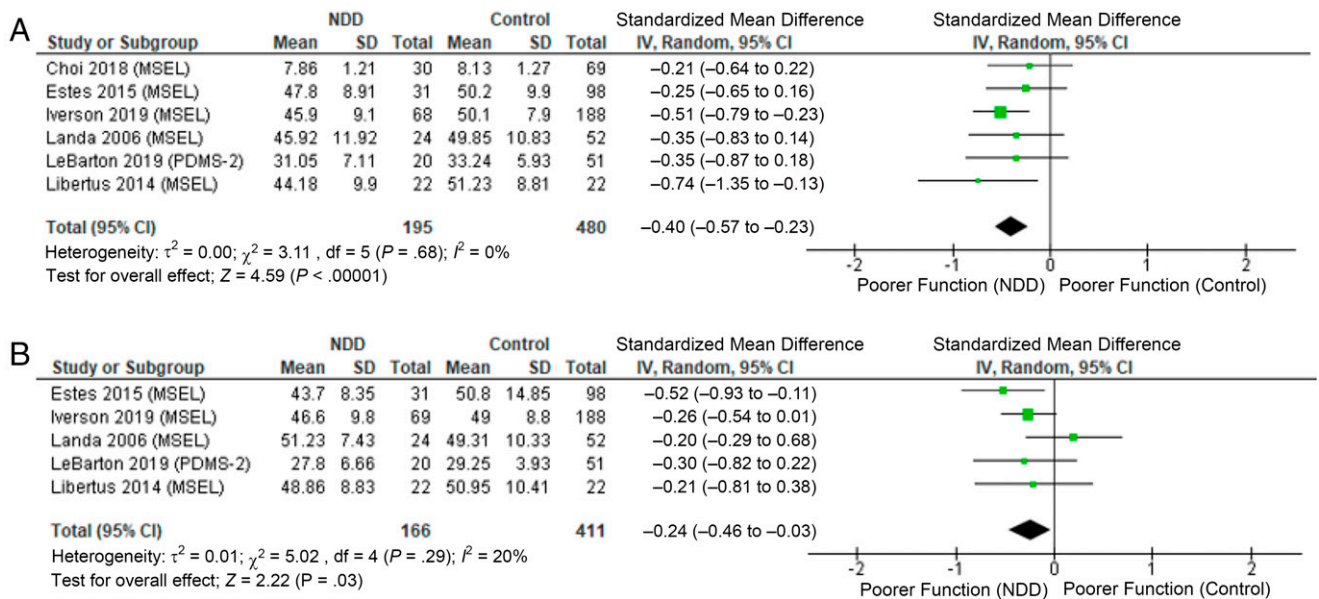


FIGURE 2

A and B. Forest plots of the comparison of fine motor function (A) and gross motor function (B) in children (0–6 months) with later diagnoses of ASD versus controls. The motor function assessment used is indicated next to each study. df, degree of freedom; IV, inverse variance.

later ASD demonstrated lower optimality scores, indicating poorer general movement function. The authors of another retrospective study⁵³ found that 87.5% (7 of 8) of children with later ASD showed abnormal general movements within the first 6 months of life. A meta-analysis of the studies involving children with later ASD was not possible because SDs could not be obtained.

Early Motor Function at 7 to 12 Months

Fine Motor

Fine motor function of children with later ADHD and ASD was examined in 8 studies by using the DDST, MSEL, and VABS-II. In 2 studies,^{48,54} the authors reported no difference in fine motor function between the later ADHD and ASD groups (ADHD, 1 study; ASD, 1 study; age range: 9–12 months) and the TD group. In contrast, the authors of 5 studies^{40–42,45,55} found that children with later ASD (age range: 7–12 months) demonstrated poorer fine motor function in relation to TD children. Statistical difference

between the later ASD and TD groups was not reported in one study.⁵⁶

A meta-analysis of 6 studies involving children with later ASD and TD children revealed an overall moderate effect size of 0.79 (95% CI -1.06 to -0.52; $P < .001$) (Fig 3A), indicating poorer fine motor function in the later ASD group. There was evidence of moderate heterogeneity of the effect size ($I^2 = 44\%$).

Gross Motor

Gross motor function of children with later ADHD, ASD, and FASD was examined in 6 studies by using the DDST, GMDS-ER, MSEL, and VABS-II. In one study,⁵⁷ the authors reported no difference in gross motor function between the later FASD (age range: 7–12 months) and TD groups. In contrast, the authors of 5 studies^{40,42,48,55,57} found that children with later ADHD, ASD, and FASD (ADHD, 1 study; ASD, 3 studies; FASD, 1 study; age range: 7–12 months) demonstrated poorer gross motor function in relation to TD children.

A meta-analysis of 3 studies involving children with later ASD and TD

children revealed an overall moderate effect size of 0.56 (95% CI -0.84 to -0.29; $P < .001$) (Fig 3B), indicating poorer gross motor function in the later ASD group. There was evidence of insignificant heterogeneity of the effect size ($I^2 = 0\%$).

Generalized Motor Function

Generalized motor function of children with later ASD and FASD was examined in 3 studies by using the BSID-II, BSFR, and VABS-II. In one study,⁵⁸ the authors reported no difference in generalized motor function between the later ASD (mean age: 9 months) and TD groups. In contrast, the authors of 2 studies^{42,50} found that children with later ASD and FASD (ASD, 1 study; FASD, 1 study; mean age: 12 months) demonstrated poorer generalized motor function in relation to TD children.

A meta-analysis of 3 studies involving children with later ASD and TD children revealed an overall nonsignificant effect size of 0.50 (95% CI -1.25 to 0.24; $P = .18$) (Fig 3C), indicating comparable generalized motor function between

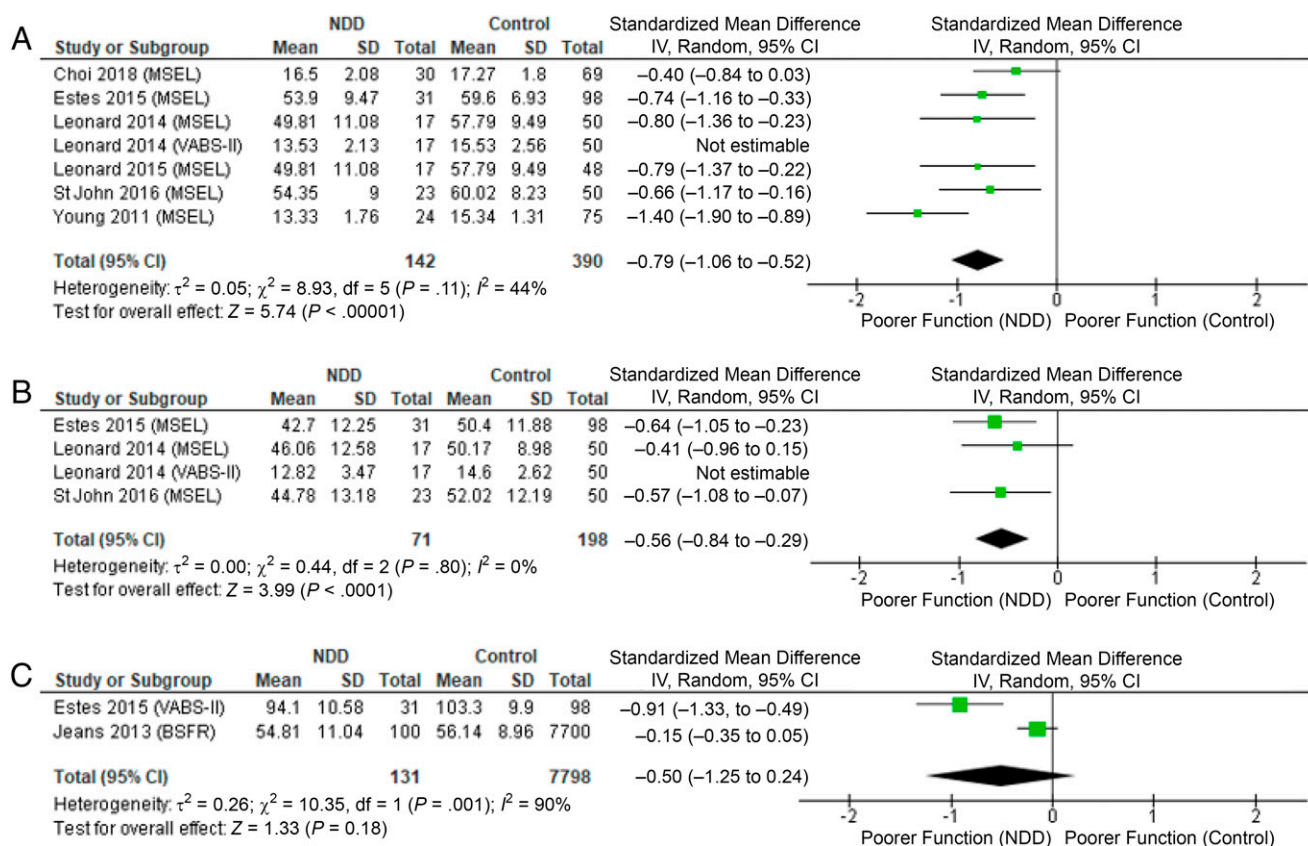


FIGURE 3

A–C, Forest plots of the comparison of fine motor function (A), gross motor function (B), and generalized motor function (C) in children (7–12 months) with later diagnoses of ASD versus controls. The motor function assessment used is indicated next to each study. df, degree of freedom; IV, inverse variance.

the later ASD and TD groups. There was evidence of considerable heterogeneity of the effect size ($I^2 = 90\%$).

Early Motor Function at 13 to 18 Months

Fine Motor

Fine motor function of children with later ASD was examined in 8 studies by using the ASQ, DDST, MSEL, and VABS-II. In 2 studies,^{48,54} the authors reported no difference in fine motor function between the later ASD and TD groups (mean age: 18 months). In contrast, the authors of 5 studies^{40,41,43,59,60} found that children with later ASD (age range: 14–18 months) demonstrated poorer fine motor function in relation to TD children. Statistical difference between the later ASD and TD groups was not reported in one study.⁶¹

A meta-analysis of 6 studies involving children with later ASD and TD children revealed an overall moderate effect size of 0.72 (95% CI -0.95 to -0.50; $P < .001$) (Fig 4A), indicating poorer fine motor function in the later ASD group. There was evidence of substantial heterogeneity of the effect size ($I^2 = 62\%$).

Gross Motor

Gross motor function of children with later ADHD and ASD was examined in 5 studies by using the ASQ, DDST, KSPD, MSEL, and VABS-II. In one study,⁴⁰ the authors reported no difference in gross motor function between the later ASD and TD groups (mean age: 14 months). In contrast, the authors of 4 studies^{43,48,49,60} found that children with later ADHD and ASD (ADHD, 1 study; ASD, 3 studies; age range: 14–18

months) demonstrated poorer gross motor function in relation to TD children.

A meta-analysis of 3 studies involving children with later ASD and TD children revealed an overall large effect size of 1.11 (95% CI -1.98 to -0.24; $P = .01$) (Fig 4B), indicating poorer gross motor function in the later ASD group. There was evidence of considerable heterogeneity of the effect size ($I^2 = 96\%$).

Early Motor Function at 19 to 24 Months

Fine Motor

Fine motor function of children with later ASD was examined in 12 studies by using the MSEL and VABS-II. In 3 studies,^{40,54,59} the authors reported no difference in fine motor function between the later ASD and TD groups

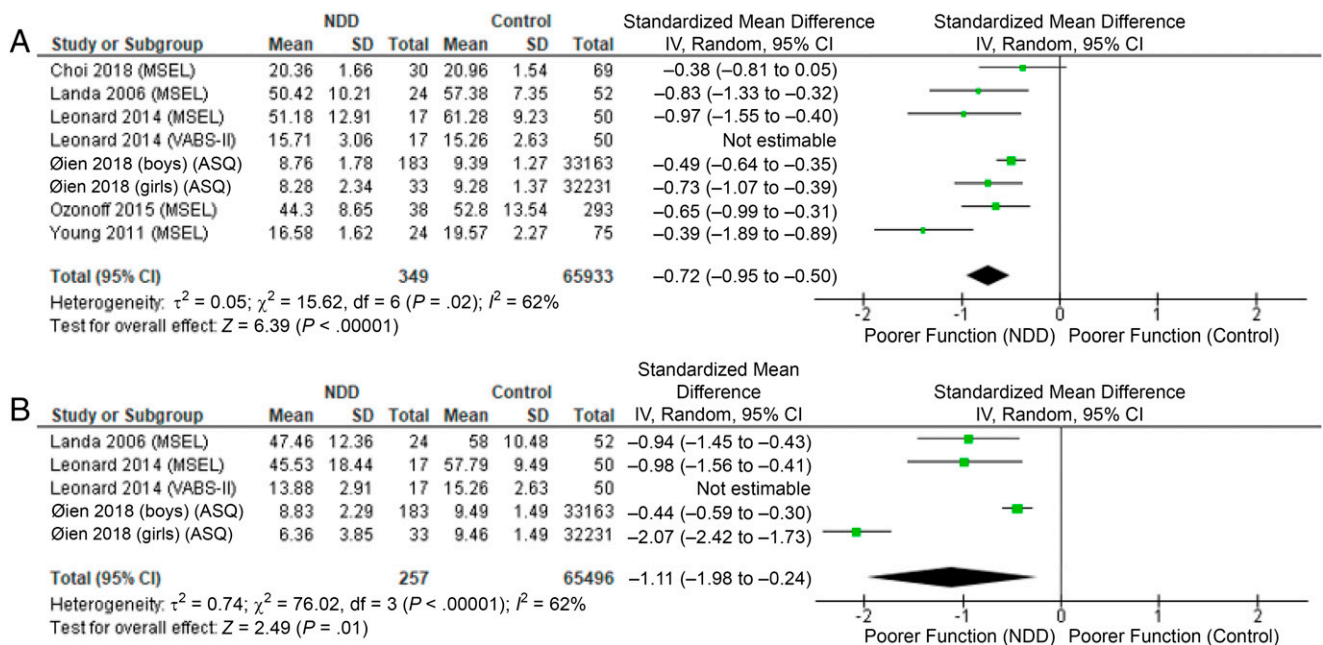


FIGURE 4

A and B, Forest plots of the comparison of fine motor function (A) and gross motor function (B) in children (13–18 months) with later diagnoses of ASD versus control. The motor function assessment used is indicated next to each study. df, degree of freedom; IV, inverse variance.

(mean age: 24 months). In contrast, the authors of 6 studies^{41–43,55,62,63} found that children with later ASD (mean age: 24 months) demonstrated poorer fine motor function in relation to TD children or normative data. Statistical differences between the later ASD and TD groups were not reported in 3 studies.^{45,61,64}

A meta-analysis of 7 studies involving children with later ASD and TD children revealed an overall large effect size of 1.14 (95% CI -1.48 to -0.81; $P < .001$) (Fig 5A), indicating poorer fine motor function in the later ASD group. There was evidence of substantial heterogeneity of the effect size ($I^2 = 71\%$).

Gross Motor

Gross motor function of children with later ASD was examined in 6 studies by using the MSEL and VABS-II. In 5 studies,^{42,43,55,62,63} the authors found that children with later ASD (mean age: 24 months) demonstrated poorer gross motor function in relation to TD children or normative data. Statistical difference between

the later ASD and TD groups was not reported in one study.⁶⁴

A meta-analysis of 4 studies involving children with later ASD and TD children revealed an overall large effect size of 1.47 (95% CI -1.74 to -1.21; $P < .001$) (Fig 5B), indicating poorer gross motor function in the later ASD group. There was evidence of insignificant heterogeneity of the effect size ($I^2 = 0\%$).

Generalized Motor Function

Generalized motor function of children with later ASD was examined in 2 studies by using the BSFR and VABS-II. In both studies,^{42,58} the authors reported that children with later ASD demonstrated poorer generalized motor function in relation to TD children.

A meta-analysis of 2 studies involving children with later ASD and TD children revealed an overall large effect size of 1.33 (95% CI -1.69 to -0.96; $P < .001$) (Fig 5C), indicating poorer generalized motor function in the later ASD group. There was

evidence of substantial heterogeneity of the effect size ($I^2 = 61\%$).

DISCUSSION

Our aim for this systematic review was to synthesize evidence of early motor functioning in children later diagnosed with NDD. Although the included studies documented early motor impairments among children later diagnosed with ADHD, ASD, DCD, FASD, and PDD-NOS, 84% (21 of 25) of the included studies in this review involved young children with later ASD. This limits our capacity to make inferences about the transdiagnostic nature of early motor impairments as an early marker of NDD risk. Accordingly, we focus the discussion on the findings of children with later ASD. Additional longitudinal studies with early motor assessments that are linked to later developmental functioning and diagnostic outcomes are essential to enable comparisons of early motor difficulties across different NDD groups.

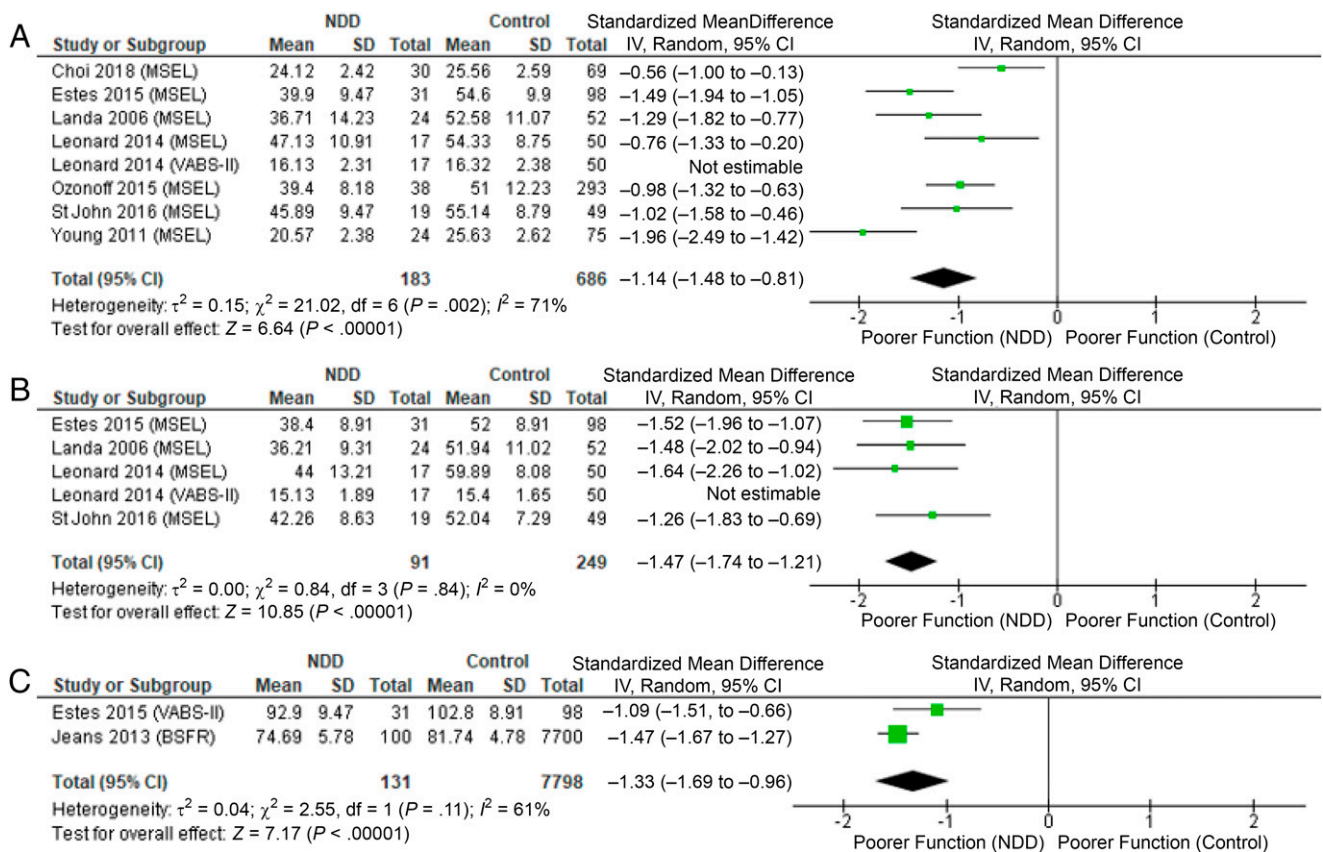


FIGURE 5

A–C, Forest plots of the comparison of fine motor function (A), gross motor function (B), and generalized motor function (C) in children (19–24 months) with later diagnoses of ASD versus controls. The motor function assessment used is indicated next to each study. *df*, degree of freedom; IV, inverse variance.

Consistent with previous findings of motor impairments in individuals with NDD,^{65–68} we found that children with later ASD exhibited early impairments in fine, gross, and generalized motor functions. Our meta-analysis indicated that children with later ASD showed increasingly poorer motor function, compared with TD children, with increasing age. During early infancy (0–6 months), those with later ASD displayed small differences in fine and gross motor functions relative to TD children. By 19 to 24 months, large effect sizes were found across fine, gross, and generalized motor functions. These findings suggest that motor impairments can be detected in children from as early as 6 months, and thus these early motor impairments could be useful to identify

children at risk for ASD. However, the predictive validity of early motor impairment should not be used alone and should be considered together with other markers of neurodevelopmental vulnerability, such as deviations in early speech and language development.⁶⁹

An important consideration in developing strategies for the early identification of at-risk children is the selection of appropriate standardized motor function assessment tools for children between 0 and 24 months. In the present review, we identified 10 different types of standardized assessments that were used to measure motor function. The use of a variety of assessment tools to measure motor function is not uncommon. Spittle et al⁷⁰ found that across the 9 assessment tools used to

measure motor development in preterm infants, all were appropriate for use, but each tool had a different purpose (ie, discriminative, predictive, or evaluative purposes). In the studies included in the current review, the MSEL was most frequently used. This is a practitioner-administered assessment that can be used on children from birth to 68 months.⁷¹ Although the MSEL has been reported to have high interrater reliability (range: 0.91–0.99) and good construct and criterion validity in a normative population,⁷² there is limited information regarding its sensitivity and specificity. More research on the psychometrics of the MSEL is needed to determine its appropriateness as a gold standard assessment tool for the measurement of motor function in

at-risk children between 0 and 24 months.

Only 3 of the 4 motor domains examined in the present review revealed early motor impairments in at-risk children. A large proportion of fine, gross, and generalized motor functions in young children with later ASD were found to be different from that of TD children; however, there were mixed findings in the general movement function. It is uncertain how the general movement function can provide meaningful information to detect motor impairments in at-risk children because only 3 included studies in the present review used the GMA to evaluate the general movement function. However, previous work has found support for the notion that GMA is a transdiagnostic measure of neurodevelopmental vulnerability. For example, among preterm infants, abnormal writhing general movements are associated later cognitive vulnerability.⁷³ Further research on the utility of the general movement function in the detection of early motor impairments in children later diagnosed with NDD is warranted.

In addition to the meta-analysis only comprising studies of children later diagnosed with ASD, this review has several limitations. First, a strict selection criterion was used to include studies in which motor function was only examined in children with later-diagnosed NDD. This led to many studies being excluded, for example, studies in which motor function was examined in at-risk children with no later diagnosis. In future work, researchers may wish to consider the association between early motor development and dimensional measures of later functioning, for example, cognitive development, or other transdiagnostic markers of neurodevelopmental vulnerability, such as dysregulated irritability.

Second, the current study contained only data from children with a later diagnosis of ADHD, ASD, DCD, FASD, and PDD-NOS; therefore, results may not be applicable to children with other types of NDD. Third, a wide range of heterogeneity was found in the meta-analyses; effect sizes with substantial and considerable heterogeneity should be interpreted with caution.

There is scope for research to further understand how early detection of motor impairments in children can be used as an early marker of ASD risk. In addition, the understanding of early motor impairment as a transdiagnostic marker of later NDD is currently limited by a paucity of studies on motor function in children later diagnosed with intellectual disability, language and speech disorder, ADHD, DCD, and FASD. Further studies in which motor function is examined in children across a wide range of NDD can be used to develop a comprehensive transdiagnostic profile of motor function in NDD. Given the heterogeneity in the clinical presentation of children with NDD, it is likely that motor profiles will be similarly heterogenous; however, transdiagnostic comparisons provide a basis for understanding latent classes of functioning that have important clinical implications.⁷⁴ In future work, researchers should also aim to determine best practice screening strategies for the early detection of motor impairments in children at risk for ASD and other NDD. This includes identifying appropriate assessment tools, standardized cutoffs for the classification of motor impairment, the recommended age for assessment, screening procedures, and cost.⁷⁵

CONCLUSIONS

With the present systematic review, we provide evidence of early motor

impairments in young children later diagnosed with ASD. With this review, we also provide mixed evidence of shared features of motor impairments across different types of NDD. Further work is needed to understand the clinical utility of motor impairment detection as a transdiagnostic early marker of NDD risk.

ABBREVIATIONS

ADHD:	attention-deficit/hyperactivity disorder
ASD:	autism spectrum disorder
ASQ-2:	Ages and Stages Questionnaire, Second Edition
BSID-II:	Bayley Scales of Infant Development, Second Edition
BSFR:	Bayley Short Form Research Edition
CI:	confidence interval
DCD:	developmental coordination disorder
DDST:	Denver Developmental Screening Test
FASD:	fetal alcohol spectrum disorder
GMA:	General Movements Assessment
GMDS-ER:	Griffiths Mental Developmental Scales-Extended Revised
ICD-11:	<i>International Classification of Diseases, 11th Revision</i>
KSPD:	Kyoto Scale of Psychological Development
MSEL:	Mullen Scales of Early Learning
NDD:	neurodevelopmental disorders
PDD-NOS:	pervasive developmental disorder not otherwise specified
PDMS-2:	Peabody Developmental Motor Scales, Second Edition
TD:	typically developing
VABS-II:	Vineland Adaptive Behavior Scales, Second Edition

Dr Lim contributed to the conceptualization of the study, conducted the literature searches for the systematic review, reviewed articles for inclusion, performed data extraction, reviewed methodology of articles using the quality appraisal tool, analyzed the data, contributed to the interpretation of results, drafted the initial manuscript, and revised the manuscript; Drs Licari and Downs contributed to the conceptualization of the study, reviewed articles for inclusion, performed data extraction, reviewed methodology of articles using the quality appraisal tool, analyzed the data, contributed to the interpretation of results, and reviewed and revised the manuscript; Drs Spittle, Watkins, and Zwicker contributed to the conceptualization of the study, analyzed the data, contributed to the interpretation of results, and reviewed and revised the manuscript; Dr Finlay-Jones conceptualized and designed the study, reviewed articles for inclusion, performed data extraction, reviewed methodology of articles using the quality appraisal tool, analyzed the data, contributed to the interpretation of results, and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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REFERENCES

- Thapar A, Rutter M. Neurodevelopmental Disorders. In: Thapar A, Pine DS, Leckman JF, Scott S, Snowling MJ, Taylor E, eds. *Rutter's Child and Adolescent Psychiatry*, 6th ed. Chichester, United Kingdom: John Wiley & Sons, Ltd; 2015:31–40
- World Health Organization. *International Classification of Diseases, 11th Revision for Mortality and Morbidity Statistics*. Geneva, Switzerland: World Health Organization; 2018
- Eklund H, Findon J, Cadman T, et al. Needs of adolescents and young adults with neurodevelopmental disorders: comparisons of young people and parent perspectives. *J Autism Dev Disord*. 2018;48(1):83–91
- Schiariti V, Mahdi S, Bölte S. International Classification of Functioning, Disability and Health Core Sets for cerebral palsy, autism spectrum disorder, and attention-deficit-hyperactivity disorder. *Dev Med Child Neurol*. 2018;60(9):933–941
- Chen CY, Liu CY, Su WC, Huang SL, Lin KM. Factors associated with the diagnosis of neurodevelopmental disorders: a population-based longitudinal study. *Pediatrics*. 2007; 119(2). Available at: www.pediatrics.org/cgi/content/full/119/2/e435
- Zwicker JG, Harris SR, Klassen AF. Quality of life domains affected in children with developmental coordination disorder: a systematic review. *Child Care Health Dev*. 2013; 39(4):562–580
- Cioni G, Inguaggiato E, Sgandurra G. Early intervention in neurodevelopmental disorders: underlying neural mechanisms. *Dev Med Child Neurol*. 2016;58(suppl 4): 61–66
- Whitehouse AJO, Varcin KJ, Alvares GA, et al. Pre-emptive intervention versus treatment as usual for infants showing early behavioural risk signs of autism spectrum disorder: a single-blind, randomised controlled trial. *Lancet Child Adolesc Health*. 2019;3(9):605–615
- Morgan C, Darrah J, Gordon AM, et al. Effectiveness of motor interventions in infants with cerebral palsy: a systematic review. *Dev Med Child Neurol*. 2016;58(9):900–909
- Zwaigenbaum L, Bauman ML, Choueiri R, et al. Early intervention for children with autism spectrum disorder under 3 years of age: recommendations for practice and research. *Pediatrics*. 2015; 136(suppl 1):S60–S81
- Adolph KE, Robinson SR. Motor Development. In: Lerner RM, Liben LS, Mueller U, eds. *Handbook of Child Psychology and Developmental Science*, 7th ed, vol. Vol 2. Hoboken, NJ: John Wiley & Sons, Inc; 2015:113–157
- Inguaggiato E, Sgandurra G, Cioni G. Brain plasticity and early development: implications for early intervention in neurodevelopmental disorders [in French]. *Neuropsychiatr Enfance Adolesc*. 2017;65(5):299–306
- Brett D, Warnell F, McConachie H, Parr JR. Factors affecting age at ASD diagnosis in UK: no evidence that diagnosis age has decreased between 2004 and 2014. *J Autism Dev Disord*. 2016;46(6):1974–1984
- Visser SN, Danielson ML, Bitsko RH, et al. Trends in the parent-report of health care provider-diagnosed and medicated attention-deficit/hyperactivity disorder: United States, 2003-2011. *J Am Acad Child Adolesc Psychiatry*. 2014;53(1):34–46.e2
- Centers for Disease Control and Prevention. Data and statistics about

- ADHD. 2019. Available at: <https://www.cdc.gov/ncbddd/adhd/data.html>. Accessed May 4, 2020
16. Finlay-Jones A, Varcin K, Leonard H, Bosco A, Alvares G, Downs J. Very early identification and intervention for infants at risk of neurodevelopmental disorders: a transdiagnostic approach. *Child Dev Perspect*. 2019;13(2):97–103
17. Guthrie W, Swineford LB, Nottke C, Wetherby AM. Early diagnosis of autism spectrum disorder: stability and change in clinical diagnosis and symptom presentation. *J Child Psychol Psychiatry*. 2013;54(5):582–590
18. Morgan AM, Aldag JC. Early identification of cerebral palsy using a profile of abnormal motor patterns. *Pediatrics*. 1996;98(4 pt 1):692–697
19. Fjortoft T, Evensen KAI, Øberg GK, et al. High prevalence of abnormal motor repertoire at 3 months corrected age in extremely preterm infants. *Eur J Paediatr Neurol*. 2016;20(2):236–242
20. Einspieler C, Sigafoos J, Bölte S, Bratl-Pokorny KD, Landa R, Marschik PB. Highlighting the first 5 months of life: general movements in infants later diagnosed with autism spectrum disorder or Rett syndrome. *Res Autism Spectr Disord*. 2014;8(3):286–291
21. Hatakenaka Y, Kotani H, Yasumitsu-Lovell K, Suzuki K, Fernell E, Gillberg C. Infant motor delay and early symptomatic syndromes eliciting neurodevelopmental clinical examinations in Japan. *Pediatr Neurol*. 2016;54:55–63
22. Sumner E, Leonard HC, Hill EL. Overlapping phenotypes in autism spectrum disorder and developmental coordination disorder: a cross-syndrome comparison of motor and social skills. *J Autism Dev Disord*. 2016; 46(8):2609–2620
23. McPhillips M, Finlay J, Bejerot S, Hanley M. Motor deficits in children with autism spectrum disorder: a cross-syndrome study. *Autism Res*. 2014;7(6): 664–676
24. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med*. 2009;6(7):e1000097
25. Kmet LM, Lee RC, Cook LS. Standard quality assessment criteria for evaluating primary research papers from a variety of fields. 2004. Available at: <https://www.ihe.ca/publications/standard-quality-assessment-criteria-for-evaluating-primary-research-papers-from-a-variety-of-fields>. Accessed June 15, 2020
26. Lee L, Packer TL, Tang SH, Girdler S. Self-management education programs for age-related macular degeneration: a systematic review. *Australas J Ageing*. 2008;27(4):170–176
27. Higgins JPT, Green S, eds. *Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1.0*. London, United Kingdom: The Cochrane Collaboration; 2011. Available at: <https://handbook-5-1.cochrane.org/>. Accessed March 23, 2020
28. *Review Manager (RevMan) [Computer Program]. Version 5.3*. Copenhagen, Denmark: The Nordic Cochrane Centre, The Cochrane Collaboration; 2014
29. Cohen J. *Statistical Power Analysis for the Behavioral Sciences*, 2nd ed. Mahwah, NJ: Lawrence Erlbaum Associates; 1988
30. Squires J, Bricker DD, Twombly E. *Ages & Stages Questionnaires*, 2nd ed. Baltimore, MD: Paul H. Brookes; 1999
31. Bayley N. *Bayley Scales of Infant Development*, 2nd ed. San Antonio, TX: Psychological Corporation; 1993
32. Bayley N. *Bayley Scales of Infant Development: Manual*, 2nd ed. San Antonio, TX: Psychological Corporation; 1993
33. Frankenburg WK, Dodds JB. The Denver Developmental Screening Test. *J Pediatr*. 1967;71(2):181–191
34. Einspieler C, Prechtl HFR. Prechtl's assessment of general movements: a diagnostic tool for the functional assessment of the young nervous system. *Ment Retard Dev Disabil Res Rev*. 2005;11(1):61–67
35. Luiz DM, Barnard A, Knoesen N, Kotras H, McAlinden P, O'Connell R. *Griffiths Mental Development Scales - Extended Revised: Administration Manual*. Oxford, United Kingdom: Hogrefe; 2004
36. Ikuzawa M, Matsushita Y, Nakase A. *Kyoto Scale of Psychological Development 2001*. Kyoto, Japan: Kyoto International Social Welfare Exchange Centre; 2002
37. Mullen E. *Mullen Scales of Early Learning*. Circle Pines, MN: American Guidance Service; 1995
38. Folio MR, Fewell RR. *Peabody Developmental Motor Scales: Examiner's Manual*, 2nd ed. Austin, TX: Pro-Ed; 2000
39. Sparrow SS, Cicchetti D, Balla DA. *Vineland Adaptive Behavior Scales*, 2nd ed. Circle Pines, MN: American Guidance Service; 2005
40. Leonard HC, Elsabbagh M, Hill EL; BASIS Team. Early and persistent motor difficulties in infants at-risk of developing autism spectrum disorder: a prospective study. *Eur J Dev Psychol*. 2014;11(1):18–35
41. Choi B, Leech KA, Tager-Flusberg H, Nelson CA. Development of fine motor skills is associated with expressive language outcomes in infants at high and low risk for autism spectrum disorder. *J Neurodev Disord*. 2018;10(1): 14
42. Estes A, Zwaigenbaum L, Gu H, et al.; IBIS Network. Behavioral, cognitive, and adaptive development in infants with autism spectrum disorder in the first 2 years of life. *J Neurodev Disord*. 2015; 7(1):24
43. Landa R, Garrett-Mayer E. Development in infants with autism spectrum disorders: a prospective study. *J Child Psychol Psychiatry*. 2006;47(6):629–638
44. LeBarton ES, Landa RJ. Infant motor skill predicts later expressive language and autism spectrum disorder diagnosis. *Infant Behav Dev*. 2019;54: 37–47
45. Ozonoff S, Young GS, Belding A, et al. The broader autism phenotype in infancy: when does it emerge? *J Am Acad Child Adolesc Psychiatry*. 2014;53(4): 398–407.e2
46. Iverson JM, Shic F, Wall CA, et al. Early motor abilities in infants at heightened versus low risk for ASD: a Baby Siblings Research Consortium (BSRC) study. *J Abnorm Psychol*. 2019;128(1):69–80
47. Libertus K, Sheperd KA, Ross SW, Landa RJ. Limited fine motor and grasping skills in 6-month-old infants at high risk

- for autism. *Child Dev.* 2014;85(6): 2218–2231
48. Gurevitz M, Geva R, Varon M, Leitner Y. Early markers in infants and toddlers for development of ADHD. *J Atten Disord.* 2014;18(1):14–22
49. Kihara H, Nakamura T. Early standard development assessment characteristics in very low birth weight infants later classified with autism spectrum disorder. *Early Hum Dev.* 2015;91(6):357–359
50. Sowell KD, Uriu-Adams JY, Van de Water J, et al.; Collaborative Initiative on Fetal Alcohol Spectrum Disorders (CIFASD). Implications of altered maternal cytokine concentrations on infant outcomes in children with prenatal alcohol exposure. *Alcohol.* 2018;68: 49–58
51. Yuge M, Marschik PB, Nakajima Y, et al. Movements and postures of infants aged 3 to 5 months: to what extent is their optimality related to perinatal events and to the neurological outcome? *Early Hum Dev.* 2011;87(3): 231–237
52. Phagava H, Muratori F, Einspieler C, et al. General movements in infants with autism spectrum disorders. *Georgian Med News.* 2008;(156): 100–105
53. Zappella M, Einspieler C, Bartl-Pokorny KD, et al. What do home videos tell us about early motor and socio-communicative behaviours in children with autistic features during the second year of life—an exploratory study. *Early Hum Dev.* 2015;91(10): 569–575
54. Young GS, Rogers SJ, Hutman T, Rozga A, Sigman M, Ozonoff S. Imitation from 12 to 24 months in autism and typical development: a longitudinal Rasch analysis. *Dev Psychol.* 2011;47(6): 1565–1578
55. St John T, Estes AM, Dager SR, et al. Emerging executive functioning and motor development in infants at high and low risk for autism spectrum disorder. *Front Psychol.* 2016;7:1016
56. Leonard HC, Bedford R, Pickles A, Hill EL; BASIS Team. Predicting the rate of language development from early motor skills in at-risk infants who develop autism spectrum disorder. *Res Autism Spectr Disord.* 2015;13–14:15–24
57. Davies LA, Cockcroft K, Olinger L, et al. Alcohol exposure during pregnancy altered childhood developmental trajectories in a rural South African community. *Acta Paediatr.* 2017;106(11): 1802–1810
58. Jeans LM, Santos RM, Laxman DJ, McBride BA, Dyer WJ. Early predictors of ASD in young children using a nationally representative data set. *J Early Interv.* 2013;35(4):303–331
59. Landa RJ, Gross AL, Stuart EA, Faherty A. Developmental trajectories in children with and without autism spectrum disorders: the first 3 years. *Child Dev.* 2013;84(2):429–442
60. Øien RA, Schjølberg S, Volkmar FR, et al. Clinical features of children with autism who passed 18-month screening. *Pediatrics.* 2018;141(6): e20173596
61. Ozonoff S, Young GS, Landa RJ, et al. Diagnostic stability in young children at risk for autism spectrum disorder: a baby siblings research consortium study. *J Child Psychol Psychiatry.* 2015; 56(9):988–998
62. LeBarton ES, Iverson JM. Fine motor skill predicts expressive language in infant siblings of children with autism. *Dev Sci.* 2013;16(6):815–827
63. Lloyd M, MacDonald M, Lord C. Motor skills of toddlers with autism spectrum disorders. *Autism.* 2013;17(2):133–146
64. Emerson RW, Adams C, Nishino T, et al. Functional neuroimaging of high-risk 6-month-old infants predicts a diagnosis of autism at 24 months of age. *Sci Transl Med.* 2017;9(393):eaag2882
65. Kaiser ML, Schoemaker MM, Albaret JM, Geuze RH. What is the evidence of impaired motor skills and motor control among children with attention deficit hyperactivity disorder (ADHD)? Systematic review of the literature. *Res Dev Disabil.* 2015;36C:338–357
66. Lucas BR, Latimer J, Pinto RZ, et al. Gross motor deficits in children prenatally exposed to alcohol: a meta-analysis. *Pediatrics.* 2014;134(1). Available at: www.pediatrics.org/cgi/content/full/134/1/e192
67. Zwicker JG, Missiuna C, Harris SR, Boyd LA. Developmental coordination disorder: a review and update. *Eur J Paediatr Neurol.* 2012;16(6): 573–581
68. Fournier KA, Hass CJ, Naik SK, Lodha N, Cauraugh JH. Motor coordination in autism spectrum disorders: a synthesis and meta-analysis. *J Autism Dev Disord.* 2010;40(10):1227–1240
69. Roche L, Zhang D, Bartl-Pokorny KD, et al. Early vocal development in autism spectrum disorder, Rett syndrome, and fragile X syndrome: insights from studies using retrospective video analysis. *Adv Neurodev Disord.* 2018; 2(1):49–61
70. Spittle AJ, Doyle LW, Boyd RN. A systematic review of the clinimetric properties of neuromotor assessments for preterm infants during the first year of life. *Dev Med Child Neurol.* 2008; 50(4):254–266
71. Gridley N, Blower S, Dunn A, Bywater T, Bryant M. Psychometric properties of child (0-5 years) outcome measures as used in randomized controlled trials of parent programs: a systematic review. *Clin Child Fam Psychol Rev.* 2019;22(3): 388–405
72. Burns TG, King TZ, Spencer KS. Mullen scales of early learning: the utility in assessing children diagnosed with autism spectrum disorders, cerebral palsy, and epilepsy. *Appl Neuropsychol Child.* 2013;2(1):33–42
73. Einspieler C, Bos AF, Libertus ME, Marschik PB. The general movement assessment helps us to identify preterm infants at risk for cognitive dysfunction. *Front Psychol.* 2016;7 :406
74. Dajani DR, Llabre MM, Nebel MB, Mostofsky SH, Uddin LQ. Heterogeneity of executive functions among comorbid neurodevelopmental disorders. *Sci Rep.* 2016;6:36566
75. Noritz GH, Murphy NA; Neuromotor Screening Expert Panel. Motor delays: early identification and evaluation. [published correction appears in *Pediatrics.* 2017;140(3):e20172081]. *Pediatrics.* 2013;131(6). Available at: www.pediatrics.org/cgi/content/full/131/6/e2016

76. Heathcock JC, Tanner K, Robson D, Young R, Lane AE. Retrospective analysis of motor development in infants at high and low risk for autism spectrum disorder. *Am J Occup Ther*. 2015;69(5):6905185070
77. Landa RJ, Gross AL, Stuart EA, Bauman M. Latent class analysis of early developmental trajectory in baby siblings of children with autism. *J Child Psychol Psychiatry*. 2012;53(9):986–996
78. Serdarevic F, Ghassabian A, van Batenburg-Eddes T, et al. Infant muscle tone and childhood autistic traits: a longitudinal study in the general population. *Autism Res*. 2017;10(5):757–768