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A systematic review and meta-analysis of the associations between motor milestone timing and motor development in neurodevelopmental conditions

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ABSTRACT

Early motor skills may be important early markers of neurodevelopmental conditions or predictors of their later onset. To explore this, we conducted a systematic review and meta-analysis of infant motor skill assessments in those who go on to gain a clinical diagnosis of autism, attention deficit hyperactivity disorder (ADHD), schizophrenia, language conditions, tic disorders, or developmental coordination disorder (DCD). In total, 63 articles met inclusion criteria. Three three-level meta-analyses were run. Meta-analysis of milestone achievement in N= 21205 individuals revealed gross motor milestones were significantly delayed compared to controls (g= 0.53, p< 0.001). Subgroup analyses revealed autism (g= 0.63) and DCD (g= 0.53) had the highest magnitude delays. Specific delays were revealed for holding the head up (g= 0.21), sitting (g= 0.28), standing (g= 0.35), crawling (g= 0.19), and walking (g= 0.71). Meta-analyses of standardised motor skill measurements in N= 1976 individuals revealed reduced performance compared to controls in autism and language conditions (g= −0.54, p< 0.001). Together, these findings demonstrate delayed milestone attainment and motor impairments in early childhood in neurodevelopmental conditions.

1. Introduction

Early motor development allows children to independently explore the environment, increase social interaction, and communicate with caregivers through joint eye contact, gestures and passing objects. Importantly, many of the first major fine and gross motor milestones in human childhood, such as walking (gross-motor) and the pincer grip (fine-motor), are typically achieved in the first two years after birth during a period of marked brain plasticity (Stiles et al., 2005). Motor and non-motor cognitive brain regions have a large number of connections with each other across the lifespan (Diamond, 2000), and sensorimotor networks develop first and reach maturity faster relative to other brain network systems (Cao et al., 2017). Motor and cognitive brain regions may thus be more vulnerable to early environmental disruption than

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other regions (Hensch and Bilimoria, 2012). Genetic factors are known to influence infant motor skills (Austerberry et al., 2022; Gui et al., 2024) and may partly overlap with genetic factors influencing some neurodevelopmental conditions (Gui et al., 2024; Hannigan et al., 2021). Motor development, therefore, has the potential to be an important early indicator of later neurodevelopmental conditions and could enable the timely initiation of early intervention.

A large-scale study by the World Health Organisation (WHO) reports typical ages of attainment for gross motor milestones (Onis, 2006). For example, crawling is typically achieved at 8 months and walking at 12 months (Onis, 2006). Evidence for fine motor skills is sparse in comparison. However, the pincer grip, for example, is typically achieved before the age of 24 months (Bedford et al., 2016). Considerable inter-individual variability is present between infants (Onis, 2006).

Much of the research in atypical infant motor development has focussed individually on motor development in groups with specific neurodevelopmental conditions rather than comparing between conditions. However, in light of recent evidence highlighting co-occurrences and overlapping genetic underpinnings between different neurodevelopmental conditions (Guilmatre et al., 2009; Ronald et al., 2008; Rujescu et al., 2009; Stergiakouli et al., 2017), as well as the differences in motor impairments across different neurodevelopmental conditions, it is important to understand if there are significant differences between neurodevelopmental conditions in motor development and milestone attainment. Doing so is important for understanding of aetiology of and developing interventions for neurodevelopmental conditions.

Independent systematic reviews of attention deficit hyperactivity disorder (ADHD, Athanasiadou et al., 2020; Havmoeller et al., 2019; Kaiser et al., 2015), autism (West, 2019), language disorders (Rechetnikov and Maitra, 2009), and schizophrenia (Burton et al., 2016; Filatova et al., 2017) have suggested that these conditions may be associated with atypical early motor skills. However, these individual reviews focused on different ages and motor skill categories. No systematic review has compared motor skills and motor developmental milestones across multiple neurodevelopmental conditions. Further, no meta-analysis or systematic review exists for motor skills for motor or tic conditions. Therefore, it is currently unclear if there are similar or unique motor delays and impairments across neurodevelopmental conditions.

Although schizophrenia is not typically a childhood-onset condition and is not defined as a neurodevelopmental disorder in the DSM-5, several lines of evidence suggest it has neurodevelopmental origins (Insel, 2010; Owen and O'Donovan, 2017). Further, studies have revealed evidence for delays in gross motor milestones in schizophrenia (Filatova et al., 2017; Murray et al., 2006). Schizophrenia will, therefore, be considered a neurodevelopmental condition for this review. In contrast, including specific learning disorders is beyond the remit of this review because this condition is explicitly defined in the DSM-5 as not attributable to motor disorders (American Psychiatric Association, 2013). Further, specific intellectual disabilities frequently co-occur with other included neurodevelopmental condition categories in this review, and thus, separating these effects is likely challenging.

Across neurodevelopmental condition diagnoses, there is a lack of consensus regarding the role or prevalence of motor impairments. A clear exception is a motor disorder, developmental coordination disorder (DCD), in which motor milestones delays and motor atypicalities such as coordination are part of its diagnostic criteria or features (DSM-5, American Psychiatric Association, 2013). The DSM-5 diagnostic criteria and features for stereotypic motor disorder also refer to "repetitive motor behaviour" that often starts in the first three years. In contrast, the only reference to motor skills for tic disorders is the criteria for "motor tics". Schizophrenia includes "grossly disorganized or abnormal motor behaviour (including catatonia)" as a key DSM-5 feature. For ADHD, excessive motor activity is the only motor-relevant criterion or feature in the DSM-5, and for autism, repetitive motor movements are the main motor-relevant component. However, recent research has revealed evidence of more extensive motor deviations or delays in autism and ADHD, indicating there may be associations of early motor markers with these conditions (Gurevitz et al., 2014; Nishimura et al., 2019; Ozonoff et al., 2008).

This review aims to fill these gaps by systematically assessing the evidence for motor atypicalities and motor milestone delay in neurodevelopmental conditions in the same review. The meta-analyses compared infant motor atypicalities and motor milestone delay across neurodevelopmental conditions and compared neurodevelopmental condition groups against controls without neurodevelopmental conditions. The meta-analyses included motor skills as assessed by standardised assessment scales, and age at fine and gross motor milestone achievement. The systematic review included other measures of gross and fine motor skills such as finger dexterity, clinical/parental motor concerns, gait, head lag, general motor skills, impaired coordination measured tests such as finger opposition, abnormal movements such as tics, and neurological soft signs from a neurological assessment. There were three primary meta-analyses to answer the following questions:

1) Do children with neurodevelopmental conditions have delays in the attainment of motor milestones in infancy compared to controls (without any neurodevelopmental condition or psychiatric illness)?
2) At what age do children with neurodevelopmental conditions reach motor milestones in infancy? – This was studied by comparing age of attainment across neurodevelopmental condition groups and/or compared to the World Health Organisation (WHO, Onis, 2006) average ages of attainment when available.
3) Do children with neurodevelopmental conditions differ significantly in standardised assessments of motor skills compared to controls (without any neurodevelopmental condition or psychiatric illness)?

2. Method

2.1. Study registration and PRISMA

Before starting the literature search, the protocol for the study was registered with PROSPERO, the International Prospective Register of Systemic Reviews (https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=175187). The review was performed in line with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) reporting guideline 2020 statement (Liberati et al., 2009).

2.2. Search methods

Database searches were conducted in MEDLINE, EMBASE and PsycINFO using OVID as a provider and Web of Science. The searches were completed individually for each condition group and in three phases between November 2020 and March 2024 (see Table S1). The searches that first took place in 2020 and 2021 (on autism, ADHD, schizophrenia, and tic disorders) were repeated in November 2022. All searches were then repeated in March 2024 (on request by reviewers) to identify more recent publications. The MEDLINE Search is presented below, where the first three terms were changed for each condition (e.g., "ADHD"). The full search terms for each neurodevelopmental condition group and database can be found in the supplement (Supplementary Data 1). In addition, reference lists of included studies were searched. There was no restriction on the date published.

1 *[Neurodevelopmental condition term1] /
2 [Neurodevelopmental condition term 2]ab. /freq=2
3 [Neurodevelopmental condition term 3].ab. /freq=2
4 Infant/
5 Infant Behavior/
6 Child Development/
7 (infan* or child*).ab.

8 Motor Skills/
9 Motor Activity/
10 Movement/
11 Walking/
12 Head Movements/
13 Locomotion/
14 Postural Balance/
15 postural control.mp.
16 (walk or walking or locomotion or gait).mp.
17 pulls.mp
18 (sitting or sit up).mp.
19 standing.mp.
20 ambulation.mp.
21 (lift* adj2 head*).mp.
22 pincer*.mp.
23 grip.mp.
24 crawl*.mp.
25 general movements.mp.
26 (fine motor or gross motor).mp.
27 (Motor adj3 skill*).mp.
28 motor development.mp.
29 motor milestone*.mp.
30 motor ability.mp.
31 motor coordination.mp.
32 1 or 2 or 3
33 4 or 5 or 6 or 7
34 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31
35 32 and 33 and 34

2.3. Search criteria

2.3.1. Inclusion criteria

1. Have a longitudinal cohort, cross-sectional, or clinical study design.
2. Assessed fine and gross infant motor milestone attainment (typically achieved between 3–24 months), motor skills, neuromotor development, or movement abnormalities.
3. Included infants aged 3–24 months (on average, if across a range).
4. Had a neurodevelopmental condition group with a diagnosis of a DSM-5 (or similar) "neurodevelopmental disorder" or schizophrenia, apart from an intellectual disability or specific learning disabilities, assessed by a gold-standard clinical tool or by own clinical assessment.
5. Included a control group (or provided an age of milestone attainment for the neurodevelopmental condition group).
6. Published in the English language.
7. Published in a peer-reviewed journal.

2.3.2. Exclusion criteria

1. Had a clinical group with a diagnosis of a learning disability.
2. Had a clinical group diagnosed with an additional neurodevelopmental or psychiatric disorder.
3. Review studies or meta-analyses.

Two reviewers (AB, TA) applied eligibility criteria and selected studies for inclusion. AB reviewed all abstracts and screened all records for inclusion, and TA checked these decisions in a random sample of 20 % of records. The researchers were blind to each other's decisions. Any disagreements were resolved by the two parties meeting and arriving at a consensus, which was reached for all cases.

2.4. Data extraction

Effect sizes and measures of variance for the primary outcome and moderator variables, in addition to supplementary data (for example, country of origin of the study), were extracted from studies where available (See Supplemental Table S3 for a complete list of extracted data). AB extracted the data using the Covidence online tool ('Covidence', 2021). CA conducted a blind data extraction on a random 20 % subset of studies. The percentage of agreement was calculated for the available data extracted for the meta-analysis. When there was insufficient data in a manuscript, contact was made with the authors to gain the data (as noted in Tables 2 and 3), or data were extracted from figures using WebPlotDigitizer, (2023), as noted in Tables 2 and 3). If data were still missing, it was noted as missing data (primary outcomes) or not reported (NR, Supplementary Data). If data was ambiguous, agreement was sought between AB and CA. For the neurodevelopmental condition group versus control milestone meta-analyses, there was the requirement for at least five effect sizes (across studies) for each milestone to be included; therefore, some data were extracted but not meta-analysed if an insufficient number of effect sizes was found (see Supplemental Methods for a discussion on power in meta-analyses). The systematic review of motor skills included motor-relevant findings that were not motor milestones and standardised motor scores that could be meta-analysed.

2.5. Quality assessment

Individual study quality was assessed using the checklist developed by Downs and Black (1998), which is considered a reliable tool (Sanderson et al., 2007). We made minor modifications in line with Filatova et al. (2017); see Supplemental Data 2 for the full items. AB conducted a quality assessment, and CA conducted a blind quality assessment on the same random 20 % subset of studies from the blind data extraction. Studies with ratings lower than 10 out of 17 will be classified as low quality.

2.6. Statistical synthesis and analysis

Before conducting the meta-analyses, we prepared the extracted means, standard deviations (SD), and other effect sizes. If convertible data for both groups was reported (for example, median and SE), a mean and SD were calculated. If no measure of variance was reported, the standardised mean differences (d) were calculated using the Practical Meta-Analysis Effect Size Calculator (Wilson, 2023) or the Estimating the Sample Mean and Standard Deviation Calculator (McGrath et al., 2020) when possible. If means or effect sizes were only given for subgroups *within* a neurodevelopmental condition diagnosis (for example, those with high and low IQ), average effect size and standard deviation were calculated as advised in the Cochrane Handbook (*Chapter 6*, 2023., p. 6).

We ran three 3-level random effects meta-analyses in the R package metafor (Viechtbauer, 2023) to account for dependency across effect sizes from the same study or cohort. The first level was sampling variance, the second was variance across outcomes within a cohort, and the third was variance across cohorts.

Data synthesis groups were based on data type (milestone or standardised measure) and if there was control milestone data. The first of the three meta-analyses was a meta-analysis of the standardised mean difference of month of milestone attainment between the neurodevelopmental condition and control group. Second, we ran a meta-analysis of the mean month of milestone attainment for the neurodevelopmental condition group. This analysis included studies that only reported the mean from the neurodevelopmental condition and not a control group, in addition to the neurodevelopmental condition group data of the studies that also reported control group means. Comparisons of 95 % confidence intervals were made between the pooled effect sizes and available World Health Organisation (WHO, Onis, 2006). Third, we conducted a meta-analysis of the standardised mean difference of standardised motor assessments between the neurodevelopmental

condition and control group.

Potential sources of heterogeneity were investigated with meta-regressions and subgroup analyses using the metafor R package. The following meta-regressions or subgroup analyses were conducted:

1. Neurodevelopmental condition group
2. Milestone (milestone meta-analysis only)
3. Test type (standardised motor meta-analysis only)
4. Study design (retrospective/prospective)
5. Age of measurement (standardised motor meta-analysis only)
6. Motor modality (standardised motor meta-analysis only)

Model comparison statistics (Bayesian information criterion, BIC; and Akaike information criterion, AIC) were used to test if there was an improvement in the model when there were three levels compared to one. Heterogeneity was assessed across levels. High heterogeneity was classified as 75 %, medium as 50 %, and low as 25 % (Borenstein et al., 2017). Differences in heterogeneity (I^2) across levels were assessed using the var.comp R function (Harrer et al., 2019). Effect sizes across neurodevelopmental conditions or milestones were compared using the "*anova*" function in Metafor, in which linear combinations of the coefficients in the model are tested using a Wald-type test (Viechtbauer, 2023).

Functions from the Metafor package were used to assess publication bias (Viechtbauer, 2023). Firstly, a funnel plot, which displays each effect estimate by its associated sample size, was created using the "*funnel*" function. Publication bias was evaluated by visually reviewing the funnel plot. Further, Egger's test of the regression intercept of the random effects analysis was used to calculate the amount of asymmetry in the funnel plot using the "*regtest*" function, a standard method measuring publication bias (Egger et al., 1997; Higgins et al., 2019). The extent of deviation from zero in the model's intercept of the regression line indicated the degree of asymmetry. If there was evidence of asymmetry, a trim and fill analysis was performed with the "*trimfill*" function. This analysis involved trimming off the asymmetric parts of the funnel plot and then estimating the new centre of the funnel plot. Once completed, the trimmed studies were replaced, and the estimated missing studies on the other side of the plot were assessed. The new mean and variance were then calculated and compared against the previous means and variances (Duval and Tweedie, 2000). Finally, cook's distance was used to assess influential cases (Cook, 1977).

2.6.1. Sensitivity analyses

Sensitivity analyses were used to see if conclusions still held when studies that did not conduct clinical assessments for diagnosis were excluded or if studies that included sample sizes less than 20 were excluded.

3. Results

3.1. Preliminary results

3.1.1. Included studies

Table 1 includes the systematic review results (30 studies), and Table 2 (23 studies) and Table 3 (14 studies) contain all studies included in the meta-analyses. There were no results for stereotypic movement disorder. Although DCD and tics come under the motor disorders classification in the DSM-5, they were treated as different neurodevelopmental conditions due to their distinct motor impairment profiles and their strong distinction in developmental research. Language disorders were included as a single condition due to differences in classification in the included studies, which weren't consistent with the present classifications used in the DSM-5. The PRISMA flow diagram can be found in Fig. 1 (also see Figs. S1–6 for PRISMA flow diagrams split by neurodevelopmental condition group). The studies that appear to meet the inclusion criteria but were excluded are listed in Supplemental Table S2, along with the explanation for exclusion.

3.1.2. Quality assessment

The range of total scores across all studies was 6–17, with a mode of 10.00 and a mean of 10.89 (Supplementary Data 2).

3.1.3. Agreement

The agreement for the data extraction was 80 %, and the quality assessment was 75 % (see Table S3).

3.2. Systematic review

The findings from the systematic review can be found in Table 1. In the 30 studies in the systematic review (4 of which were also included in the meta-analyses, and 14 originated from the USA), there were 40 relevant findings on infants across 3–24–month–olds, including those with autism, ADHD, schizophrenia, tics, and language disorders. Findings were divided into 16 topics (see Table S18 in the supplement for a table grouped by motor trait type and neurodevelopmental condition group).

Studies of infant motor skills in individuals who go on to gain diagnoses of autism (27 findings) tended to reveal the most consistent differences relative to controls, predominately revealing poorer motor skills than controls. However, many of these studies were rated low-quality or had small samples. The findings included greater motor difficulties in general and gross motor areas. These include head lag measured from a small-scale, rated as low-quality, study (N=27) of videos (Flanagan et al., 2012), greater clumsiness in a small, rated as low-quality, study (N=36) reporting differences in individual questionnaire items (Dewrang and Sandberg, 2010), more impairments in motor coordination compared to controls (Baranek et al., 2022), lower general motor skills at 24 months measured in a large-scale prospective study (Jeans et al., 2013). Further, there was evidence for motor developmental delay in autism up to 24 months (Kochav-Lev et al., 2023), more referrals for gross motor milestone delay (Gurevitz and Leisman, 2023), impaired gross motor skills at six months (LeBarton and Landa, 2019), and lower longitudinal trajectories of gross motor skills from 6 to 36 months compared to controls (Patterson et al., 2022). Additionally, impairments were found in autism compared to control groups for posture (at 6, 9, and 12 months, Nickel et al., 2013), and gait (observed at 20 months, Esposito and Venuti, 2008). Further, in children who went on to gain autism diagnoses, compared to those who did not, parents reported more general motor concerns at two years (Sacrey et al., 2015).

Moreover, in relation to later diagnoses of autism, fine motor impairments were additionally revealed for fine motor skills in a small study (N=20) of reach-to-grasp movements (Sacrey et al., 2018), a larger study (N=71) of motor subscales (Dewrang and Sandberg, 2010), and in a bubble-popping tablet game (Perochon et al., 2023), where performance was more variable and less accurate. Furthermore, those who went on to gain diagnoses of autism had lower longitudinal trajectories indicating poorer fine motor skills (Patterson et al., 2022). Two studies also found decreased performance in autism compared to control participants in imitating motor skills, movement imitation at 18 months (Dewrang and Sandberg, 2010), and motor symmetry whilst sitting in a small study (N=24) of home videos (Esposito and Venuti, 2009). Additionally, greater motor activity was found for the autism group compared to controls at 18 and 24 months (Reetzke et al., 2022). Lastly, altered developmental trajectories of motor skills were found for autism compared to controls (Landa et al., 2012).

Alternatively, there were multiple findings of no motor impairments in individuals who go on to gain diagnoses of autism. Firstly, although rated as low-quality, one study examined clinical motor difficulties and did not find evidence of differences across the autistic, control and "mildly learning disabled" groups (M. H. Johnson et al., 1992). Similarly, individual studies reported no autism compared to control differences in

Table 1
Studies included in the systematic review.

Study	NDC	Country	Cohort	Design	Age(s) (m)	Sample Size		*n* Female		Motor Assessment	Outcome Detail
						NDC	Control	NDC	Control		
Baranek (2022)	Autism	USA	NA	P	Total sample 12	72	1904	Total sample 1123	Total sample 1123	**General Motor Skills** Motor coordination & milestones (MCM) subscale of the First Years Inventory (3.1), parent-report - frequency of behaviours on a 5-point Likert scale- higher scores indicated higher features or difficulties. Items: put sounds together, use consonants, walk, pincer grasp on small objects, body stuck in position, switch object from hand to hand, blowing raspberries	Autism group had higher MCM scores than the control group • Mean difference: autism/control - 0.73 SD (0.10), **p < 0.001**
Bradshaw (2023)	Autism	USA	NA	P	1–6 m	20	40	NR	NR	**Gross Neurological** Pull-to-sit - assessment of motor and neurological functioning (the NNNS) administered monthly at 1–6 months. Evaluates response to being pulled from a supine to sitting position: increase in shoulder and body tone, muscular resistance to stretching the neck, lower musculature and attempts at righting the head when in an upright position. Scored on a scale of 1–9. Latent growth curve models used to compare trajectories of pull-to-sit skills	Higher proportion of infants later diagnosed with autism demonstrated greater head lag in pull-to-sit at 4 months or later compared with and typically developing infants • Autism – 74 %, control 44 %, $X^2 = 4.65$, **p =.049** Pull-to-sit trajectories did not differ in infants with ASD compared with typically developing infants
Comings and Comings (1987)	Tic	USA	NA	R	NA	347	47	NR	NR	**Toe Walking**	No significant group differences in the presence of toe walking in childhood
Dewrang (2010)	Autism	Sweden	NA	R	18	23	13	4	7	Movement Imitation Clumsiness Fine Motor Gross Motor Five items on movements and motor skills from the Symptoms of Autism Before Age 2 scale (SAB−2; Dahlgren and Gillberg, 1989)	Autistic group, compared to controls, had: • More difficulties imitating movements, F= 30.43, ***p*<.001** • Was more clumsy and ill-coordinated, F= 19.63, ***p*<.001** No significant group differences for: • Would point to objects with the whole of his/her hand, F= 0.21, *p*=ns • His/her movements were agile and graceful: F= 0.01, *p*= ns • Once s/he started to walk, s/he did it perfectly at once: F-value: 0.01, *p*= ns
Esposito and Venuti (2008)	Autism	Italy	ODFLab	R	20	16	16	0	0	**Gait** Walking Observation Scale (Esposito and Venuti, 2004). 11 items in 3 categories: foot movements, arm movements, global movements.	• Significant differences across all groups (autistic, mental retardation, typical development): F (2,43)= 21.01, ***p*< 0.001,** n^2=.22) Tukey post hoc comparisons: • Autistic group greater severity of disturbance than controls (no *p* value given)
Esposito and Venuti (2009)	Autism	Italy	ODFLab	R	NA	10—12	10—12	NR	NR	**Motor Symmetry** symmetry for sitting or standing positions assessed by retrospective home videos where random still images were taken and coded by blind coders	Sitting: • The level of symmetry showed significant differences among the groups (F(2,30)= 4.12**, *p*< 0.05)**

(*continued on next page*)

Table 1 (*continued*)

Study	NDC	Country	Cohort	Design	Age(s) (m)	Sample Size		*n* Female		Motor Assessment	Outcome Detail
						NDC	Control	NDC	Control		
											• KMeans cluster analysis: All participants in the lower level of symmetry cluster belonged to the autistic group Standing • the level of symmetry showed no significant group differences
Flanagan et al. (2012)	Autism	USA	NA	P	6—36	10	17	0	5	**Head Lag** Archived videos of the pull-to-sit task from the gross motor scale of the Mullen Scales of Early Learning (Mullen, 1995) coded for head lag in all children	More infants later diagnosed with autism exhibited head lag than infants without diagnoses of autism (no risk and social/comm delay, Fisher's exact test, ***p*= .02**)
Gurevitz and Leisman (2023)	Autism	Israel	MHO	R	NR	1105	1105	189	189	**General Motor Skills** Referral for motor milestone delay to Child Development Centre. OR association with autism, and multivariate logistic regression analysis for association of motor referral, and other variables, with later autism diagnosis	• 72 (6.5 %) control, 406 (36.7 %) autism referred for motor milestone delay • OR 8.33, 95 % C (6.30–10.89), **p <0.001** Multivariate model: • Diagnosis of motor delay associated with autism- B = 2.04 95 % CI (5.60, 10.45), SE(0.16), **p<0.001**
Isohanni et al. (2001)	Schiz	Finland	NFBC	P	12	100	10457	35	5184	**Gross Neurological** Public health nurses and GPs judged deviations in movements in posture, abnormal muscle tone, or other neurological symptoms (yes vs no)	Percent of Schizophrenia group identified as having some form of developmental deviance in at least one domain: • 4.6 %. x^2= 10.66(1), ***p*< 0.01**
Jaspers et al. (2013)	ADHD	Neth	TRAILS	P	1—15	419	1245	166	702	**Gross Motor** **Fine Motor** Van Wiechen Scheme: GM and FM subscales. If problem present, coded as "yes" or "no" if not.	Gross motor skills: • Higher scores associated with ADHD: OR:0.73, 95 % CI(0.61,0.88), *p* value not provided Fine motor skills: • No significant association with ADHD– OR: 0.88, 95 % CI(0.56,1.38), *p*= ns
Jeans et al. (2013)	Autism	USA	ECLS-B	P	9,24	100 (rounded)	7700 (rounded)	30	3927	**General Motor Skills** Motor Index Score (GM and FM composite) of the Bayley Short Form–Research Edition (BSF-R; Bayley, 1993)	Significantly lower motor score compared to controls at 24 m, but not 9 m: • 9 m: β= -0.01, SE= 0.30, *p*=.982 • 24 m: β= −1.13, SE= 0.15, ***p*<.0001**, OR= 0.32, 95 % CI(0.24, 0.44)
Johnson et al. (1992)	Autism	UK	NA	R	6, 12, 18	7—10	3—19	NR	N R	**Clinical Motor Difficulties** One or more clinical motor problems from screening test records coded as (1) referral to a specialist, (2) a note made to re-check a test, (3) a note made that the infant appeared unusual in a particular respect.	Comparisons across autistic, mildly learning disabled and control groups: • No significant group differences at 6 months • 12 months not tested • 18 months – Significant differences across all groups(x^2= 5–97, *p*= **0.051**): autism, 2/7; control, 0/11; mildly learning disabled, 7/17
Johnson et al. (2014)	ADHD	UK	ALSPAC	P	12	16	120	2	38	**Motor Activity** Thirteen motion summaries were created to determine robust indices of general motor activity, summarizing speed, acceleration, variability of speed and acceleration, periodicity, and restlessness.	No significant association between the motion variables measured at age 12 months and diagnosis of ADHD at age 7 years
Kochav-Lev et al. (2023)	Autism	Israel	MHS	R	Before 24	1821	238478	NR	NR	**General Motor Skills** Early childhood motor developmental delay (MDD) – defined as having at least one recorded developmental physiotherapy visit before the age of 2 years	Association between MDD and ASD: • OR 4.1 (95 % CI 3.6, 4.6)

(*continued on next page*)

Table 1 (*continued*)

Study	NDC	Country	Cohort	Design	Age(s) (m)	Sample Size		*n* Female		Motor Assessment	Outcome Detail
						NDC	Control	NDC	Control		
Landa and Garrett-Mayer (2006)	Autism	USA	NA	P	6, 14, 18, 24 (+30,36)	23	53	NR	NR	**Trajectories of motor development** Longitudinal modelling of Mullen fine and gross motor scores	Fine and gross motor: • No significant group differences at 6 months. • Autistic group had poorer motor skills than controls at 14 months through to 24 months
	Lang					11					Fine motor: • Language group showed poorer motor skills than controls at 6–14 months, • 18–24 months - no significant group differences Gross motor: • No significant difference between groups
Landa et al. (2012)	Autism	USA	NA	P	6, 14, 18, 24 (+ 30, 36)	52	121	9	68	**Trajectories of motor development** Latent class growth model membership for subscales of the Mullen Scales of Early Learning (Mullen, 1995) was related to diagnostic outcome at 36 months	Six classes: 1, accelerated; 2, normative; 3, language/motor delay; 4, developmental slowing • Not-autistic group primarily in class 1 and 2 • Autistic group: Spread across classes 2, 3, and 4 • Class 4 almost entirely included autistic individuals • Class 4 contained a higher proportion of autistic children than either class 1, 2, or 3 (***p's* < 0.001**)
LeBarton and Landa, (2019)	Autism	USA	NA	P	6	20	51	8	24	Fine Motor Gross Motor Visual-Motor Integration Peabody Developmental Motor Scales - 2 (PDMS−2; Folio and Fewell, 2000)	Poorer motor skills predicted autism diagnosis at 24–36 m in: • Stationary (gross motor, Chi-square= 7.756, ***p*= .021**; R^2=.060) • Grasping (fine motor, Chi-square= 6.286, ***p*= .043**; $R^{2=}$.05) Motor skills did not predict autism diagnosis at 24–36 m in: • Visual-Motor Integration (Chi-square= 4.958, *p*=.084)
Marin-Mendez et al. (2017)	ADHD (Trait measure)	Spain	NA	R	0—36	NR	Total sample 1426	NR	Total sample 719	**Fine and Gross Motor** Parental questionnaire about the presence of problems in FM and GM (and other areas)	Group differences: • Gross motor: *p*= ns Fine motor: • ADHD group more differences than controls, ***p*< 0.05**
Nickel et al. (2013)	Autism	USA	NA	P	6, 9, 12, 14	4	18	1	10	**Posture** Infants were videotaped at home during everyday activities and play. All infant postures were coded and classified as to whether they were infant-initiated.	Mann-Whitney U tests - 6, 9, and 12 months, but not 14 months, autistic infants' posture repertoires were significantly smaller than those of infants in the HR and LR groups combined: • 6 m, U= 8, ***p*= .004** • 9 m, U= 21, ***p*= .023** • 12 m, U= 18.5, ***p*=.014** • 14 m, *p*= ns
Nishimura et al. (2019)	Autism	Japan	HBC	P	1, 4, 6, 10, 14, 18, 24	32	1120	NR	NR	**Trajectories of motor development** MSEL (GM, FM, Expressive Lang, Receptive Lang, Visual Reception). Parallel process latent class growth analysis (across all ages) distinguished distinct trajectory groups based on scores of five MSEL domains. Markedly Delayed latent class was associated with early marked delays in motor domains then somewhat later delays in language domains.	Probability of autism diagnosis at 32 months according to latent classes: • High Normal: 0 % autistic, 100 % Not autistic, *n*=110 • Normal: 0 % autistic, 100 % Not autistic, *n*= 468 • Low Normal: 4.0 % autistic, 96.0 % Not autistic, *n*=202 • Delayed: 6.4 % autistic, 93.6 % Not autistic, *n*=134

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Table 1 (*continued*)

Study	NDC	Country	Cohort	Design	Age(s) (m)	Sample Size		*n* Female		Motor Assessment	Outcome Detail
						NDC	Control	NDC	Control		
											• Markedly Delayed: 32.6 % autistic, 67.4 % Not autistic, *n*=38
Ozonoff et al. (2008)	Autism (Autism: No, Autism: Reg*	USA	NA	R	9—12	26+28	24	1+5	12	**Gross Neurological** Groups split depending on regression in language or social interest or engagement (ADI-R). Movement Abnormalities and Protective Responses: coded from home videos	No significant differences between groups
Patterson et al. (2022)	Autism	Canada	CISS	P	Gross Motor:6 −36 m Fine Motor: 6–24 m	137	176	NR	NR	**Fine Motor** **Gross Motor** Mullen Scales of Early Learning: Fine and Gross motor. Group-based trajectory modelling (GBTM) using latent class mixed modelling. Linear and quadratic polynomials for gross motor scores, and linear, quadratic, and cubic polynomials for fine motor scores. Cramer's V calculated for the strength of association.	Fine Motor -autism group overrepresented in lower trajectory groups • Group 1 (75.6 % autism) low and stable trajectory, with low mean scores at 24 months; Group 2 (25.1 % autism) mid-level stable trajectory, mid-level mean scores from 12 to 24 m; Group 3 (10.6 % autism) less steep incline to group 4–12 m; Group 4 (5.0 % autism) • Diagnosis associated with trajectory membership ($\chi^2 = 153.29$, **p < 0.001**, moderate association; Cramer's V = 0.34) Gross Motor -autism group overrepresented in lower trajectory groups • Group 1 (38.0 % autism) low and stable trajectory, low mean scores from 6 to 24 m; Group 2 (20.0 % autism) mid-range stable trajectory, moderate mean scores from 6 to 24 m; Group 3 (26.3% autism) peak decelerate trajectory pattern; Group 4 (14.9 % autism) high and stable trajectory; high mean scores at 12 m and 24 m. • Diagnostic category associated with group trajectory membership ($\chi^2 = 15.40$, **p < 0.05**), weak association (Cramer's V = 0.11).
Perochon et al. (2023)	Autism	USA	NA	CS	Total sample 24	23	128	Total sample 37.5	Total sample 37.5	**Fine Motor** Tablet-based motor skills - pop the bubble game: infants popped bubbles presented for 20 seconds on an iPad screen. Measures extracted: 1. number of touches; 2. number of pops; 3. bubble popping rate; 4. double touch rate; 5. screen exploratory percentage; 6. number of targeted bubbles;7. number of transitions; 8. repeat percentage; 9. mean/ median/standard deviation touch duration Group comparison ANCOVAs. Benjamini–Hochberg correction. covariates: Age and IQ Logistic regression - performance motor features predict group membership in AUC.	Autism group, compared to controls were slower and more variable. • Lower bubble-popping rate (F(1, 148) = 15.14, **p <.001**, $\eta^2 = 0.09$) • Larger median distance to the centre (mm) (F (1148) = 20.14, p = 1.7e–4, $\eta^2 = 0.12$) • Longer average touch length (,F(1, 148) = 23.56, p **<.001**, $\eta^2 = 0.14$) • Greater variability in touch length (F(1, 148) = 32,70, p **<.001**, $\eta^2 = 0.18$) • More time to pop a targeted bubble (F(1, 148) = 18.56, p **<.001**, $\eta^2 = 0.11$). • The AUC using three-motor features - 0.73 (95 % CI, 0.63–0.83
Reetzke et al. (2022)	ADHD	USA	NA	P	12, 18, 24, (+36)	17	77	6	41	**Motor Activity** Continuous motion-based activity was recorded using tri-axial accelerometers. Two dependent variables of activity level were derived: Mean activity (MA) and mean	Significantly higher MA and MI compared to the control group from 18 m: • 12 m MA: *p*= 0.40, d= -0.03, MI: *p*= 0.37, d= -0.04

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Table 1 (*continued*)

Study	NDC	Country	Cohort	Design	Age(s) (m)	Sample Size		*n* Female		Motor Assessment	Outcome Detail
						NDC	Control	NDC	Control		
										intensity (MI). Estimates were derived using linear contrasts from linear mixed-effects models with fixed effects for outcome group (ADHD, autism, control), linear, age, and interactions between variables. Pairwise comparisons.	• 18 m - MA: p= **0.047**, d= 1.04, MI: p= **0.03**, d= 0.91 • 24 m - MA: p= **0.03**, d= 1,42, MI: ***p***= **0.02**, d= 1.06 • Fixed effects for ADHD groups were significant, indicating greater MA and MI than TD group across age (18–36 m)
	Autism					19		8			Significantly higher MA and MI compared to the TD group from 18 m: • 12 m MA: p= 0.63., d= 0.38, MI: p= 0.76., d= 0.38 • 18 m: MA: ***p*< 0.001,** d= −0.52, MI: ***p*= 0.001**, d= −0.37 • 24 m: MA: ***p*< 0.001**., d= −0.81, MI: ***p*< 0.001**, d= −0.44 Fixed effects for autistic groups were significant, indicating greater MA and MI than TD group across age (18–36 m)
Rosso et al. (2000)	Autism	USA	NCPP	P	8	19	5415	8	3955	**Gross Neurological** Unusual movements—derived from standardised psychological and neurological examinations	Significantly higher MA and MI compared to the TD group from 18 m: • 12 m MA: p= 0.63., d= 0.38, MI: p= 0.76., d= 0.38 • 18 m: MA: ***p*< 0.001,** d= −0.52, MI: ***p*= 0.001**, d= −0.37 • 24 m: MA: ***p*< 0.001**., d= −0.81, MI: ***p*< 0.001**, d= −0.44 • Fixed effects for autistic groups were significant, indicating greater MA and MI than TD group across age (18–36 m)
Sacrey et al. (2015)	Autism	Canada	NA	P	6, 9,12, 15, 18, 24 (+36)	62	69	14	28	**Parental Motor Concerns** Interview to collect information about parent concerns during the first 2 years: "Are there any current concerns about motor development?" Yes/no	Percentage of reported concerns for motor skills compared between groups: • Group effect: more concerns in the autism group than controls (F^2,1196 • 40.1, ***p*< 0.001**) • Effect significant at all time points between 6 and 24, p **< 0.05**
Sacrey et al. (2018)	Autism	Canada	GRH	Ret	6, 9, 12, 15, 18, 24 (+36)	10	10	4	3	**Fine Motor** Reach-to-grasp movement was measured using the qualitative Skilled Reaching Rating Scale to determine the presence of any group-related differences in the mechanics of the reach-to-grasp movement.	Autistic group performed worse compared to children in the LR and HR not autistic groups (Benjamini and Hochberg corrections for multiple comparisons; q, adjusted alpha for posthoc comparisons): • Reach-to-grasp movement, ***q*< .033**, d= 0.74 • Orient, ***q*< 0.033,** d= 0.47 • Lift, ***q*< 0.017,** (d not reported) • Pronation, ***q*< 0.033**, d= 0.66 No significant group differences: • Advance and grasp, p= ns
Tobarra-Sanchez et al. (2022)	ADHD	UK	ALSPAC	P	18	174	7947	27	27	**Fine motor** **Gross Motor** Denver Developmental Screening Test. 16 fine motor and 12 gross motor skills rated on a three-point scale (0 = not	Fine motor -ADHD diagnosis associated with fine motor delay • OR 1.89, 95 % CI(1.29, 2.77), **p <.001**

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Table 1 (*continued*)

Study	NDC	Country	Cohort	Design	Age(s) (m)	Sample Size		*n* Female		Motor Assessment	Outcome Detail
						NDC	Control	NDC	Control		
										yet started, 1 = once or twice, 2 = yes, can do well). Dichotomous variable created for each score with motor skills >1 SD below the mean, indicating the presence or absence of motor delays.	• Adjusted for sex and SES - OR 1.84, 95 % CI (1.21, 2.79), **p= 0.004** • Motor score not a predictor of ADHD diagnosis in multivariate model (with ADHD PRS, vocabulary, grammar, activity; OR 1.36, 95 % CI (0.75, 2.48) p=.305) Gross motor -ADHD diagnosis associated with gross motor delay once covariates controlled for • OR −1.54, 95 % CI(0.99, 2.38), p =0.52 • Adjusted for sex and SES OR 1.78, 95 % CI (1.11, 2.87), **p= 0.016**
Uljarevic et al. (2017)	Autism	Aus	WAABR	R	NR	147	NA	28	NA	**Toe Walking** Parental questionnaire: Early developmental milestones questionnaire - Presence of toe walking	Percentage toe walked: • 51 % of children never toe walked • 33.8 % child toe walked in the past but no longer does • 15.2 % child currently toe-walks
Walker et al. (1994)	Schiz or MAD	USA	AOP	R	0—24	23/30	15/21	7/30	14/21	**General Motor Skills** home videos coded by examiners for the presence of skills: Mean rating from crawling, grasping, head control, manual manipulation, sitting, walking	• No significant group differences (F=1.24(5,70), *p*= 0.30)

Note: All studies were included in the systematic review and their associated findings. *, two autism subgroups: Autism: No, no language regression, Autism: Reg, language regression; LR, no family history of autism; HR, have an older biological sibling diagnosed with autism; NDC, neurodevelopmental condition; P, prospective; R, retrospective; Schiz, Schizophrenia; DCD, developmental coordination disorder; ADHD, attention deficit hyperactivity disorder; MAD, major affective disorder; SAD, schizoaffective disorder; USA, United States of America; Neth, Netherlands; UK, United Kingdom; Den, Denmark; Aus, Australia; NFBC, NCPP, Philadelphia National Collaborative Perinatal Project; Northern Finland Birth Cohort; WAABR, Western Australian Autism Biological Registry; AOP, Archival-Observational Project; PLD, Perm Longitudinal Database; ODFLab, Observational and Functional Diagnosis Lab; TRAILS, The TRacking Adolescents' Individual Lives Survey; ECLS-B, Early Childhood Longitudinal Study–Birth Cohort; ALSPAC, Avon Longitudinal Study of Parents and Children; GRH, Autism Research Centre at the Glenrose Rehabilitation Hospital; HBC, Hamamatsu Birth Cohort for Mothers and Children; MHS, Meuhedet Health Services; MHO, Maccabi Health Organization; CISS, Canadian Infant Sibling Study; NA, not applicable; NR, not reported; +, sample sizes across subgroups; -, range of sample size across measures or ages; /, n out of total sample (not subsample for the measure); FM, fine motor; GM, gross motor; OR, odds ratio.

Table 2
Studies included in the milestone meta-analyses.

Study	NDC Group	Country	Cohort	Design	DG	Sample Size		*n* Female		Milestones Measured
						NDC	Control	NDC	Control	
Studies included in neurodevelopmental condition versus control standardised mean difference meta-analysis										
Comings and Comings(1987)	Tic	USA	NA	R	clinical	347	47	NR	NR	walking unaided
Farran et al., (2020)	ADHD	UK	NA	R	parental report and traits	13–16 + 13–19	27–32	9	9	walking unaided, sitting unaided, standing unaided, holding head up
Jones et al., (1994)[d]	Schiz	UK	NSHD	R	clinical	30	4716	10	2259	walking unaided
Keskinen et al., (2015)	Schiz	Finland	NFBC	R	clinical	152	10131	NR	NR	walking unaided, sitting unaided, standing unaided, hold head up
Lavenne-Collot et al., (2021)	Autism	France	NA	R	clinical	79	100	30+6	54	walking unaided, sitting unaided, hold head up
Lee et al., (2021)	DCD	UK	NA	R	parental report and traits	23–50	17–29	13	16	walking unaided, sitting unaided, standing unaided, hold head up, roll back to front, crawling
	ADHD					34–61 + 2–7		13		
Manicolo et al., (2019)	Autism	Switz	NA	R	clinical	32	36	5	5	walking unaided, sitting unaided
Ozonoff et al., 2008	Autism	USA	NA	R	clinical	26+28	24	6	12	walking unaided, sitting unaided, rolling, crawling
Sorensen et al., (2010)	Schiz	Denmark	CPC	R	clinical	92	4982	44	2444	walking unaided, sitting unaided, standing unaided, holding head up, roll back to front, crawling
Sumner et al., (2016)[a]	DCD	UK	NA	R	clinical	28	33	9	9	walking unaided, sitting unaided, crawling
	Autism		NA		parental report and traits	28		5		
West(2019)	Autism	USA	NA	P	clinical	15	25	4	10	walking unaided
West et al. (2023)[b]	Autism	USA	NA	P	clinical	15	25	4	15	walking unaided
Additional studies included in the meta-analysis of mean age (no control mean)										
Arabameri and Sotoodeh (2015)[a]	Autism	Tehran	NA	R	clinical	88	NA	18	NA	standing unaided, sitting unaided, standing
Bishop et al., (2016)	Autism	USA	NA	R	clinical	903	NA	NR	NA	walking unaided
Chawarska et al., (2007)	Autism	USA	NA	R	clinical	51	NA	NR	NA	walking unaided
Havdahl et al., (2021)[c]	Autism	Norway	MOBA	P	clinical	148+ 64	NA	22	NA	walking unaided
Ketcheson et al., (2020)	Autism	USA	SPARK	R	clinical	13182	NA	NR	NA	walking unaided, sitting unaided, crawling
Kim (2008)	Autism	USA	NA	R	clinical	32	NA	6	NA	walking unaided, crawling
Lloyd et al., (2013)	Autism	USA	NA	R	clinical	162	NA	22	NA	walking unaided, sitting unaided
Matson et al., (2010)	Autism	USA	NA	R	clinical	331	NA	85	NA	walking unaided, crawling
Reindal et al., (2020)	Autism	Norway	BUPgen	R	clinical	376	NA	84	NA	walking unaided
Uljarevic et al., (2017)	Autism	Aus	WAABR	R	clinical	147	NA	28	NA	walking unaided, sitting unaided, standing unaided, crawling
Wang et al., (2023)	Autism	China	NA	P	clinical	151	NA	24	NA	walking unaided

Note: All studies were included in the meta-analysis of mean age (only the NDC group mean was included for studies with a control group mean); NDC, neurodevelopmental condition; P, prospective; R, retrospective; DG, diagnosis method; [a], data extracted from figure; [b], data retrieved from contacting authors; [c], means converted from medians and interquartile ranges; [d], NDC group Cohen's d converted from mode and p-value and thus not included in the meta-analysis of mean age; DG, diagnosis; Schiz, Schizophrenia; DCD, developmental coordination disorder; ADHD, attention deficit hyperactivity disorder; USA, United States of America; UK, United Kingdom; Switz, Switzerland; Aus, Australia; NSHD, Medical Research Council National Survey of Health and Development; CPC, Copenhagen Perinatal Cohort; NFBC, Northern Finland Birth Cohort; WAABR, Western Australian Autism Biological Registry; MOBA, Norwegian Mother, Father and Child Cohort Study; SPARK, Simons Foundation Powering Autism Research; CD confirmed diagnosis; PR, parental report of diagnosis; T, traits; NA, not applicable; NR, not reported; +, sample sizes across subgroups; -, range of sample size across measures or ages.

Table 3
Studies included in the standardised assessment of motor scores meta-analyses.

Study	NDC Group	Country	Cohort	Design	Sample Size		*n* Female		Age(s) (m)	Motor Measure	Outcome Measure
					NDC	Control	NDC	Control			
Choi et al. (2018)	Autism	USA	NA	P	30	67	9	31	6, 9, 12, 24	Mullen	FM, GM
Estes et al. (2015)	Autism	USA	IBIS	NR	49	98	8	43	6, 12, 24	Mullen, VABS	FM, GM
Foster (2023)	Autism	USA	NA	P	20	40	5	18	24	Mullen	FM
Iverson et al. (2019)	Autism	USA	BSRC	P	69	188	20	81	6	Mullen	FM, GM
James et al. (2023)	Autism	USA	NA	CS	269	44	NR	NR	24	Mullen, VABS	FM
Landa and Garrett-Mayer (2006)	Lang Autism	USA	NA	P	11 23	53	NR NR	NR	6, 14, 24	Mullen	FM, GM
Leonard et al. (2014)	Autism	UK	BASIS	NR	17	24	6	17	7, 14, 24	Mullen, VABS	FM, GM
Leonard et al. (2015)	Autism	UK	BASIS	NR	17	48	6	31	7	Mullen	GM
Libertus et al. (2014)	Autism	USA	NA	NR	22	22	5	13	6	Mullen	FM, GM
Li et al. (2023)	Autism	UK	BASIS	P	46	137	NR	NR	10, 14, 24	VABS	FM, GM
Ozonoff et al. (2014)[b]	Autism	USA	NA	NR	51	116	8	53	6, 12, 18, 24, (and 36)	Mullen	FM
Pecukonis et al. (2022)	Autism	USA	BSRC	P	114	248	34	116	12	Mullen	FM
Pusponegoro et al. (2016)	Autism	Inds	NA	CS	40	40	8	20	12–24	VABS	GM
St John et al. (2016)	Autism	USA	NA	NR	23–19	50–49	6–5	21–25	12,24	Mullen	FM, GM

Note: NDC, [b], data from communication with authors; NDC, neurodevelopmental condition; Lang, language and communication disorders; USA, United States of America; UK, United Kingdom; Inds, Indonesia; BASIS, The British Autism Study of Infant Siblings; IBIS, The Infant Brain Imaging Study; BSRC, Baby Siblings Research Consortium; NA, not applicable; NR, not reported; CS, cross-sectional; P, prospective; R, retrospective; -, range of sample size across measures or ages; ASQ, Ages and Stage Questionnaire; Mullen, Mullen Scales of Early Learning; VABS, Vineland Adaptive Behavior Scales; FM, fine motor; GM, gross motor.

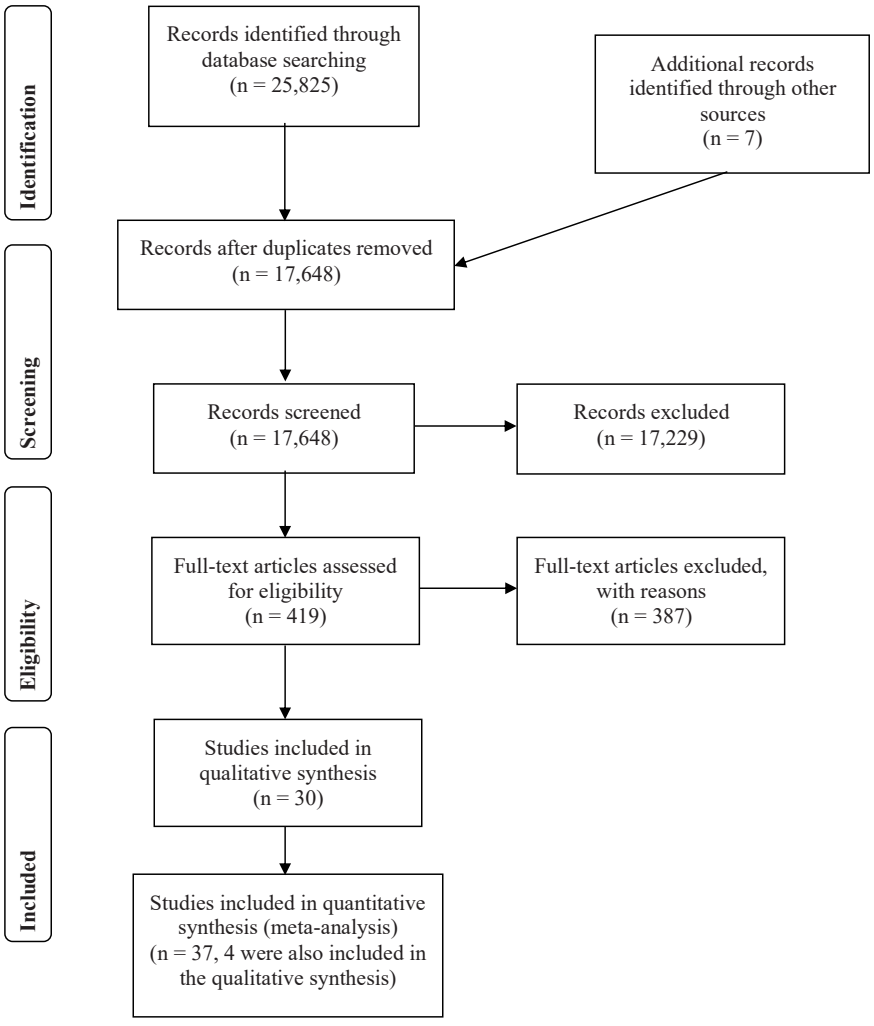

Fig. 1. PRISMA flow diagram

Table 4
Neurodevelopmental condition versus control meta-analysis of motor milestone attainment.

Domain	k^{est}	g (95 % CI)	*p*	Q (df)	p_Q	I^2 L2	I^2 L3
Hold Head up	5	0.21 (0.05, 0.37)	**0.012**	5.27 (4)	0.261	0.00	32.69
Rolling	13	0.23 (−0.15, 0.60)	0.240	10.56 (3)	**0.014**	72.20	0.70
Sitting Unaided	9	0.28 (0.10, 0.47)	**0.003**	16.25 (8)	**0.039**	20.31	32.62
Crawling	6	0.19 (0.02, 0.37)	**0.030**	3.58 (5)	0.611	0.00	12.48
Standing Unaided	5	0.35 (0.11, 0.60)	**0.005**	9.70 (4)	**0.046**	68.39	0.00
Walking Unaided	14	0.71 (0.48, 0.95)	**<0.001**	57.42 (13)	**<0.001**	0.00	79.80

Note. Higher Hedges g refers to late attainment compared to the control group. k^{est}, number of effect sizes; Q, Test for Residual Heterogeneity; I^2 L2, % of total variance accounted for by variation within samples/cohorts; I^2 L3, % of total variance accounted for by variation between samples/cohorts; p_Q refers to the significance test of the heterogeneity statistic (Q).

pointing at 18 months (fine motor, Dewrang and Sandberg, 2010), precision in the initiation of walking (gross motor, Ozonoff et al., 2008), gross neurological skills at 9–12 months (Ozonoff et al., 2008), motor activity at 12 months (Reetzke et al., 2022), motor symmetry for standing (Esposito and Venuti, 2009), or visual motor integration at six months (LeBarton and Landa, 2019).

For ADHD (7 findings), there was mixed evidence for motor differences. For fine motor skills, one large (*N*=1426) study reported evidence of an association of retrospective parental concerns of a fine motor impairment with ADHD traits (Marin-Mendez et al., 2017) and fine motor delays were associated with ADHD diagnosis at 18 months (Tobarra-Sanchez et al., 2022). However, another large (*N*= 1664) study found no significant group differences in general fine motor skills measured at 1–15 m between ADHD and controls (Jaspers et al., 2013). Further, two studies found evidence for later (18 and 24 months) but not early (12 months) increased activity levels in ADHD cases compared to controls (P. Johnson et al., 2014; Reetzke et al., 2022). In contrast to the findings for autism, one study reported evidence of superior gross motor skills compared to controls, although this study was rated as low-quality (Jaspers et al., 2013). Furthermore, ADHD diagnosis was only associated with gross motor delay at 18 months when SES and sex were controlled for (Tobarra-Sanchez et al., 2022).

For schizophrenia (4 findings), there was mixed evidence of impairment in motor skills. One study found evidence for more head lag in the pull-to-sit position in the later-daignosed schizophrenia group compared to controls (Bradshaw et al., 2023). However, a respective home video study found no evidence of impaired general motor skills compared to controls across 0–24 months (Walker et al., 1994). For gross neurological skills, there were no statistically significant differences at eight months (Rosso et al., 2000), and only a small subset (4.6 %) of the schizophrenia group (*N*=100) were identified as having gross neurological deviance at 12 months (Isohanni et al., 2001).

For tic disorders (1 finding), there was only one finding from a study rated as low-quality that found no significant group differences in early toe walking (Comings and Comings, 1987).

For language disorders (1 finding), a small longitudinal modelling study (*N*=64) found impairments in fine motor skills across 6–14 months compared to controls, but no differences compared to controls at 18 and 24 months. No gross motor skills impairments were found across 6–24 months (Landa and Garrett-Mayer, 2006).

3.3. Meta-analyses

3.3.1. Neurodevelopmental condition group-control meta-analysis of motor milestone attainment

The meta-analysis of milestone attainment between cases and controls (K_{est}= 43) revealed significantly delayed motor milestone attainment for the neurodevelopmental condition groups compared to controls (g= 0.53, 95 % CI[0.30, 0.76], *p*< 0.001, Figure S7) with significant heterogeneity Q(42)= 190.78, p< 0.001. To understand the source of the significant heterogeneity, we looked at the heterogeneity across levels, which suggested the source of heterogeneity was mainly from differences between study cohorts (I^2 Level 2= 24.54 %, I^2 Level 3= 61.76 %). Model comparison statistics revealed a larger BIC and AIC for the more parsimonious model (removing level 3, Table S4), suggesting that the results were not homogenous across levels. The likelihood ratio test comparing the models was significant (*p*= 0.046, Table S4). The results were thus reported from the three-level model. Inspection of the funnel plot (Figure S8) and Egger's test of funnel plot asymmetry (z= 0.43, p= 0.667) suggested no evidence of asymmetry or publication bias.

Moderation and subgroup analyses were conducted to investigate the sources of the heterogeneity in effects of delayed motor milestone attainment for the neurodevelopmental condition groups compared to controls. Milestone type moderated the effect of delayed motor milestone attainment for the neurodevelopmental condition groups compared to controls (Q(5)= 19.49, *p*= 0.002). Subgroup analyses revealed delays in holding the head up, sitting, standing, crawling and walking, but not rolling (see Table 4 for the model results, Table S5 for model comparison statistics, Fig. 2 for a spider plot, Figure S7 for the forest plot). Comparing across milestones, only walking unaided had a significantly larger neurodevelopmental condition group/control difference compared to the other milestones (hold head up, *p*= 0.001; rolling, *p*= 0.001; sitting unaided, *p*= 0.004; crawling, *p*= 0.002; standing unaided, *p*= 0.026).

The neurodevelopmental condition group also moderated the effect (Q(4)= 17.65, *p*= 0.001, Fig. 3). Tics (k^{est}=1) had significantly later motor milestone attainment than all other neurodevelopmental conditions (ADHD, *p*= 0.01; DCD, *p*= 0.039; Autism, *p*= 0.019;

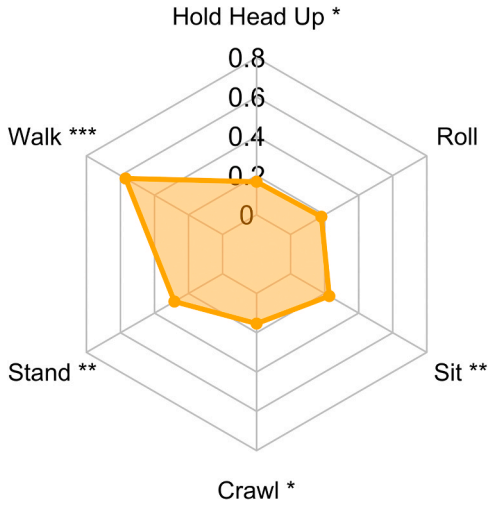

Fig. 2. Spider plot of multilevel random effects model for standardised mean difference in motor milestone attainment between neurodevelopmental condition groups with milestone type subgroups. *Note*, Meta-analysis of the standardised mean difference in age of attainment of motor milestones between neurodevelopmental condition groups and controls. Hedges' g, ***, *p*< 0.001, ** *p*< 0.001, * *p*< 0.05.

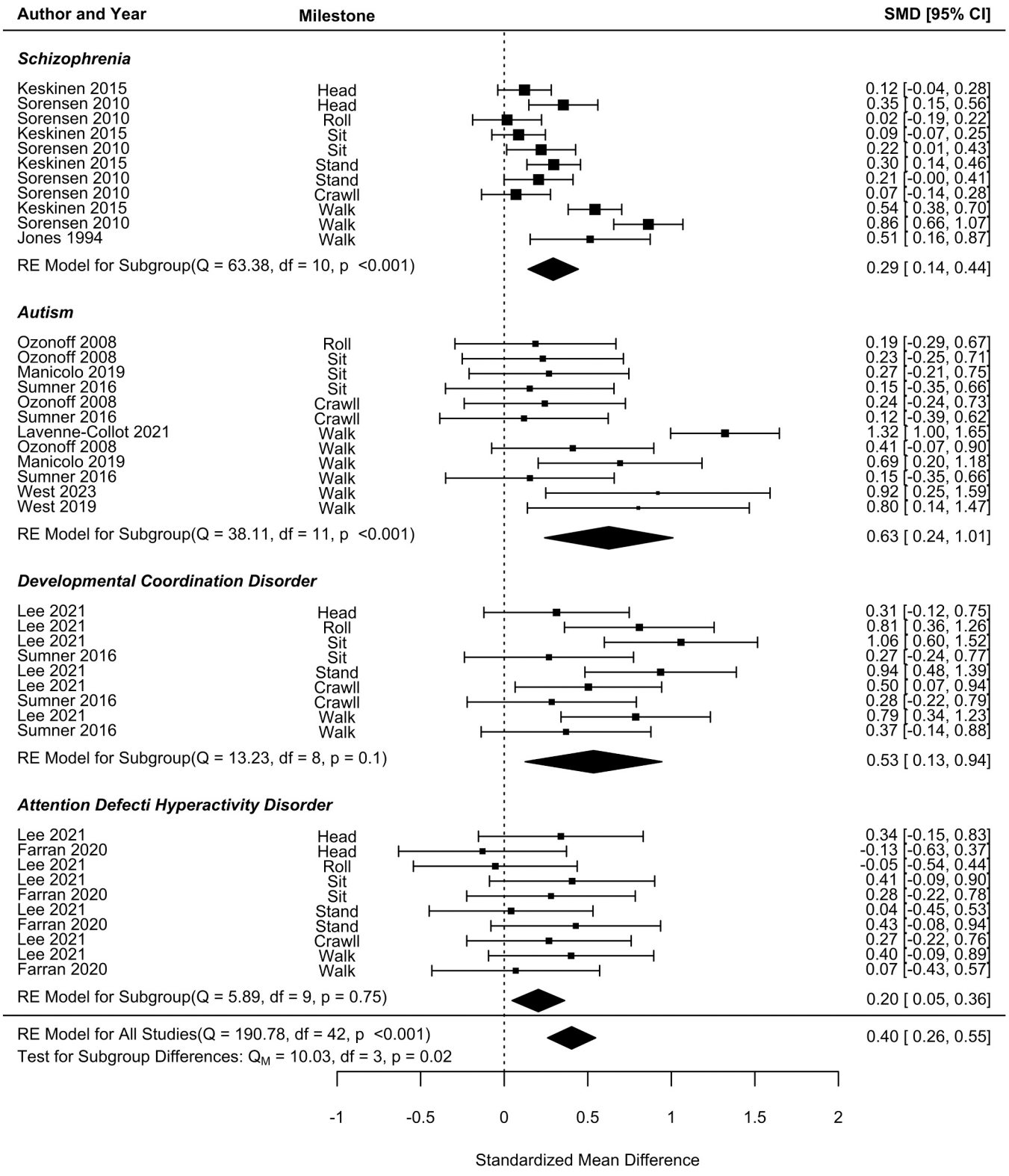

Fig. 3. Forest plot of multilevel random effects model for standardised mean difference in motor milestone attainment with neurodevelopmental condition group subgroups. *Note*, Positive effect sizes denote later milestone attainment compared to controls. SMD, standardised mean difference; CI, 95 % confidence intervals.

Schizophrenia, p= 0.004). Additionally, the DCD group had later milestone attainment than the ADHD group (p= 0.003), and the autism group had later milestone attainment than the ADHD group (p= 0.048). Subgroup analyses revealed autism was associated with the largest delay in motor milestone attainment based on the magnitude of hedges g (although confidence intervals overlap), followed by DCD, schizophrenia, and ADHD (see Table 5 for the model results and Table S6 for model comparison statistics). There was only one effect size for tics conditions, so this group was excluded from this subgroup analysis.

Sensitivity analyses that excluded studies that did not conduct

Table 5
Meta-analysis of individual neurodevelopmental condition group differences in motor milestone attainment compared to controls.

NDC	k^{est}	g (95 % CI)	*p*	Q (df)	p_Q	I^2 L2	I^2 L3
ADHD	10	0.20 (0.05, 0.36)	**0.011**	5.89 (9)	0.751	0.00	0.00
DCD	9	0.53 (0.13,0.94)	**0.011**	13.23 (8)	0.104	5.79	52.43
Autism	12	0.63 (0.24,1.01)	**0.001**	38.11 (11)	**<0.001**	0.00	74.79
Schizophrenia	11	0.29 (0.14, 0.44)	**<0.001**	63.38 (10)	**<0.001**	84.91	0.00

Note. Higher Hedges g refers to late attainment compared to the control group. NDC, neurodevelopmental condition; k^{est}, number of effect sizes; Q, Test for Residual Heterogeneity; I^2 L2, % of total variance accounted for by variation within samples/cohorts; I^2 L3, % of total variance accounted for by variation between samples/cohorts. p_Q refers to the significance test of the heterogeneity statistic (Q).

clinical diagnosis procedures were conducted, which excluded all ADHD studies. Conclusions for the main effect (g= 0.60, *p*<.001) and subgroup analyses did not change (see Table S7). Further sensitivity analyses were also conducted, which excluded studies with sample sizes under 20 (neurodevelopmental condition group or control; k^{est}= 2: West, 2019 and West et al., 2023, age of walking in autism). Conclusions did not change for the neurodevelopmental condition group comparison (g= 0.50, *p*< 0.001), the autism subgroup (g= 0.55, *p*< 0.001), or the walking subgroup (g= 0.69, *p*< 0.001, Table S8).

3.3.2. *One-mean meta-analysis of the age of motor milestone attainment*

The individual meta-analyses revealed that, on average, individuals with neurodevelopmental conditions started to lift their head at 1.94 months, roll at 5.06 months, sit at 7.25 months, crawl at 8.89 months, stand at 11.58 months, and walk at 13.96 months (Table S9). The effect sizes for independent sitting, crawling, independent standing, and walking were higher (meaning later) than the upper 95 % confidence interval from the World Health Organisation (WHO) mean age of attainment (Table S9, WHO and Onis, 2007). Subgroup analyses of differences between neurodevelopmental conditions were conducted for all milestones (see Table S9 for model results and S10 for model comparison statistics). Analyses of the differences between neurodevelopmental conditions in walking are presented below and in Fig. 4. Results from the other subgroup analyses can be found in the supplement.

3.3.2.1. Walking. There were 24 effect sizes for walking, so an unpreregistered subgroup analysis of walking across neurodevelopmental condition groups was conducted. The neurodevelopmental condition group moderated the pooled age of attainment (Qm(4)= 11.36, *p*= 0.023). DCD (k^{est}= 2) was associated with reaching the walking milestone at the latest age (g[pooled age]= 15.99, which was later than Schizophrenia *p*= 0.019 and ADHD *p*= 0.032, and autism *p*= 0.022), followed by autism (g[pooled age]= 14.03 which was later than Schizophrenia, *p*= 0.040), ADHD (g= 13.70) which was later than Schizophrenia, *p*= 0.025, then Schizophrenia (g[pooled age]= 12.61, Fig. 4, Table S11 for model results, S12 for model comparison statistics,). All the neurodevelopmental condition groups except for schizophrenia were above the WHO 95 % confidence intervals for the mean attainment age of walking (11.98, 12.22; WHO and Onis, 2007).

The funnel plot (Figure S9) revealed evidence of publication bias, and Egger's test of funnel plot asymmetry suggested there was evidence of asymmetry (z= 2.28, *p*= 0.023). A trim and fill analysis did not suggest any asymmetry. However, an inspection of the forest plot and funnel plot indicated that the Arabameri and Sotoodeh, (2015) effect size has a lower standard error than expected for the effect size (mean). Inspection of Cooks' distance (0.30) suggested it was moderately influential. A leave-one-out analysis showed that the average age of walking would be slightly reduced to 13.87 (95 % CI: 13.48, 14.25, *p*< 0.001) if this effect size was left out.

3.3.2.2. Neurodevelopmental condition group versus controls meta-analysis of standardised motor measurement. Effect sizes were only found for autism (k^{est}= 56) and language disorders (k^{est}= 6). A 3-level random-effects meta-analysis (k^{est}= 62) revealed significantly impaired motor skills for these two neurodevelopmental condition groups compared to controls (g= −0.54, 95 % CI[−0.65, −0.44], *p*< 0.001, Fig. 5) with significant heterogeneity (Q(61)= 168.02, *p*< 0.001). Within-cohort heterogeneity was medium (I^2 Level 2= 31.44 %), and between-cohort heterogeneity was close to zero (I^2 Level 3= 0.00 %). Inspection of the funnel plot (Figure S15) and Egger's test of funnel plot asymmetry (z= −1.58, *p*= 0.114) suggested no evidence of asymmetry or publication bias.

Model comparison statistics revealed a smaller AIC and BIC for the more parsimonious model (removing level 3, Table S13). In addition, the likelihood ratio test comparing the models was not significant (χ2= 0.07, *p*= 0.792), which suggests that the results are homogenous across models. However, as there were correlations between the clustered effect sizes, the results from the three-level model were reported.

Age of measurement was a significant moderator, with later age of assessment being associated with greater motor impairment (QM(1)= 18.89, *p*< 0.001, g= −0.02, 95 % CI[−0.04, −0.01], *p*< 0.001). The age moderator effect was broken down into three age of measurement brackets (6–12, 12–18, and 18–24 months), and the effect size increased as the measurement age increased (See Table S14). The age moderator effect was explored further in the bubble plot, which shows a greater (negative) standardised mean difference in motor scores (relative to controls) across measurement age for autism (g= −0.03, 95 % CI[−0.04, −0.01], *p*< 0.001, but not for language conditions (g= 0.01, 95 % CI [−0.06, 0.09], *p*= 0.728, See Fig. 6).

Neurodevelopmental condition group, motor modality, or test type did not moderate the overall neurodevelopmental condition group versus control motor attainment effect (*p*= 0.37, *p*= 0.526, *p*= 0.173, respectively). Subgroup analyses were conducted within the neurodevelopmental condition group to investigate the differential motor scores for each condition. For autism (k^{est}= 56), there was evidence for significantly impaired motor skills compared to controls (g= −0.55, 95 % CI[−0.66, −0.43], *p*< 0.001, Table S16). There was a similar effect for language conditions but with a greater 95 % confidence interval (k^{est}= 6, one study; g= −0.54, 95 % CI[−1.03, −0.05], *p*= 0.031).

4. Discussion

This is the first cross-condition systematic review and meta-analysis of infant motor skills in neurodevelopmental conditions. The review revealed important similarities and differences between neurodevelopmental conditions for motor milestones and motor skills, thus contributing new insight into the early signs and clinical presentation of neurodevelopmental conditions.

The meta-analysis identified walking as the most delayed motor milestone in infants later diagnosed with neurodevelopmental

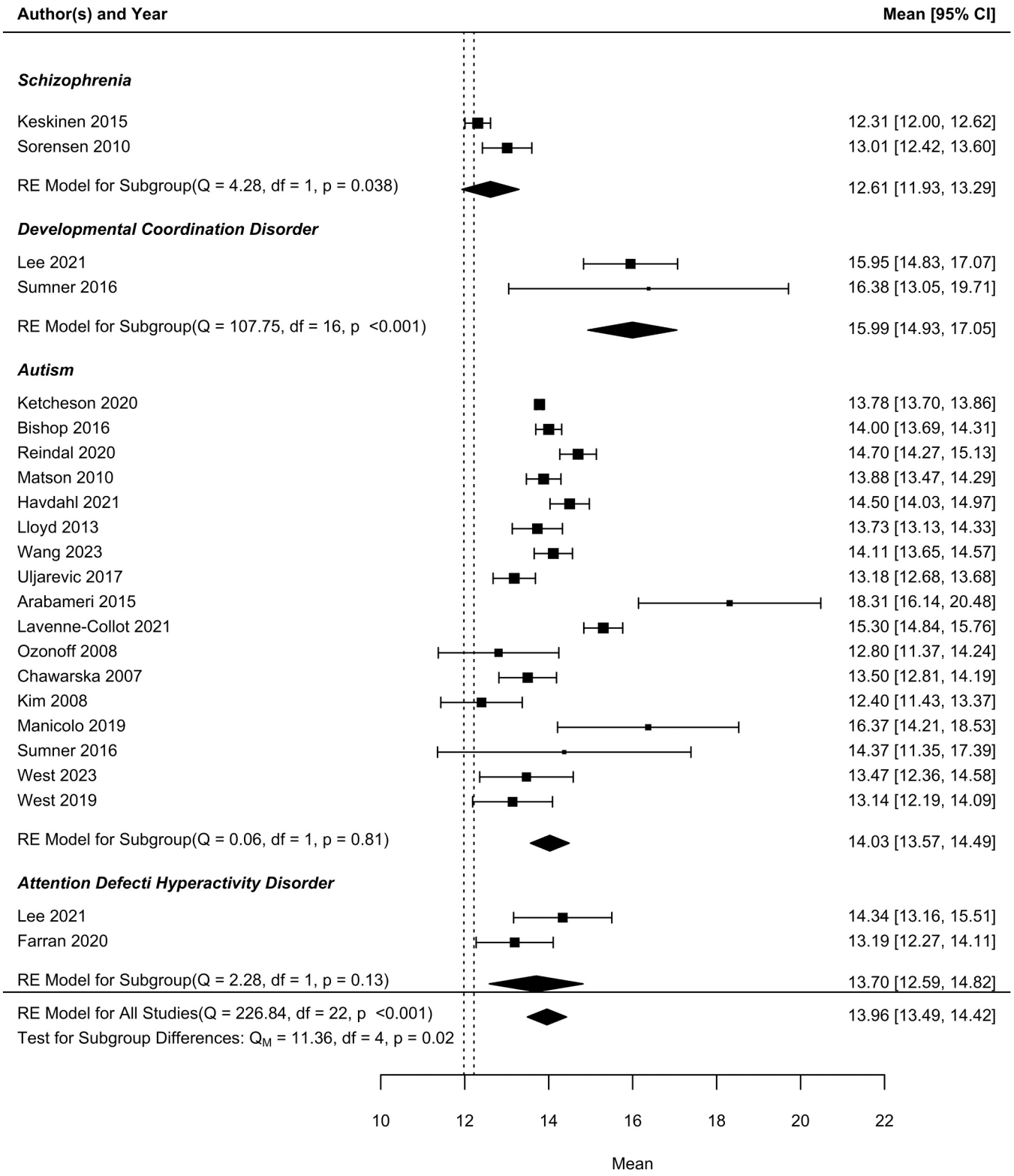

Fig. 4. Forest plot of multilevel random effects model for mean age of walking with neurodevelopmental condition subgroups. *Note.* Mean refers to pooled age of walking unaided. Dotted lines represent the WHO 95 % confidence intervals for mean age of walking. CI, 95 % confidence intervals.

conditions. However, walking age also varied significantly between conditions. Infants later diagnosed with schizophrenia walked the earliest at approximately (13 months on average), and those later diagnosed with DCD walked the latest at (16 months on average). All other included milestones were delayed in infants with neurodevelopmental consitionss compared to controls, apart from rolling, and all other milestones apart from crawling had significant heterogeneity across neurodevelopmental conditions.

Tics had the most delayed milestones compared to controls, although this was based on one walking finding from a single sample. DCD had later milestones, on average, than ADHD, and subgroup analyses revealed autism was associated with the highest magnitude delay in

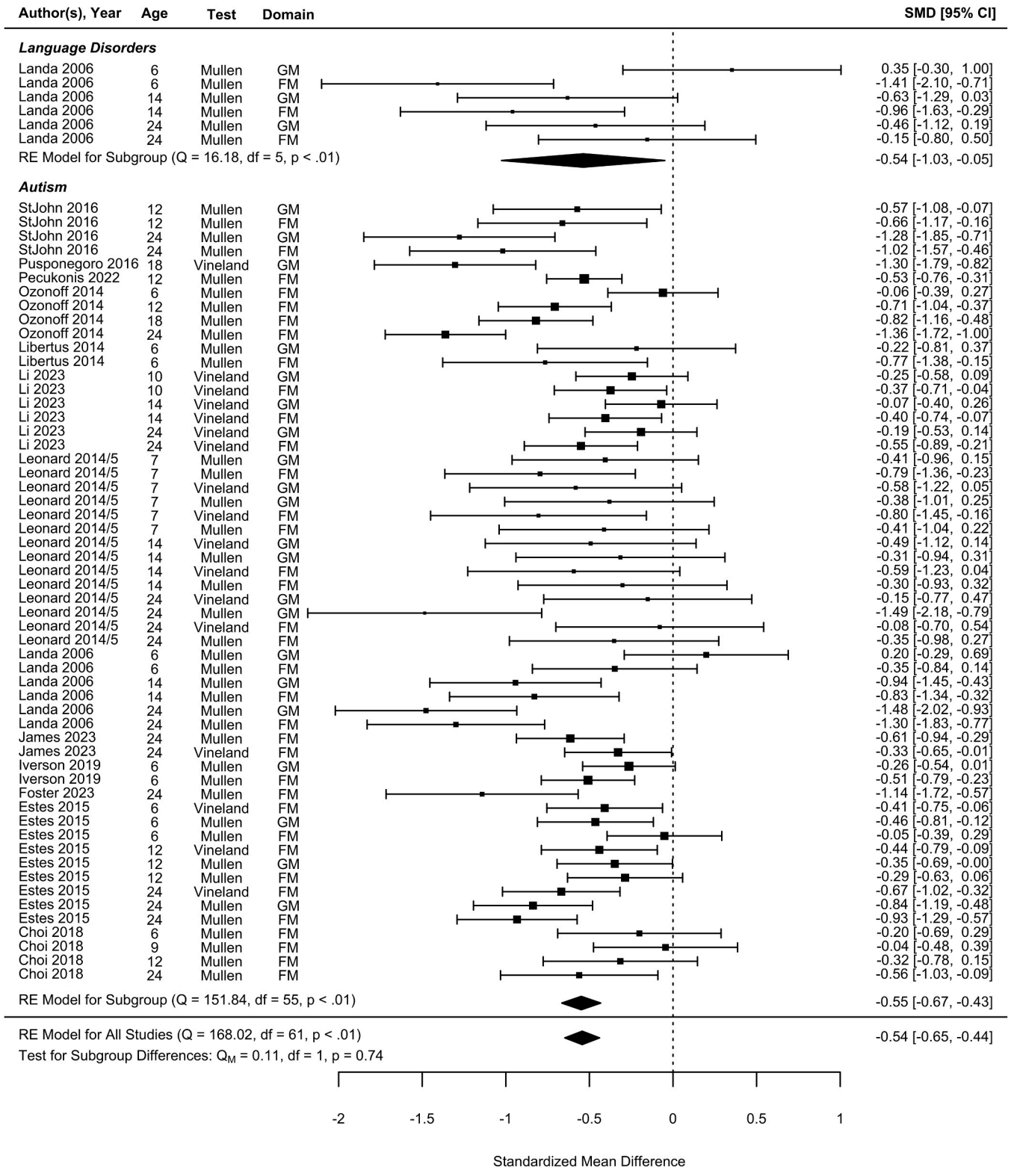

Fig. 5. Forest plot of multilevel random effects model for standardised motor assessments between neurodevelopmental condition groups with neurodevelopmental condition group subgroups. *Note*, Negative standardised mean difference indicates lower scores on standardised motor measures for cases compared to controls. Leonard 2014/15 refers to two studies from the same cohort. Vineland, Vineland, Vineland Adaptive Behaviour Scales; Mullen, The Mullen Scales of Early Learning; SMD, standardised mean difference; CI, 95 % confidence intervals.

motor milestone attainment, followed by DCD, schizophrenia, and ADHD. The significant heterogeneity in the amount of milestone delay for autism and schizophrenia is likely due to having a greater delay in attaining the walking milestone than other motor milestones. In contrast, ADHD and DCD had low heterogeneity in the delay in the attainment across all the motor milestones studied.

The evidence of slight motor delays, typical development, or, in some cases, even enhanced motor skills associated with ADHD suggests that,

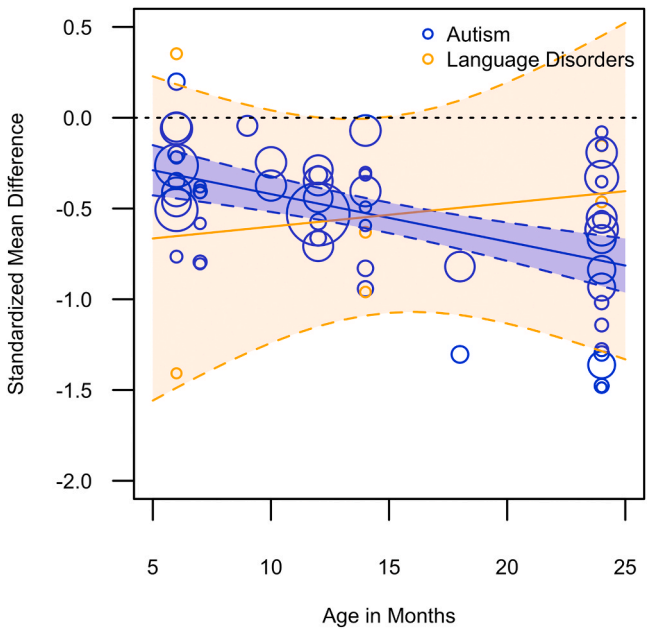

Fig. 6. Bubble plot of standardised mean difference in standardised motor assessments across age of measurement. *Note*, Negative standardised mean difference indicates lower scores on standardised motor measures for cases compared to controls. Bubbles represent individual effect sizes; the sizes of bubbles are proportional to the weight of the effect size in the meta-analysis. Highlighted areas refer to 95 % confidence intervals for each group.

although there may be similarities in the aetiology of ADHD and autism, motor development diverges in these conditions from an early age. Previous meta-analysis indicated limited or no evidence of early motor delays or impairments in ADHD (Athanasiadou et al., 2020), and a genome-wide association analysis (GWAS) of age at onset of walking showed earlier walking was genetically correlated with ADHD (Gui et al., 2024). It is unclear if there are later delays or impairments in motor skills in ADHD, as existing reviews have drawn contrasting conclusions (Havmoeller et al., 2019; Kaiser et al., 2015). This, therefore, warrants further comprehensive investigation.

The present study's results relating to autism suggested delays and impairments across many motor domains and impairments that also increase over age. These findings are consistent with a systematic review of the motor development between 3 and 42 months of individuals who go on to gain a diagnosis of autism, which revealed evidence for atypical motor development across domains, with effect sizes increasing with age (West, 2019). There is, therefore, strong evidence for early and increasing motor delays and impairments for individuals who later gain a diagnosis of autism.

We found some evidence of impairments in general motor skills in language disorders, but these impairments were not as large as those found for autism. Further, the systematic review revealed evidence of impaired early- but not late -infancy fine motor skills. This is in keeping with the findings of a non-systematic review of later motor skills, which also suggested some motor impairments in language disorders (Hill, 2001). Similarly, a meta-analysis comparing children with speech and language impairments against controls found evidence of more motor performance errors, slower motor task performance, and lower motor assessment scores in the children with speech and language impairments (Rechetnikov and Maitra, 2009). More research is needed to understand the profile of early motor skills and their development in individuals later diagnosed with language disorders.

We found evidence for significant and extensive gross motor milestone delay in infants later diagnosed with DCD, which is consistent with the clinical description for DCD in the DSM-5. However, the search did not find sufficient studies on tics disorders to draw any conclusions about this neurodevelopmental condition group.

A significant gap in the literature on fine motor skill assessment before 24 months led to no fine motor skill effect sizes in the milestone meta-analyses. However, the systematic review revealed mixed findings for autism and ADHD in fine motor impairments compared to controls, and the meta-analysis of standardised assessments revealed no motor modality moderation of group differences in motor skills. Preschool (2–4 years of age) fine motor skills are associated with genetic liabilities to ADHD and later traits for ADHD and autism (Bowler et al., 2024). Therefore, more research is needed to explore this important motor sub-domain earlier in development. Furthermore, more research is needed on tics disorders and DCD as they make up a small proportion of the literature, limiting the ability to compare conditions.

This study has several strengths. We included multiple neurodevelopmental conditions and motor assessments in meta-analyses and systematic reviews. We used multilevel models to account for the relatedness of effect sizes and explored multiple sources of heterogeneity.

This study also had several limitations. First, although all the primary meta-analyses had sufficient overall power (K range: 43–62), the subgroup analyses were unbalanced and had lower relative power (main subgroup analyses, K range 5–; walk subgroup 2–17). Second, there was a bias in the included studies, which mainly originated from Western countries (57 of 63 studies were from North American or European countries), which limits generalisability to non-Western cultures and highlights a need for research across a wider geographical range. Further, many studies used different methods of collecting motor data, often not giving sufficient detail in their manuscripts to compare to other methods. Third, conclusions drawn from the meta-analyses depend on the methodological rigour of the included studies, and it must be noted that fifteen studies included in the meta-analyses and systematic review were rated as low quality.

Our review and meta-analyses suggest that neurodevelopmental conditions involve delayed or impaired infant motor skills and highlight important distinctions across conditions. Walking is the most delayed across most included conditions. Tic disorders, Autism and DCD, had the highest magnitude impairment or delays in attainment compared to other conditions. There is also evidence of increases in motor impairments as children later diagnosed with neurodevelopmental conditions mature over infancy. Our work also shows that more research is needed for underrepresented conditions, such as tic disorders and DCD, to understand the similarities and differences in motor skills in neurodevelopmental conditions.

This study has several implications. In this first systematic review of motor milestone timing and motor development across neurodevelopmental conditions, we see that differences in the motor domain in infancy are pervasive both in terms of being present across many neurodevelopmental conditions and in terms of a range of skills and milestones being affected. Future research should investigate the potential for early interventions focused on the motor domain to improve outcomes and symptom severity in children who are at elevated likelihood of neurodevelopmental conditions. Second, our findings should instigate further research to understand the mechanistic underpinnings of the strong associations between atypical motor development and neurodevelopmental conditions. Finally, prediction modelling could be used to test whether signs of motor delay or differences in infancy can predict onset of neurodevelopmental conditions, in combination with other known factors such as genetic predisposition, family history and birth complications.

Data Availability

All data used in the article is secondary data taken from published articles. Data may be requested from the corresponding author.

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Disclosures

AB, TA, and CA have nothing to disclose. AR is a Joint Editor of the Journal of Child Psychology and Psychiatry, for which she receives an honorarium. PF is Deputy Editor in Chief of the Journal of Child Psychology and Psychiatry, for which he receives an honorarium.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.neubiorev.2024.105825.

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