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SYSTEMATIC REVIEW

Predictors of upper-extremity motor outcomes after constraint-induced therapy or bimanual training in children with cerebral palsy: A systematic review

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Abstract

Aim: To systematically review the factors that predict changes in upper-extremity motor function in response to constraint-induced movement therapy (CIMT) or bimanual training in children with cerebral palsy (CP).

Method: The PubMed, Cochrane, Embase, Scopus, CINAHL, and PEDro databases were searched. Studies were included if predictor variables were measured at baseline and were linked to an upper-extremity motor function outcome after intervention. Studies investigating only neurophysiological biomarkers were excluded. Two independent reviewers conducted study selection, risk of bias assessment, data extraction, and synthesis.

Results: The electronic search yielded 4317 articles, of which 23 were included (14 of 23 were randomized controlled trials). The most frequently studied factors were baseline motor outcomes (19 studies), age (19 studies), behavior (six studies), sex (six studies), and affected side (six studies), with inconsistent evidence to support an association with changes in upper-extremity motor function after CIMT or bimanual training. Cognitive deficits, somatosensory deficits, and mixed effects of predictive factors were rarely studied.

Interpretation: Based on current evidence, it is inconclusive whether children with CP benefit from CIMT or bimanual training, regardless of their baseline upper-extremity motor function, age, sex, affected side, or behavior.

Cerebral palsy (CP)[1] is the leading cause of motor disability in children, affecting approximately 2 to 4 per 1000 worldwide.[2,3] Children with CP frequently experience upper-extremity impairments, including deficits in tactile sensation, proprioception, and both unimanual and bimanual motor control.[4,5] These deficits contribute to difficulties in performing daily activities and restrict social participation.[6]

In the last decades, two interventions focusing heavily on the intensity of practice with the more-affected arm have been developed for children with CP: constraint-induced movement therapy (CIMT) and bimanual training.[7,8] CIMT involves restricting the less-affected upper extremity while engaging the more-affected one in structured practice, guided by motor learning principles such as shaping and repetitive task practice.[7] Likewise, bimanual training involves the principles of motor learning embedded in a structured practice of bimanual tasks, without a constraint.[8] Studies have shown that both therapies yield similar outcomes, although CIMT is more effective in

Abbreviation: CIMT, constraint-induced movement therapy enhancing the more-affected side, while bimanual training is particularly beneficial for improving bimanual coordination.[9–11] A hybrid approach has also been tested, combining both methods, with CIMT followed by bimanual training.[7] The two therapies have been extensively studied and well recommended in the management of the upper extremities in children with CP (typically the unilateral form associated with hemiparesis).[12,13] However, there are some interindividual differences in the responses to the two therapies.[14,15] Some studies explored the relationship between clinical factors (e.g. age and motor deficit severity) or neurophysiological factors (e.g. axonal integrity and corticospinal tract reorganization) and the response to CIMT or bimanual training, but the findings remain controversial.[15–19]

Identifying the factors influencing the response to CIMT or bimanual training is essential for personalizing treatment, and for optimizing therapy time, costs, and effort for families, clinicians, and policymakers. Additionally, it can guide the development of more effective therapies for individuals who respond less favorably. To the best of our knowledge, no studies have comprehensively summarized the evidence on factors associated with the response to these interventions. Therefore, this study aimed to systematically review the factors predicting the change in upper-extremity motor function in response to CIMT or bimanual training in children with CP. We limited the scope of this review to personal and clinical factors because neurophysiological factors are not consistently accessible in clinical practice worldwide. Moreover, only observational assessment tools of upper-extremity motor function were considered because they provide a more objective evaluation than self-reported outcomes, which are more susceptible to social desirability bias.[20]

What this paper adds

- Evidence on factors predicting response to constraint-induced movement therapy (CIMT) or bimanual training remains inconclusive.
- Statistically powered studies predicting response to CIMT or bimanual training are needed.
- The mixed effects of several predictive factors require further investigation.

METHOD

This systematic review followed the methods provided in the Cochrane Handbook for Systematic Review of Interventions,[21] and was reported according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement.[22] The protocol of the review was prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO) (2022 CRD42022309358). Deviations from protocol, with reasons, are presented in Appendix S1.

Research question and eligibility criteria

The research question of this prognostic systematic review was: What are the factors predicting the change in upper-extremity motor function in response to CIMT or bimanual training in children with CP? For that perspective, studies were included if they met the following criteria: (1) at least 50% of the participants were children with CP; (2) at least 50% of the intervention duration involved CIMT or bimanual training; (3) a clinician-based observational assessment tool (excluding self-report tools) measuring upper-extremity motor function was used as an outcome measure; (4) at least one factor (e.g. age, sex, or motor severity) was included as a predictive factor to this upper-extremity motor function outcome. Studies including mixed samples of CP and other diagnoses, without reporting separate results for the CP subgroup, were excluded. No exclusions were made based on study design or language. Studies published in languages other than English or French were translated using DeepL Translator (DeepL SE, Cologne, Germany).

Literature search

The search was conducted with the assistance of a scientific librarian (ML). The search strategy was developed using keywords related to 'cerebral palsy', 'constraint-induced movement therapy', and 'bimanual training'. It was then adapted for each database, including PubMed, Cochrane, Embase, Scopus, CINAHL, and PEDro (see Table S1 for details). The bibliographic references of the studies included in the review were also examined to identify additional relevant articles. The full search strategy for each database was initially conducted in January 2022 and updated in July 2025.

Study selection and data extraction

The references from the databases were extracted to the Rayyan online software (https://www.rayyan.ai/). Two independent authors (ESS and ED) removed duplicates and conducted the first screening based on the titles and abstracts of the studies. Afterward, they completed the screening phase based on the full text of the articles. The two authors met to discuss discrepancies at the end of each screening phase.

The first author (ESS) performed the data extraction, which was double-checked by the other authors (ED, ECZ, CH, and TFA). The extracted data encompassed study type, sample description (including age, sex, and type of CP), intervention details and dosage, predictive factors, upper-extremity motor function outcomes, statistical analyses performed, and key findings.

Risk of bias assessment

Risk of bias in the studies included in this review was assessed using the Downs and Black Scale, a valid and reliable tool for evaluating both randomized and non-randomized study designs.[23] This 27-item scale assesses four domains: (1) reporting quality (10 items); (2) external validity (three items); (3) internal validity (13 items); and (4) statistical power (one item). The total score ranges from 0 to 28 and is interpreted as follows: excellent (26–28 points); good (20–25 points); fair (15–19 points); and poor (≤ 14 points).[24] Two authors (ESS and GE) independently conducted the assessment and later met to resolve any discrepancies.

Data analysis

Because of the heterogeneity in outcome measures selected as the dependent variable and the statistical analyses used in the studies included in this review, the synthesis was conducted according to the Synthesis Without Meta-analysis (SWiM) guidelines.[25] First, the studies included were grouped according to each extracted predictive factor. Second, vote counting based on the direction of effects method was used to estimate the effect of each predictive factor.[26] This approach was chosen because of considerable inconsistencies among studies in reporting effect estimates or statistical significance using p-values.[26] For this work, vote counting compares the number of studies reporting a positive association between outcome and upper-extremity motor improvement versus those reporting a negative association, grouping studies based on the direction of the effect rather than the statistical significance reported by the studies.[26] Consequently, studies that did not report the direction of the effect were excluded from the synthesis. Regarding the quantitative nature of the predictive factor, the direction of the effect was considered 'positive' when better performance in the predictive factor correlated with greater improvements in upper-extremity motor function. Conversely, a 'negative' association indicated that better performance was linked to smaller improvements. In studies with multiple dependent variables, we focused on the Assisting Hand Assessment because it has been reported as the most reliable upper-extremity motor outcome measure in children with unilateral CP and was the most used across studies.[27] The Peabody Developmental Motor Scales was considered in one study,[28] and the use of ratio metric from accelerometry in another.[29]

No conclusions were drawn for the predictive factors examined in only one study. Three authors (ESS, ECZ, and CH) independently conducted the data synthesis and then discussed and finalized it in plenary sessions.

Lastly, we used the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach to assess the certainty of the evidence for the following outcomes at the end of the intervention: baseline motor outcomes; age; behavior; sex; affected side; somatosensory deficits; and the interaction between age and baseline motor outcomes.[30] This method allowed us to assign a level of evidence—high, moderate, low, or very low—based on study limitations, inconsistency, indirectness, imprecision, and publication bias. For each domain, the certainty of evidence was downgraded by one level for serious concerns and by two levels for very serious concerns.

For outcomes where a pooled analysis was available for more than three studies, we conducted a sensitivity analysis to assess the robustness of the decision we made to include studies with fair methodological quality.

In the vote counting process, we observed that studies reporting no statistically significant effect of the predictive factor were more likely to omit statistics on the direction of the effect. Therefore, Table S2 summarizes the studies according to the reported significance of the predictive factor.

RESULTS

Study selection

The search strategy identified 4317 records. After removing 2002 duplicates, title and abstract screening resulted in 174 eligible records. After a full-text review, 23 articles were included in the review. The study selection process is illustrated in Figure S1.

Study characteristics

The characteristics of the studies are presented in Table S3. The studies were mostly randomized controlled trials (14 of 23 studies) conducted in several countries from four continents (Europe [11 studies], North America [eight studies], Asia [three studies], and Australia [two studies]). Sample size varied between 11 and 96 participants, with a pooled total of 937 participants. Participants' age ranged from 13 weeks to 16 years. Almost all studies (22 of 23 studies) included children with unilateral CP and only one included both unilateral and bilateral CP.[31] Most children were classified in levels I to III on the Manual Ability Classification System (reported in 7 of 11 studies) and levels I and II on the Gross Motor Function Classification System (reported in 3 of 4 studies). The most common intervention was CIMT (13 of 23 studies). Five studies combined CIMT with bimanual training, three studies compared bimanual training to CIMT, one study implemented bimanual training alone,[29] and another incorporated both bimanual and locomotor training.[32] The upper-extremity motor outcomes used as the dependent variable were predominantly the Assisting Hand Assessment (12 of 23 studies), followed by the Jebsen–Taylor Test of Hand Function (6 of 23 studies).

The quality of the studies, assessed using the Downs and Black Scale, ranged from poor to good (see Table S4 for details). Eight studies had good methodological quality, 14 had fair quality, and one had poor quality. The most frequently unmet items of the Downs and Black Scale in the studies were: item 8 (reporting of adverse events, 5 of 23 studies); items 11 and 12 (sample representativeness in relation to the entire population, 0 of 23 studies for both); item 13 (representativeness of treatment as the most frequently received intervention, 3 of 23 studies); item 14 (blinding of participants to the intervention, 0 of 23 studies); item 22 (simultaneous recruitment of different groups, 4 of 23 studies); and item 24 (concealment of randomization from patients and staff, 9 of 23 studies) (Table S4).

Factors associated with changes in upper-extremity motor function

The results of the individual studies on the predictive factors associated with changes in upper-extremity motor function are presented in Table S5. Tables 1 and 2 summarize the findings on predictive factors according to the vote counting method (Table 1) and the certainty of the evidence (Table 2). Presentation of the predictive factors is structured according to the number of studies performed, from the most to the least studied. The effects of predictive factors on upper-extremity motor function immediately after therapy and at the follow-up are reported in the corresponding tables (Tables 1, S2, and S5). For clarity, only the immediate post-therapy results are presented in this article because the follow-up findings were comparable and derived from fewer studies.

Baseline motor outcomes

Baseline motor outcomes were primarily assessed using the Assisting Hand Assessment (11 studies), and the Jebsen–Taylor Test of Hand Function and Manual Ability Classification System (five studies each). Additionally, 14 studies used the baseline score of the same dependent variable of upper-extremity motor function.

Immediately after the intervention, 19 studies assessed the effect of baseline motor outcomes on changes in upper-extremity motor function.[14–17,29,31,33–45] Ten studies reporting the direction of the effect were included in vote counting,[14,17,29,34,35,37,40,43–45] with a pooled sample size of 312 children. The methodological quality of the studies was rated as fair (six) and good (four). The proportion of studies reporting larger improvement in children with lower baseline motor outcome was 60% (95% confidence interval [CI] = 31.27–83.18, $p = 0.75$).

Overall, this led to the conclusion that there may be little to no consistent negative association between baseline motor impairments and changes in upper-extremity motor function after CIMT or bimanual training, although the results are uncertain (very low level of evidence; Table 2).

Sensitivity analysis

Exclusion of six studies with fair quality[14,29,37,43–45] left four studies (all with good quality). Pooled analysis of these studies showed a similar effect (p = 75%, 95% CI = 30.01–95.44, $p = 0.63$).

Age

Immediately after the intervention, 19 studies assessed the effect of age on changes in upper-extremity motor function.[14–17,28,29,31,33,34,36–43,45,46] Nine studies reporting the direction of the effect were included in vote counting[14,17,28,29,38,39,41,43,46] with a pooled sample size of 385 children. Methodological quality was judged as fair (seven studies) and good (two studies). The proportion of studies reporting larger improvement in older children was 55.56% (95% CI = 26.66–81.12, $p = 1$).

Overall, this led to the conclusion that there may be little to no consistent positive association between age and changes in upper-extremity motor function after CIMT or bimanual training, although the results are uncertain (very low level of evidence; Table 2).

Sensitivity analysis

Exclusion of seven studies with fair quality[14,28,29,38,39,41,43] left two studies (all with good quality). Pooled analysis of these studies showed a different direction of effect, but still not significant (p = 100%, 95% CI = 34.23–100, $p = 0.5$).

Behavior

Children's behavior was assessed using the number of redirections during assessment,[15,35] restraint time,[17,31] and the Dimension for Mastery Questionnaire.[33,37]

Immediately after the intervention, six studies evaluated the effect of behavior on changes in upper-extremity motor function.[15,17,31,34,35,38] Three studies reporting the direction of the effect were included in vote counting,[31,34,35] with a pooled sample size of 93 children. Methodological quality was rated as poor (one study) and good (two studies). The proportion of studies reporting larger improvement in children showing high adherence was 66.67% (95% CI = 20.77–93.85, $p = 1$).

Overall, this led to the conclusion that there may be little to no consistent positive association between adherence and changes in upper-extremity motor function after CIMT or bimanual training, although the results are uncertain (very low level of evidence; Table 2).

TABLE 1 Vote counting summary of the associations between predictive factors and upper-extremity motor function changes according to Cochrane guidelines[26].

Factor	Studies	Significant association		Statistics
Immediately after the intervention				
Baseline motor outcome	10[14,17,29,34,35,37,40,43–45] $n = 312$	Positive association	4[34,37,43,44]	Probability of larger improvement in children with lower baseline motor outcome (negative association) = 60%, 95% CI = 31.27–83.18, $p = 0.75$
		Negative association	6[14,17,29,35,40,45]	
Age	9[14,17,28,29,38,39,41,43,46] $n = 385$	Positive association	5[14,29,39,41,43]	Probability of larger improvement in older children (positive association) = 55.56%, 95% CI = 26.66%–81.12%, p-value = 1
		Negative association	4[17,28,38,46]	
Behavior	3[31,34,35] $n = 93$	Positive association (with high adherence)	2[31,35]	Probability of larger improvement in children showing high adherence = 66.67%, 95% CI = 20.77–93.85, $p = 1$
		Negative association (with high motivation)	1[34]	
Sex	1[44] $n = 20$	Female	1[44]	NA
		Male	–	
Affected side	None for vote counting			NA
Somatosensory deficit (tactile deficits, stereognosis, proprioception)	None for vote counting			NA
Cognitive deficit	None for vote counting			NA
Interaction between age and baseline motor outcome	2[15,41] $n = 75$	Younger age + lower baseline motor outcomes (high changes)	1[41]	NA
		Younger age + higher baseline motor outcomes (higher changes)	1[15]	
Interaction between age and behavior	1[15] $n = 20$	Younger age + high adherence (high changes)	1[15]	NA
At follow-up				
Baseline motor outcome	4[14,17,32,37] $n = 155$	Positive association	1[37]	Probability of larger improvement in children with lower baseline motor outcomes (negative association) = 75%, 95% CI = 30.06–95.44, $p = 0.63$
		Negative association	3[14,17,32]	
Age	4[14,17,28,32] $n = 144$	Positive association	1[14]	Probability of larger improvement in children with lower baseline motor outcomes (negative association) = 75%, 95% CI = 30.06–95.44, $p = 0.63$
		Negative association	3[17,28,32]	
Affected side	1[47] $n = 45$	Left	–	NA
		Right (not responders)	1[47]	
Behavior (adherence)	None for vote counting			NA
Sex	None for vote counting			NA
Somatosensory deficit (tactile and stereognosis deficits)	None for vote counting			–
Cognitive deficit	None for vote counting			–
Stroke type according to the affected side	1[47] $n = 45$	Arterial stroke + left-side-affected (responders)	1[47]	–

Abbreviation: CI, confidence interval.

Sex

Immediately after the intervention, six studies explored the effect of sex on changes in upper-extremity motor function.[29,33,39,41,42,44] Only one study of fair methodological quality reported the direction of the effect in favor of females.[44] The remaining five studies of fair methodological quality reported no association between sex and changes in upper-extremity motor function (Tables 2 and S2).

Overall, this led to the conclusion that there is high uncertainty regarding the association between sex and changes in upper-extremity motor function after CIMT or bimanual training (very low level of evidence; Table 2).

TABLE 2 Factors influencing changes in upper-extremity motor function after constraint-induced therapy or bimanual training in children with cerebral palsy in the hospital, home, or clinic (constraint-induced therapy or bimanual training interventions).

Outcome	Absolute effect	Number of participants (studies)	Certainty of the evidence	Comment
Baseline motor outcome	Proportion of studies reporting larger improvement in children with lower baseline motor outcome: 60% (95% CI = 31.27–83.18)	Vote counting: 312 (10)	Very low[a,b,c]	There may be little to no consistent negative association between baseline motor impairments and changes in UE motor function, but the results are uncertain
Age	Proportion of studies reporting larger improvement in older children = 55.56% (95% CI = 26.66–81.12)	Vote counting: 385 (9)	Very low[d,e,f]	There may be little to no consistent positive association between age and changes in UE motor function, but the results are uncertain
Behavior	Proportion of studies reporting larger improvement in children showing high adherence = 66.67% (95% CI = 20.77–93.85)	Vote counting: 93 (3)	Very low[g,h,i,j]	There may be little to no consistent positive association between adherence and changes in UE motor function, but the results are uncertain
Sex	See comment	Vote counting: 20 (1) Narrative synthesis: 207 (5)	Very low[k,l,m]	There is high uncertainty regarding the association between sex and changes in UE motor function One study found positive correlations between female sex and gains on UE motor function scales; three studies reported that sex was not a predictor; one study reported that recovery was not affected by sex; and one study found no significant recovery difference between males and females
Affected side	See comment	Vote counting: 0 (0) Narrative synthesis: 221 (6)	Very low[n,o,p]	There may be no consistent association between the affected side and changes in UE motor function, but the results are uncertain Three studies reported that the affected side was not a predictor; two studies reported that recovery was not affected by side; and one study found no significant motor recovery difference between left-sided and right-sided children with CP.
Somatosensory deficit	See comment	Vote counting: 0 (0) Narrative synthesis: 105 (2)	Very low[q,r,s]	There is high uncertainty regarding the association between somatosensory deficits and changes in UE motor function One study reported that tactile deficits were not a predictor; another study reported no significant interaction between proprioception and UE motor recovery

TABLE 2 (Continued)

Outcome	Absolute effect	Number of participants (studies)	Certainty of the evidence	Comment
Interaction between age and baseline motor outcome	See comment	Vote counting: 75 (2)	Very low[t,u,v,w]	There is high uncertainty regarding the interaction between age and baseline motor outcomes in predicting changes in UE motor function One study found larger improvement in younger children with lower baseline motor outcomes; another study found larger improvement in younger children with higher baseline outcome

[a]Downgraded one level for risk of bias due to fair (six studies) and good (four studies) methodological quality, as assessed with the Downs and Black Scale.

[b]Downgraded one level for inconsistency due to heterogeneity because four studies found a positive association whereas six studies found a negative association.

Certainty of evidence was not downgraded further down for imprecision (even if the effect was not significant); as with the vote counting method, heterogeneity always leads to imprecision.

[c]Downgraded one level for indirectness because most of the included studies were not primarily designed to answer our research question.

[d]Downgraded one level for risk of bias due to fair (seven studies) and good (two studies) methodological quality, as assessed with the Downs and Black Scale.

[e]Downgraded one level for inconsistency due to heterogeneity because five studies found a positive association, whereas four studies found a negative association.

Certainty of evidence was not downgraded further down for imprecision (even if the effect was not significant); as with the vote counting method, heterogeneity always leads to imprecision.

[f]Downgraded one level for indirectness because most of the studies included in the review were not primarily designed to answer our research question.

[g]Downgraded one level for risk of bias due to poor (one study) and good (two studies) methodological quality, as assessed with the Downs and Black Scale.

[h]Downgraded one level for inconsistency due to heterogeneity because two studies found a positive association, whereas one study found a negative association.

[i]Downgraded one level for imprecision because of the limited sample (93 participants, 3 studies).

[j]Downgraded one level for indirectness because most of the included studies were not primarily designed to answer our research question.

[k]Downgraded one level for risk of bias due to fair (six studies) methodological quality, as assessed with the Downs and Black Scale.

[l]Downgraded one level for imprecision due to the limited sample (20 participants, 1 study) for vote counting.

[m]Downgraded one level for indirectness because most of the studies included in the review were not primarily designed to answer our research question.

[n]Downgraded one level for risk of bias due to poor (one study), fair (four studies), and good (one study) methodological quality, as assessed with the Downs and Black Scale.

[o]Downgraded one level for imprecision because of the limited sample (0 participants, 0 studies) for vote counting.

[p]Downgraded one level for indirectness because most of the studies included in the review were not primarily designed to answer our research question.

[q]Downgraded one level for risk of bias due to fair (one study) and good (one study) methodological quality, as assessed with the Downs and Black Scale.

[r]Downgraded one level for imprecision because of the limited sample (0 participants, 0 studies) for vote counting.

[s]Downgraded one level for indirectness because most of the included studies were not primarily designed to answer our research question.

[t]Downgraded one level for risk of bias due to fair (both studies) methodological quality, as assessed with the Downs and Black Scale.

[u]Downgraded one level for imprecision due to the limited sample (75 participants, 2 studies) for vote counting.

[v]Downgraded one level for indirectness because the included studies were not primarily designed to answer our research question.

[w]Downgraded one level for inconsistency due to heterogeneity because one study found larger improvement in younger children with lower baseline motor outcomes. whereas another found larger improvement in younger children with higher baseline outcomes.

Abbreviations: CI, confidence interval; CP, cerebral palsy; UE, upper extremity.

Affected side

Immediately after the intervention, six studies assessed the effect of the affected side on changes in upper-extremity motor function.[15,29,31,33,39,42] None reported the direction of the effect for vote counting. The studies were of poor (one), fair (four), and good (one) methodological quality. None reported an association between the affected side and changes in upper-extremity motor function (Tables 2 and S2).

Overall, this led to the conclusion that there may be no consistent association between the affected side and changes in upper-extremity motor function after CIMT or bimanual training, although the results are uncertain (very low level of evidence; Table 2).

Somatosensory deficits

Immediately after the intervention, two studies assessed the effect of somatosensory deficits (tactile and stereognosis,[16,42] and proprioception[16]) on changes in upper-extremity motor function. Neither reported the direction of the effect for vote counting. The two studies were rated as fair (one) and good (one) in methodological quality. Neither reported a significant association between somatosensory deficits and changes in upper-extremity motor function (Tables 2 and S2).

Overall, this led to the conclusion that there is high uncertainty regarding the association between somatosensory deficits and upper-extremity motor recovery after CIMT or bimanual training (very low level of evidence; Table 2).

Interaction between age and baseline motor outcomes

Immediately after the intervention, two studies of fair methodological quality investigated the effect of the interaction between age and baseline motor outcomes on changes in upper-extremity motor function, with a pooled sample size of 75 children.[15,41] One study reported larger changes in younger children with lower baseline motor outcomes,[15] while the other reported larger changes in younger children with higher baseline motor outcomes.[41]

Overall, this led to the conclusion that there is high uncertainty regarding the interaction between age and baseline motor outcomes in predicting changes in upper-extremity motor function after CIMT or bimanual training (very low level of evidence; Table 2).

Factors investigated in only one study

Immediately after the intervention, learning disability,[42] mirror movement,[16] time since the lesion was acquired,[33] birthweight,[34] and the interaction between age and behavior[15] were each explored in one study. Only the interaction between age and behavior[15] was associated to changes in upper-extremity motor function. Younger age with high adherence was associated with larger changes.[15] Lastly, one study explored the effect of the interaction between stroke type and affected side at follow-up.[47] The authors reported larger changes in left-side involvement combined with arterial stroke type.

As those factors were investigated in only one study, no conclusions were reached.

DISCUSSION

This systematic review summarized 23 studies investigating related predictive factors associated with changes in upper-extremity motor function after CIMT or bimanual training in children with CP. To our knowledge, this is the first systematic review on that topic. The 23 articles mostly assessed the effect of children's baseline motor outcomes and age, followed by sex, affected side, and behavior. Other variables, such as somatosensory deficits, learning disability, and mirror movement, were investigated less. There is insufficient evidence to support an association between any of the investigated predictive factors and changes in upper-extremity motor function after CIMT or bimanual training. This discussion addresses the predictive factors evaluated in at least two studies. Factors assessed in only one study (mirror movement, time since the lesion was acquired, topography, and birthweight) need to be explored further.

Most of the studies included in this review were randomized controlled trials, which were not statistically powered to identify predictors of treatment response. Instead, secondary post hoc analyses were conducted to explore potential predictive factors, using different approaches such as linear and binary regression models with cutoff values for the dependent variable. These methodological limitations weakened the overall strength of the evidence, as reflected in the GRADE assessment, and highlight the need for future studies specifically designed to evaluate predictors of response to CIMT and bimanual training. Such research is particularly important given the clear evidence of interindividual variability in treatment response, despite the strong recommendations for both therapies.[14,17,42]

One might have expected that children with lower baseline motor outcomes would have greater potential for improvement compared to those with higher baseline outcomes. However, it is also possible that children with lower baseline motor outcomes engage in fewer repetitions of task practice compared to those with higher baseline outcomes. Repetitive task practice is a key principle of motor learning, which is incorporated in both therapies.[7,8] Consequently, these opposing effects of baseline motor outcomes could potentially counterbalance their influence on changes after the interventions.

Regarding children's age, based on young children exhibiting a higher degree of brain plasticity, it would have been expected that early intervention could result in larger responses to therapies like CIMT and bimanual training.[48,49] However, both therapies are generally oriented toward functional goals defined in collaboration with children and their parents.[7,8] Therefore, older children might be more aware of the reasons for their participation and exhibit greater engagement in the therapies. In motor learning, active engagement of the learner is crucial.[50] Thus, this high level of engagement from older children might compensate for the lower potential for neuroplasticity, making age an unreliable predictor of changes after the therapies. Notwithstanding, the contralateral development of the corticospinal tract is activity-dependent, with a more probable bilateral projection of the contralesional corticospinal tract to both the less-affected and more-affected hands in children with severe hand impairments.[51] Therefore, initiating intervention at a very early stage (3–6 months of age) may enhance outcomes by promoting greater use of the more-affected hand during this critical phase of corticospinal tract maturation.[46,51] This could reflect the influence of age (early vs late initiation), as demonstrated by Boyd et al.[46] Nevertheless, further longitudinal studies are required to confirm these findings.

As for the children's behavior, it would be expected that children with less adherence would have lower engagement, leading to smaller improvements. The insufficient evidence to support an association between children's behavior and changes in upper-extremity motor function might be related to the inconsistency in the methods of assessment of children's behavior across studies. The assessment included the number of redirections during assessment,[15,35] restraint time,[17,31] and the Dimension for Mastery Questionnaire.[34,38] While the number of redirections during assessment and restraint time may be more indicative of adherence during the intervention, they may not fully capture adherence across all aspects of the intervention (restraint, task practice, shaping). Additionally, the Dimension for Mastery Questionnaire assessed motivation, which is less directly related to adherence. Future studies could consider incorporating other outcome measures, such as the Therapy Behavior Scale, which better reflect adherence during intervention.[52] Moreover, the impact of adherence on therapy outcomes is more relevant to the CIMT approach. Although CIMT has been adapted for children, for example, by using mitts instead of casting, it is clear that restraining the less-affected upper limb can be potentially invasive.[7] Thus, some children may experience more frustration, leading to a reduced therapeutic response.[35] This CIMT-specific limitation does not apply to bimanual training, which is performed without any restraint.

Results showed inconclusive evidence to support an association between children's sex or the affected side and upper-extremity motor changes. The hypothesis of a possible prognostic effect of sex and affected side were not argued in the studies involved in this review, but the findings are consistent with a previous review in adults with stroke, which showed no association between sex or affected side and upper-extremity recovery.[53]

Somatosensory deficits were assessed in only two studies with inconsistent results. Regarding somatosensory deficits, previous reviews reported a significant association between tactile sensory and stereognosis with upper-extremity motor function in children with CP.[4,54] It would be interesting to explore more extensively the possible impact of somatosensory deficits. However, it is noteworthy that some studies included very young children in whom somatosensory testing is difficult to perform.

The interactions among several factors may be more predictive of changes after the intervention than each factor in isolation. Two studies suggested the combined effects of children's age and baseline motor outcomes, although the results were inconsistent.[15,41] For example, younger children with lower baseline motor outcomes tend to experience greater frustration and lower therapy adherence, resulting in less progress.[15] Future research should further investigate the mixed effects of these factors.

Limitations

It is noteworthy that the studies included in this review primarily focused on children with the unilateral form of CP. Thus, the generalizability of the findings to the bilateral form of CP is limited. Additionally, the high proportion of randomized controlled trials and the small sample sizes in some studies included in this review may have limited the certainty of the evidence. Moreover, the characteristics of the children involved in randomized controlled trials may not fully represent those observed in population-based studies. Differences in intervention characteristics, such as dosage (grouped vs distributed), intervention providers (professional therapists vs parents), and settings (home vs laboratory), might also have affected the reliability of the pooled conclusions. The upper-extremity motor functions used as the dependent variable are mostly clinical-observation-based outcome measures (such as the Assisting Hand Assessment and Box and Block Test). It would be interesting to use outcome measures that assess spontaneous use of the more-affected limb, such as accelerometry, because it is less dependent on the observer and would better reflect the transfer of changes into daily life.[55] Some studies used the same motor outcome measure as both a predictor and a dependent variable, which may have introduced bias into their results. The methodological quality of most studies was rated as fair, which limits the certainty of the evidence.

Future research should further investigate the somatosensory, cognitive, and behavioral factors that influence responses to CIMT and bimanual therapy. Additionally, the effects of interactions between these several factors warrant further exploration.

Conclusions

This systematic review shows that there is inconclusive evidence to support an association between predictive factors such as baseline motor outcome, age, sex, and affected side and changes in upper-extremity motor function in response to CIMT or bimanual training. Future statistically powered exploratory studies are needed to identify predictive factors for these well-recommended interventions.

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DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

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SUPPORTING INFORMATION

The following additional material may be found online:
Appendix S1: Deviations from protocol.
Appendix S2: Articles excluded at the full-text stage.
Figure S1: Flowchart of the systematic review.
Table S1: Search strategies.
Table S2: Summary of the significant associations between the predictive factors and changes in the upper-extremity motor function as reported in the studies.
Table S3: Study characteristics.
Table S4: Black and Downs checklist items.
Table S5: Study sample characteristics and findings.

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