Predictive validity of spontaneous early infant movement for later cerebral palsy: a systematic review

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ABBREVIATIONS

ATNR	Asymmetric tonic neck reflex
GMA	General Movements Assessment
NPV	Negative predictive value
PPV	Positive predictive value
QUADAS-2	Quality Assessment of Diagnostic Accuracy Studies

AIM To systematically review the predictive validity of spontaneous early infant movements for later cerebral palsy (CP).
METHOD Cohort studies with published data to calculate predictive validity of early spontaneous movements for later CP were searched in four electronic databases: CINAHL, Embase, MEDLINE, and PsycINFO.
RESULTS Forty-seven studies met inclusion criteria. The Prechtl General Movements Assessment (GMA) during the fidgety period (10–20wks corrected age) had the strongest sensitivity: 97 per cent (95% confidence interval [CI] 93–99) and specificity: 89% (95% CI 83–93). The sensitivity and specificity of the Prechtl GMA during the writhing period (birth–6wks) was 93% (95% CI 86–96) and 59% (95% CI 45–71) respectively. Cramped-synchronized movements in the writhing period according to Prechtl had the best specificity (sensitivity: 70% [95% CI 54–82]; specificity: 97% [95% CI 74–100]). Hadders-Algra's method of assessing general movements had a pooled sensitivity and specificity of 89% (95% CI 66–97) and 81% (95% CI 64–91) respectively. Presence of asymmetric postures and movement quality/quantity were reported under the Hammersmith Infant Neurological Examination, Hammersmith Neonatal Neurological Examination, and Movement Assessment of Infants but had weak associations with later CP.
INTERPRETATION Fidgety movements assessed by the Prechtl GMA have the strongest predictive validity for later CP, but cannot be considered in isolation because of the presence of false positive results.

There is growing evidence that early management of cerebral palsy (CP) can lead to improved functional outcomes.[1] However, timely intervention can only occur with early identification of infants at high risk of developing CP.[2] Definitive diagnosis and classification of CP stabilizes after 2 years of age[3] with the average age of CP diagnosis occurring at approximately 19 months.[4] However, delaying intervention until the time of diagnosis may result in missed opportunities to implement intervention during a period of brain 'plasticity', and maximize functional outcomes from the earliest possible age.[5,6]

Spontaneous infant movement has been reported to have prognostic value for CP since the early works of Amiel-Tison et al.[7] and Prechtl.[8] With recent advances in smartphone technology, capturing spontaneous movements using video has improved accessibility,[9,10] which has the potential to provide remote professional assessments for isolated and vulnerable families. While existing studies have explored the clinical utility of brain imaging or neurobehavioural assessments to predict later CP,[11,12] the predictive validity of a range of early spontaneous movements should be determined to facilitate accurate and early detection of infants at risk of developing CP.

Previous studies have indicated that postures such as persistent asymmetric tonic neck reflex (ATNR) or non-midline patterns may be suggestive of unilateral CP.[13,14] In addition, persistent cramped-synchronized features, which are simultaneous stiff limb and trunk movements,[15] appear to have predictive validity for spastic CP.[16,17]

There has been particular interest in the predictive validity of the Prechtl General Movements Assessment (GMA)[15] with a recent systematic review[12] reporting a high sensitivity of 98% (95% confidence interval [CI] 73–100) and specificity of 91% (95% CI 83–95) to predict later CP.[12] However, these predictive values did not distinguish between writhing and fidgety general movements (see classifications, Table I), and the difference between these two movements has been suggested to be critical

when interpreting results to guide clinical practice, as abnormal writhing movements can normalize in later infancy.[18] General movements have also been defined according to Hadders-Algra, with observed movements classified as per Table I.[19] Apart from the general movements (assessed using the Prechtl or Hadders-Algra method), no previous systematic review has reported on the predictive validity of any other spontaneous early movement described above. The aim of our systematic review is to determine the predictive validity of any observable spontaneous infant movement between 37 weeks' gestational age to 5 months' corrected age for later CP and conduct a meta-analysis to determine the sensitivity and specificity of different spontaneous movements for a later diagnosis of CP.

METHODS

Initially, four systematic reviews[11,12,20,21] were assessed to collate infant assessment tools that had components that were purely observed without any assessor interaction. Assessments that tested infants at under 37 weeks' gestation or over 5 months' corrected age were excluded. The age range of infant assessment was selected based on the age at which infants begin to develop a complex repertoire of movement.[15] Assessment tools were screened by two authors (AK, AS).

All included assessment tools, 'general movement*' or 'motor repertoire' were combined with the term 'cerebral palsy' and searched in MEDLINE (1946–December 31st, 2016), CINAHL (1981–December 31st, 2016), Embase (1947–December 31st, 2016), and PsycINFO (1966–December 31st, 2016) databases, with searches updated on November 6th, 2017 as per Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines (Appendix S1, online supporting information).[22] Titles, abstracts, and full texts were screened by two independent assessors (AK, TF) and any conflicts were resolved by a third assessor (AS). We included English language cohort studies of any infant population that reported on the predictive validity of any observational movement between the ages of 37 weeks' gestation to 5 months' corrected age for later CP at any age. Where published articles reported on repeated cohorts, we considered data from the latest published study, or from the latest study where data were available to reconstruct 2×2 tables for further analysis if not available in the latest study itself.

The reference lists of all included articles were screened to identify additional studies. Reference lists of three other systematic reviews assessing the Prechtl GMA[12,23,24] and a key review article[25] were also screened.

What this paper adds

- Fidgety general movements (Prechtl) are most predictive for later cerebral palsy compared with other spontaneous movements.
- False positive results are high among all spontaneous movement assessments.

Data extraction

Data were extracted by two independent authors (AK, TF) from included articles using an extrapolated list based on the Standards for Reporting of Diagnostic Accuracy Studies (Appendix S2, online supporting information).[26] Studies were also assessed for bias using the Quality Assessment of

Table I: Characteristics of included assessments tools

Assessment tool	Age of assessment	Movements observed	Presence of assessor handling	Number of studies that report separate observational components	Number of studies with 2x2 data available
Prechtl GMA writhing	Preterm age to 9wks CA	Normal writhing movements$^{(-)}$ Poor repertoire$^{(+)}$, cramped-synchronized$^{(+)}$ or chaotic movements$^{(+)}$	None	21	13
Prechtl GMA fidgety	9–16wks CA	Normal fidgety movements$^{(-)}$ Absent$^{(+)}$ or abnormal fidgety movements$^{(+)}$	None	33	26
GMs (Hadders-Algra) writhing	Preterm age to 6–12wks CA	Normal optimal GMs$^{(-)}$ Normal suboptimal GMs$^{(-)}$ Mildly abnormal GMs$^{(+)}$ Definitely abnormal GMs$^{(+)}$	None	3	2
GMs (Hadders-Algra) fidgety	2–12wks to 14–18wks CA	Normal optimal GMs$^{(-)}$ Normal suboptimal GMs$^{(-)}$ Mildly abnormal GMs$^{(+)}$ Definitely abnormal GMs$^{(+)}$	None	8	7
MAI	0–12mo	ATNR, tremors, head centring, hand posture	Some items elicited	2	–
HINE	3mo, 6mo, 9mo, 12mo	Movement quality and quantity	Some items elicited	2	–
HNNE	Preterm–term age	Resting posture Movement quality and quantity	Some items elicited	1	–

$^{(-)}$Negative test result, $^{(+)}$positive test result. GMA, General Movements Assessment; CA, corrected age; GMs, general movements; MAI, Movement Assessment of Infants; ATNR, asymmetric tonic neck reflex; HINE, Hammersmith Infant Neurological Examination; HNNE, Hammersmith Neonatal Neurological Examination.

Diagnostic Accuracy Studies (QUADAS-2) (Appendix S3, online supporting information).[27] The QUADAS-2 tool measures the risk of bias for cohort selection, the index test (observational assessment tools), the reference standard (method of CP diagnosis), and the flow of participants including loss to follow-up and consistency of methodology across the cohort. We considered follow-up rates of greater than or equal to 85% as having a low risk of bias for follow-up. We considered studies that documented a consistent process between assessors to diagnose CP according to a standardized neurological examination and classification according to Palisano et al.[28] or Hagberg et al.[29] criteria as having a low risk of bias. Unclear classifications were applied where studies did not specify the neurological assessment used to diagnose CP. Data were extracted to reproduce 2×2 tables for analysis of sensitivity, specificity, positive predictive value (PPV), negative predictive values (NPV), positive likelihood ratios, and negative likelihood ratios. Where extracted data did not match published data or where predictive validity for CP was not the primary aim of the study, data were crossed checked by a second author (TF). Positive and negative test results for the Prechtl GMA and general movements according to Hadders-Algra were dichotomized as per Table I. Cramped-synchronized movements according to the Prechtl GMA were considered in the writhing period only. Any conflicts in data extraction or scoring were resolved by a third assessor (AS).

The methods for this systematic review were registered with PROSPERO International Prospective Register of Systematic Reviews (CRD42016042551, July 12th, 2016).

Data analysis

Data for sensitivity (the proportion of those with CP who were identified as having early abnormal movements) and specificity (the proportion of those without CP who were identified as having early normal movements) of observed infant movement to predict later CP were extracted from published data and reproduced with 95% CIs using RevMan 5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark). Studies with insufficient published data to reproduce 2×2 tables were not included in quantitative analysis.

Where sufficient data were available, we used statistical packages Stata 14 (StataCorp, College Station, TX, USA) or R (R Foundation for Statistical Computing, Vienna, Austria) to complete meta-analyses for diagnostic accuracy studies to determine the pooled sensitivity and specificity for observed movements. Heterogeneity between studies was assessed with the I^2 statistic and random-effects analyses were used because the heterogeneity was substantial between studies.[30] Analyses were summarized visually with forest plots of sensitivity and specificity, with summary points using STATA 14, or with RevMan 5.3 for studies that could not be pooled visually. As PPVs and NPVs are dependent on CP prevalence within a population, PPVs and NPVs were not pooled as any summary value would be related to an unknown CP prevalence and therefore have minimal clinical utility.[31,32] Instead, PPV and NPV were quoted as ranges for each spontaneous movement. Positive and negative likelihood ratios were also summarized for each spontaneous movement.

RESULTS

Twenty-five assessment tools had infant observation as part of the assessment and are detailed in Appendix S4 (online supporting information). Only one tool (Peabody Developmental Motor Scales)[33] required infant handling for the whole assessment and two tools assessed infants outside the specified age range (Lacey Assessment of the Preterm Infant; Primitive Reflex Profile)[34,35] and thus were not included in the database search terms. One additional tool (Infant Motor Profile)[36] was identified in the secondary electronic database search strategy.

From database and grey literature searches, 880 titles and abstracts were retrieved after removal of duplicates (Fig. 1). Fifty-five records met inclusion criteria and represented 47 study cohorts, of which 31[16,18,37–68] were prospective studies, five[69–74] were retrospective studies, five[13,14,75–79] were studies of selections from previous cohorts, and two were follow-up studies[80–83] from randomized controlled trials where outcomes between intervention arms did not differ. Finally, four cohort studies[17,84–86] were unclear if they were retrospective or prospective. The characteristics of each study are summarized in Table SI (online supporting information). From the 47 included studies, we reproduced 2×2 data for 13 studies[13,17,18,38,41–44,52,64,68,77,83] for writhing movements, 26 studies[13,14,16–18,38,39,41–44,46,48,52,54,56,59,64–66,68,69,72,77,83,84] fidgety movements, and five studies[13,18,42,51,59] for cramped-synchronized movements under the Prechtl GMA for prediction of later CP. One study[79] reported on two cohorts for writhing general movements and seven studies[37,50,57,61,78–80] for fidgety general movements using Hadders-Algra's method.

Movements that were included in qualitative analysis included presence of ATNR posture, asymmetric postures, and quality/quantity of movements assessed as part of the Hammersmith Infant Neurological Examination,[87] Movement Assessment of Infants,[85,88] or Hammersmith Neonatal Neurological Examination[89] (Table I).

Seventeen studies[16,18,37,39,41–43,54,57,58,60,61,69–72,82,83] defined the type and topography of later CP but did not relate specific observed items to the type of CP that developed. Only four studies[13,17,52,77] contained data to correlate specific movements for the type or topography of CP. However, all four articles appeared to be derived from the same sample and we could not be sure if crossover of participants between articles existed.

Two studies[47,76] had a CP rate of 0% and were included in the current systematic review for qualitative analysis only. CP rate varied between 1.6%[63,64] and 52.4%[18] for all other studies of high-risk infant populations.

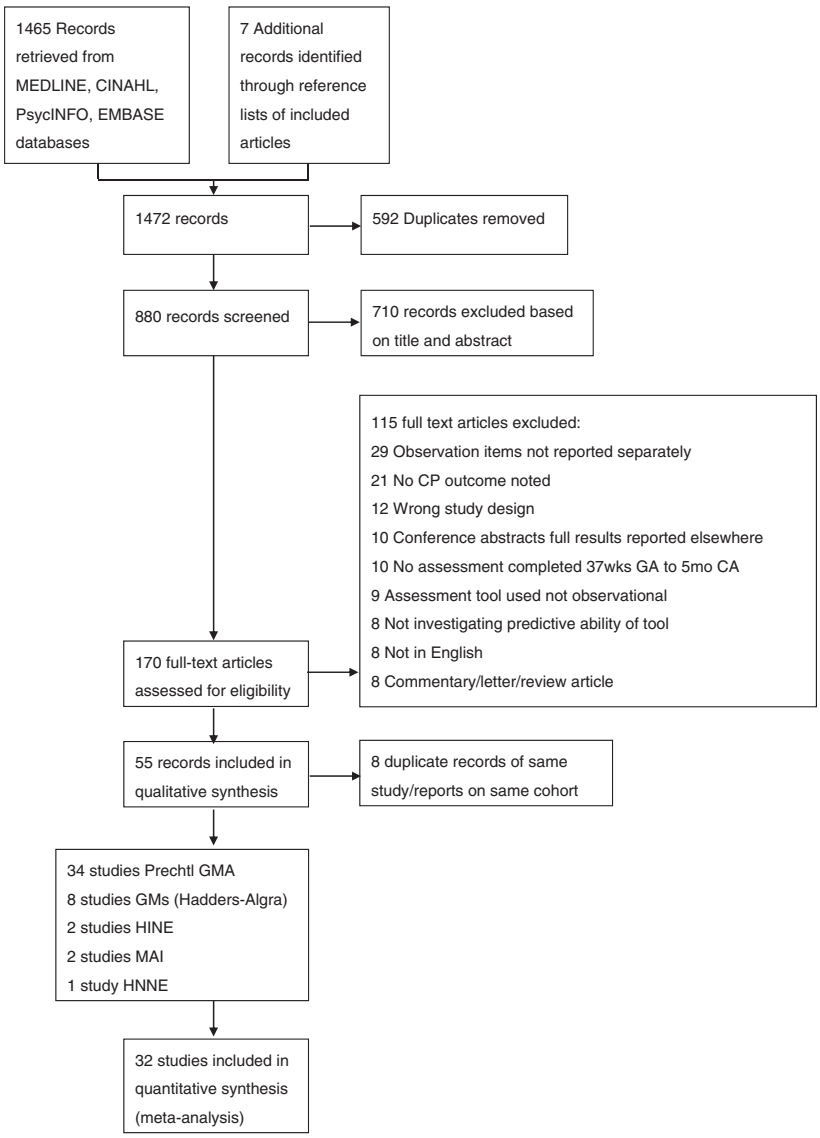

Figure 1: Preferred Reporting Items for Systematic Reviews and Meta-Analysis flowchart for article screening. CP, cerebral palsy; GA, gestational age; CA, corrected age; GMA, General Movements Assessment; GMs (Hadders-Algra), general movement classification according to Hadders-Algra; HINE, Hammersmith Infant Neurological Examination; MAI, Movement Assessment of Infants.

Methodological quality

The methodological quality of individual studies as assessed by the QUADAS-2 are detailed in Table SII (online supporting information) and overall combined bias summarized in Figure 2. Study quality was variable with concerns regarding the selection of patients, the reference standard, and the flow and timing of assessment. Four studies[39,49,54,56,59] had a low risk of bias in all four QUADAS-2 domains.

Consecutive participant recruitment was reported in only 16 studies.[37–41,43,44,48,49,51,54–56,59,63,64,74,82,83] Initial index assessments of spontaneous infant movement were generally well conducted with consistent thresholds defined by Prechtl or Hadders-Algra with the exception of one study[60] that used writhing instead of fidgety classifications for 3-month Prechtl GMA. Where studies noted partial blinding among scorers, the studies were rated as having an overall low bias.[46,48,57,82,83] Participant selection affected the representativeness of high-risk infants in one study[80,81] as participants were selected based on abnormal general movements according to Hadders-Algra at the start of the fidgety period. This led to concerns regarding applicability of participants to the research question.

Studies varied with their methods of CP diagnosis. Three studies used Hagberg or Palisano criteria to diagnose CP.[14,37,55,56,75] A standard neurological examination (e.g. Touwen, Amiel-Tison, and Grenier) or a standard test of reflexes, tone, etc., were used to determine CP in 27

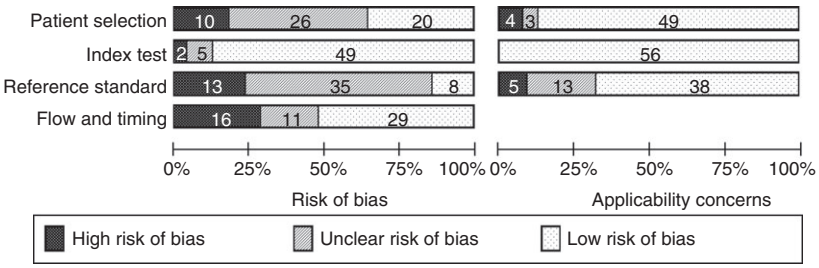

Figure 2: Summary of Quality Assessment of Diagnostic Accuracy Studies scores across all included articles. Numbers on graph sections represent the number of articles with high, unclear, or low risk of bias.

studies.[16–18,38–42,44,45,48,51–54,57–59,61,62,68,70,71,73,74,78–80] Ten studies[13,43,46,50,63,64,67,72,76,77,85] used a non-specific neurological examination and were classified as unclear. Three studies[69,82–84] did not use standardized examinations between assessors and these were assigned a high risk of bias rating for the administration of the reference standard.

Only 10 studies[39,43,45,49,54–56,59,63,64,79–83] reported blinding of assessors at follow-up. Flow and timing of assessments were poorly reported. Twelve studies excluded infants if they had incomplete assessments.[13,16,44,51,53,61,67–71,77] Therefore, flow and follow-up rates could not be calculated accurately.

Predictive validity of spontaneous movements

Table II summarizes the sensitivity, specificity, PPV and NPV ranges, positive likelihood ratios and negative likelihood ratios of cramped-synchronized, writhing, and fidgety movements assessed according to the Prechtl GMA and fidgety general movements according to Hadders-Algra, with individual study sensitivity and specificity detailed in Figure S1 (online supporting information).

The Prechtl GMA

Cramped-synchronized movements had the highest positive likelihood ratio compared with other spontaneous movements but had the lowest sensitivity of 70% (95% CI 54–82), indicating substantial rates of false negative results within the test. Consequently, the negative likelihood ratio was the poorest (0.31 [95% CI 0.20–0.49]) compared with other spontaneous infant movements.

Writhing movements had the lowest specificity of 59% (45%–71%) with a PPV range of 8% to 68%, indicating the highest proportion of false positive results within this test. Consequently, writhing movements had the lowest positive likelihood ratio of 2.28 (95% CI 1.67–3.20).

Fidgety movements assessed by the Prechtl GMA had the strongest sensitivity (97% [95% CI 93–99]) for predicting CP. The specificity was 89% (95% CI 83–93) and PPV ranged between 36% to 100% indicating a variable but notable rate of false positive results. The negative likelihood ratio was 0.04 (0.02–0.08) and NPV range was 80 per cent to 100%, indicating a lower presence of false negative results and that presence of fidgety movements (Prechtl GMA) were mostly to be associated with normal outcome.

General movements according to Hadders-Algra

We extracted data for writhing general movements according to Hadders-Algra from two cohorts within one study.[79] Both cohorts reported a sensitivity of 100% (cohort A 95% CI 3–100; cohort B 95% CI 63–100). The specificities of cohorts A and B were 38% (95% CI 22–56) and 55% (95% CI 39–70) respectively. Data were not pooled because of a small number of studies.

The sensitivity for fidgety general movements according to Hadders-Algra for predicting later CP was 89% (95% CI 66–97) and specificity was 81% (95% CI 64–91). The range for PPV was 6% to 56% and for NPV the range was narrow, from 96% to 100% (Table II). The positive likelihood ratio was 4.77 (2.49–9.15) and negative likelihood ratio was 0.14 (0.04–0.44).

Table II: Summary of predictive scores for the Prechtl GMA writhing, fidgety; GMs (Hadders-Algra) writhing, fidgety; cramped-synchronized movements

Test	Sensitivity, % (95% CI)	Specificity, % (95% CI)	PPV range, %	NPV range, %	LR+ (95% CI)	LR- (95% CI)
Cramped-synchronized movements[a]	70 (54–82)	97 (74–100)	36–100	74–94	23.43 (2.33–235.49)	0.31 (0.20–0.49)
Prechtl GMA writhing[b]	93 (86–96)	59 (45–71)	8–68	80–100	2.28 (1.67–3.20)	0.13 (0.07–0.25)
Prechtl GMA fidgety[a]	97 (93–99)	89 (83–93)	8–100	80–100	8.80 (5.7–13.5)	0.04 (0.02–0.08)
GMs (Hadders-Algra) fidgety[a]	89 (66–97)	81 (64–91)	6–56	96–100	4.77 (2.49–9.15)	0.14 (0.04–0.44)

[a]Analysis conducted in STATA. [b]Analysis conducted in R. GMA, General Movements Assessment; GMs, general movements; CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value; LR+, positive likelihood ratio; LR-, negative likelihood ratio.

Presence of persistent/dominant ATNR

Predictive scores for ATNR for later CP were derived from two studies,[14,80] and were 54%[14] (95% CI 25–81) and 30%[80] (95% CI 7–65)[80] for sensitivity; and 85%[14] (95% CI 73–93)[14] and 76%[80] (95% CI 59–89) for specificity. Prechtl[52] noted that of the 11 infants developing CP in the studied cohort, eight showed persistent ATNR postures. Harris[85] reported that 19 out of 36 (reported as 53.8%) infants with CP demonstrated ATNR postures and 34 out of 118 (28.8%) infants without CP also demonstrated ATNR postures (p=0.029) when assessed by the Movement Assessment of Infants. Harris[85] did not specify if ATNR was dominant.

Asymmetrical postures

Asymmetry scores were assessed under the Assessment of Motor Repertoire in one study.[13] Marked asymmetrical movement at term age was noted in 5 out of 15 infants who had CP and 5 out of 19 infants who did not have CP. At the fidgety period, 9 out of 15 infants who developed CP and 5 out of 19 who did not develop CP showed asymmetrical movement at 49 to 56 weeks postmenstrual age. The correlation of asymmetry scores and CP outcome were not reported with statistical significance values. Another study[77] noted that five out of six infants that eventually developed hemiplegia also showed asymmetrical signs at fidgety age (p<0.001).

According to Harris,[85] 4 out of 36 (reported as 11.8%) infants who developed CP had asymmetrical movement at 4 months' corrected age versus 17 out of 118 (14.4%) infants who later developed without CP (p=0.917). An infant's inability to hold their head in midline was found to be significant (p<0.001) as 17 out of 36 (reported as 48.6%) infants who developed CP had difficulty with midline head postures compared with 21 out of 118 (reported as 17.1%) who did not have eventual CP as assessed by the Movement Assessment of Infants.

Overall movement quality and quantity

Groen et al.[78] found that there was no relationship to later CP where discrepancies in arm and leg movement quality existed. Similarly, Philippi et al.[50] showed that slow or periodic leg movements had low predictive validity for later CP (receiver-operating characteristic [ROC] 0.73 for slow leg movements, 0.53 for periodic leg movements).

Hamer et al.[80] investigated the presence of stiff movements without jerky movements and its relationship to later CP. Stiff movements without jerky movements were present in 8 out of 10 children who developed CP (p<0.001).

Pizzardi et al.[51] found a strong relationship between movement quality and quantity components of the Hammersmith Infant Neurological Examination (ROC approximately 0.96 and 0.97 respectively) at 3 months' corrected age. Similar results were reported by Romeo et al.[54,73] where the median score for movement quality and quantity assessed as part of the Hammersmith Infant Neurological Examination was 6 out of 6 (IQR 3–6) for those without CP and 1 out of 6 (IQR 0–5) for those who developed CP (p<0.001). In the study by Ricci et al.[53] fewer than 50% of infants with tetraplegia showed movement quality and quantity outside the normal range when assessed under the Hammersmith Neonatal Neurological Examination.

DISCUSSION

The results of this study indicate that spontaneous infant movement can be a strong predictor of later CP. The predictive validity of fidgety movements using the Prechtl GMA in this study is consistent with the results of previous reviews of the Prechtl GMA.[12,23,24] However, when comparing with the existing systematic reviews, our findings highlight the low specificity of the Prechtl GMA writhing movements, indicating a high presence of false positive results. To our knowledge, this is the first systematic review to use meta-analysis to assess the predictive validity of writhing and fidgety movements under the Prechtl GMA and general movements according to Hadders-Algra separately, with Prechtl's method having better predictive validity for CP. The distinction between the predictive validity of writhing and fidgety periods is critical. The results of our systematic review confirm that abnormal writhing movements (assessed using Prechtl's method) can normalize[18] and clinicians should focus on ensuring that they obtain a trajectory of general movements including the fidgety age. As the majority of infants are no longer hospital inpatients during the fidgety period, concerted effort for infants to be assessed at this age is of high importance. Capturing infant movements remotely at this critical age within the family home can be facilitated by technologies such as parent-operated smartphone applications.[9,10]

There was inconsistent reporting of studies' interpretation of pathological postures such as ATNR or limb movement quality, resulting in variable threshold levels that limited the ability to pool predictive validity of these postures. There was also insufficient detail in studies to establish whether certain postures or asymmetries resulted in specific types or topography of CP. However, the distribution of type/topography of CP, especially for ataxic, dyskinetic, and diplegic forms, are few in comparison to spastic and hemiplegic types,[90] such that studies would require very large sample sizes to accurately establish any relationship between certain movement behaviours and their correlation to specific types/topographies of CP.

However, it may be possible that asymmetrical postures and/or poor limb movement have more predictive validity when considered in combination. For example, assessments such as the General Movement Optimality Score[91] or the observational section of the Test of Infant Motor Performance[92] may provide higher predictive validity when abnormal or normal movements and postures appear together rather than in isolation.

Limitations of the review

Many studies had insufficient information to draw clear conclusions about study methodology, therefore limiting the ability to accurately assess bias under the QUADAS-2. Most study bias concerns arose from studies' cohort selection, CP diagnosis, and follow-up rates. A consecutively recruited cohort reduces selection bias within a sample as a truer representation of the population can be studied.[27] While consecutive recruitment was an issue with the majority of studies, the sensitivity of individual studies with lower risk of bias showed consistency with pooled results. However, specificity varied more among studies with lower risk of bias (Fig. S1).

With respect to the variable specificity and wide range of PPVs across all spontaneous movements, clinicians should be wary of false positive results when presented with concerning spontaneous movements. As CP is not diagnosed contemporaneously, a positive test may needlessly cause stress and anxiety in parents, or increase unnecessary demand on follow-up services. Clinicians should also refer to recent guidelines and consider results of spontaneous movement assessments with brain imaging and physical examinations such as the Hammersmith Infant Neurological Examination, in addition to clinical history and parent interviews to guide further diagnosis of CP.[6,93,94] Conversely, normal spontaneous movements had consistently higher NPVs despite varying degrees of study quality and CP prevalence. This has important implications for ensuring that CP diagnosis is not missed because of false negative tests. In the absence of other concerning factors, such as poor environment, low social risk, or significant clinical history, it may be appropriate for clinicians to reduce their frequency of service for those with normal spontaneous movements.

When considering participant selection, a group of studies[13,16,17,52,71] appeared to use the same cohort but split participants into different risk groups. Therefore, potential crossover of participants across these six studies may have artificially increased participant numbers. Given that four studies[13,16,17,52] were included in the analysis of our review, the results from these studies should be treated with caution.

Studies varied with regard to their method of CP diagnosis. CP diagnosis is currently based on clinical assessment and there is currently no criterion standard test to definitively diagnose CP.[95] Where standardized assessment procedures between assessors were not reported, we could not be sure that consistency was maintained between assessments of individual CP cases, therefore introducing potential assessor bias. Reporting of blinded assessment at follow-up was also poor. This has potential to introduce assessment bias to studies as knowledge of prior index test results may influence the diagnosis of any borderline CP cases.

Another limitation in this review lies in the inclusion of studies that diagnosed CP as early as 12 months,[39,43,46,47,65,66] potentially missing milder CP cases. However, as there are fewer functional limitations associated with milder CP,[28] the ability for spontaneous movements to identify those who are showing more severe forms of CP remains important to ensure early intervention resources are directed appropriately. Additionally, in studies where cohorts were reviewed at two time points, the number of cases that developed CP did not change for four studies,[14,55,56,63,64,75,82,83] but did change for two studies.[49,59,80,81] However, for the latter two studies, the method of CP diagnosis differed between earlier and later studies. Future studies should consider longer follow-up periods and note the severity of CP identified at different ages to better assess the predictive validity of spontaneous movements.

As we were not able to access translators for this study, non-English language studies were excluded and therefore could not be considered for analysis, which is another limitation of the study. However, the number of such studies is likely to be small relative to the large number included in this review, and thus any bias is likely to be small.

Finally, it is important to consider the time of recruitment when comparing findings with contemporaneous participants. One study[85] recruited their cohort as early as 1976, one study[77] had a recruitment period of 10 years, and two studies[76,86] recruited at two time points. Changes in neonatal practices and survival rates have potential to alter CP prevalence over time and affect prevalence-dependant PPVs and NPVs.

CONCLUSION

Clinical implications

The findings of this study indicate that observable spontaneous early infant movement can play an important role in predicting later CP, in particular, fidgety movements assessed by the Prechtl GMA. However, clinicians should be wary of the presence of false positive and false negative results when providing test feedback to families. Therefore, these early predictors should not be used in isolation as definitive diagnostic tests for CP but should be used in conjunction with other clinical assessment methods to guide diagnosis.

Suggestions for future research

Further studies with larger consecutively recruited cohorts with longer follow-up periods are required to establish relationships between specific observed movements and the type and topography of CP. Assessments with cumulative scores of multiple observed infant movements may have superior predictive validity than single observable postures alone and require further investigation. Finally, the utility of spontaneous infant movement recorded by parents and transmitted remotely to predict later CP needs to be determined.

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SUPPORTING INFORMATION

The following additional material may be found online:

Appendix S1: Search string used in electronic databases.

Appendix S2: Data extraction items based on Standards for Reporting of Diagnostic Accuracy Studies.

Appendix S3: Quality Assessment of Diagnostic Accuracy Studies items.

Appendix S4: List of infant assessment tools that observe infant movement.

Table SI: Summary of study characteristics for the Prechtl General Movements Assessment, general movements according to Hadders-Algra, Movement Assessment of Infants, Hammersmith Infant Neurological Examination, Hammersmith Neonatal Neurological Examination

Table SII: Quality Assessment of Diagnostic Accuracy Studies ratings for Prechtl General Movements Assessment, general movements according to Hadders-Algra, Movement Assessment of Infants, Hammersmith Infant Neurological Examination, Hammersmith Neonatal Neurological Examination

Figure S1: Forest plots of Prechtl General Movements Assessment (GMA) writhing, Prechtl GMA fidgety, Prechtl GMA cramped-synchronized, and general movements according to Hadders-Algra fidgety.

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