Effectiveness of motor interventions in infants with cerebral palsy: a systematic review

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ABBREVIATIONS

AACPDM	American Academy of Cerebral Palsy and Developmental Medicine
CIMT	Constraint-induced movement therapy
GAME	Goals, Activity and Motor Enrichment
GRADE	Grading of Recommendations Assessment, Development and Evaluation
ICF	International Classification of Functioning, Disability and Health
NDT	Neurodevelopmental therapy
RCT	Randomized controlled trial
TIDieR	Template for Intervention Description and Replication

AIM To systematically review the evidence on the effectiveness of motor interventions for infants from birth to 2 years with a diagnosis of cerebral palsy or at high risk of it.

METHOD Relevant literature was identified by searching journal article databases (PubMed, Embase, CINAHL, Cochrane, Web of Knowledge, and PEDro). Selection criteria included infants between the ages of birth and 2 years diagnosed with, or at risk of, cerebral palsy who received early motor intervention.

RESULTS Thirty-four studies met the inclusion criteria, including 10 randomized controlled trials. Studies varied in quality, interventions, and participant inclusion criteria. Neurodevelopmental therapy was the most common intervention investigated either as the experimental or control assignment. The two interventions that had a moderate to large effect on motor outcomes (Cohen's effect size>0.7) had the common themes of child-initiated movement, environment modification/enrichment, and task-specific training.

INTERPRETATION The published evidence for early motor intervention is limited by the lack of high-quality trials. There is some promising evidence that early intervention incorporating child-initiated movement (based on motor-learning principles and task specificity), parental education, and environment modification have a positive effect on motor development. Further research is crucial.

Cerebral palsy (CP) is the most common physical disability of childhood, with a worldwide prevalence of 2.1 per 1000 live births.[1] The impairments of CP always involve motor function, while cognitive and sensory impairments often co-occur. By definition, CP starts early in infancy because of a lesion or injury to the developing brain,[2] and it is generally accepted that targeted intervention for children with CP should start early, in the period of rapid neural development.[3,4]

Lesions of either the brain or spinal cord during fetal and neonatal development may dramatically alter the formation and function of sensorimotor pathways, depending on the extent, location, and timing of the lesions.[5] Lack of movement and reduced neural drive in sensorimotor pathways can negatively impact neural circuit development and skill acquisition, whereas normal activity provides a substrate for circuit refinement and plasticity.[6,7] Evidence now exists that the corticospinal system, a major circuitry for skilled motor behaviours, is already active and shaping spinal circuits by the late prenatal period but that these dynamics are derailed by prenatal to postnatal insults.[6] Therapeutic interventions that motivate movement are potential substrates for driving these circuits during their most dynamic phase of plasticity.[6,8]

Therapeutic interventions for children with CP broadly encompass the breadth of the International Classification of Functioning, Disability and Health (ICF). Intervention aims to address body function/structure deficits, minimize activity limitations and improve functional skills, and encourage participation in age-appropriate settings. In the early years, intervention focuses on the promotion of milestone attainment across all affected developmental

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domains. Motor interventions targeting fine and gross motor skills are often initiated for infants at risk of, or diagnosed with, CP.

Knowledge about effective motor interventions in older children with CP has increased during the past 10 years (Novak et al.[9]) with high-level evidence available particularly for upper-limb motor interventions.[10] Although systematic reviews about the effectiveness of a variety of motor interventions for older children with CP abound, most reviews of motor interventions are not specifically of young infants and toddlers with CP. Rather, they report on heterogeneous groups of 'at risk' infants, and results reported to date show very limited effect. The systematic review and meta-analyses by Spittle et al.[11] supported the idea that early intervention programmes improve the cognitive outcomes of preterm infants; however, any advantages in motor outcomes were minimal and were not sustained into the school years. An earlier review of the effects of early intervention on motor development of high-risk infants reported mixed results, with very few studies reporting benefits of the experimental intervention.[12] Infants included in the review were at various levels of risk of developmental delay, with most individual study samples including infants with typical outcomes. Only four of the 34 included studies in this review were confirmed samples of infants with CP.

Since children with CP reach 90% of their gross motor potential by age 5, with most potential achieved in the first 2 years,[13] current evidence summaries specifically for infants and toddlers with CP are important for clinicians in order to provide effective motor interventions. Previous studies with wide age ranges of children with CP do not help to determine the specific effects for infants under 2 years of age who may be included in the sample. Given that the first 2 years are regarded as a critical period for development of the corticospinal tract, activity-based interventions during this period[14] are vital for optimizing outcomes.

To date there has been no systematic review of the effectiveness of early motor interventions with inclusion criteria limited to infants at the highest risk of CP or with a diagnosis of CP. With increasing use of sensitive tools including magnetic resonance imaging and the General Movements Assessment, earlier identification of those infants with CP and at the highest risk of it is now possible.[15] The aim of this systematic review is to evaluate the evidence for the effectiveness of motor interventions for infants aged 0 to 2 years with CP or at very high risk of it.

What this paper adds

- Updated review of early motor intervention studies of infants with cerebral palsy found evidence of efficacy was weak.
- Promising approaches involve child-initiated movement, task specificity, and environmental modification.

METHOD

Search strategy

The method used was a systematic review with reporting according to the preferred reporting items for systematic reviews and meta-analyses statement.[16] A search of six databases (PubMed, Embase, CINAHL, Cochrane, Web of Knowledge, and PEDro) was conducted by two authors (CM and RJ). Dates included were 1980 to December 2014. No limit was placed on article type. Index terms and keywords included cerebral palsy; hypoxic ischemic encephalopathy; hemiplegia; physical therapy; occupational therapy; exercise; movement therapy; motor training, neurodevelopmental therapy; treatment outcome; gait; and age groups. All relevant systematic reviews were manually searched. A second search was completed in August 2015; of the 211 studies identified in this search, two met the eligibility criteria and were included. See Appendix S1 (online supporting information) for search terms by database.

Selection criteria

Selection criteria included: (1) infants between the ages of birth to 2 years diagnosed with CP or at risk of it, with 'at high risk' defined as absent fidgety movements on the General Movements Assessment,[17] or positive brain imaging, or diagnosed hypoxic–ischemic encephalopathy; (2) those infants who received early motor intervention; and (3) an outcome assessment of motor skills/development. Motor intervention is defined as a therapeutic intervention with motor development or skills as one primary outcome. Studies of mixed age groups were included if data of participants aged 0 to 24 months were reported separately within the publication. Exclusion criteria were articles where the primary intervention was medical, pharmaceutical, or surgical, or where the article was not in English.

Selection of studies, data extraction, and quality ratings

Three pairs of reviewers completed study selection, appraisal of study validity, and data extraction. Reviewers scored all steps independently after reliability was determined for each pair and each step. The inclusion of studies was completed from the title and abstract or, when necessary, from the full text article. Disagreements were resolved by the pairs and, if necessary, brought to the larger group for resolution. Study validity was appraised using 17 questions for group designs based on Sackett et al.,[18] PEDro,[19] American Academy of Cerebral Palsy and Developmental Medicine (AACPDM) Systematic Review Methodology,[20] Fetters and Tilson,[21] and 14 questions for single-subject designs developed by the AACPDM. Questions included in the rating scales for the different study designs can be found in Appendices S2 and S3 (online supporting information). Study designs were appraised and assigned a level of design rigor (level I, most rigorous, to level V, least rigorous) according to criteria from the AACPDM Systematic Review Methodology[20] separately for group (Appendix S4, online supporting information) and single-subject (Appendix S5, online supporting information) designs. Data extraction was completed using a form that was designed and pilot tested by the authors before establishing reliability for the data extraction process (Appendix S6,

online supporting information). Authors were contacted for additional information as necessary for complete and uniform data extraction across studies.

Data analysis

Characteristics of the interventions in the included studies were categorized according to all outcomes across the domains of the ICF. A descriptive summary of the results of the individual studies was compiled for all outcomes. For motor outcomes, we computed the effect size (Cohen's *d*)[22] for each of the level II studies at all time points for the primary motor measure. The effect size expresses the magnitude of the effect of the intervention regardless of statistical significance. Cohen suggests $d=0.2$ is a small effect, 0.5 is a medium effect, and 0.8 is a large effect size. The quality and strength of recommendation of the entire body of evidence was evaluated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system.[23]

RESULTS

The results of the search and extraction of studies are included in Figure 1. A total of 4343 articles were identified, with 3196 remaining after duplicates were removed. Forty-eight conference abstracts without articles were removed. There were 2887 articles eliminated, including narrative reviews and opinion pieces, from title and abstract review, with the remainder of 225 articles eliminated after full text review. A total of 36 articles representing 34 studies were included in this systematic review. Studies where data were reported in more than one publication were considered single studies.[24–27]

Tables SI and SII (online supporting information) contain the characteristics of all included studies. These 34 studies included 10 randomized controlled trials (RCTs), 4 cohort, 10 single-subject design, and 10 case studies or case series designs. There were no level I, 10 level II, 1 level III, 13 level IV, and 10 level V studies (Tables SI and SII). Appraisal scores ranged from 3/17 to 15/17) for group studies (Appendix S4) and 4/14 to 11/14 for single-subject designs (Appendix S5).

Considered collectively using GRADE methodology, the body of evidence was graded as low quality.[23]

Level II and III included studies

A total of 379 infants participated in the 10 level II studies, with sample sizes ranging from 10[28] to 105[29] participants. The single level III study[35] included a further 23 infants with CP for a total of 402 participants in level II and III studies. The median sample size across all level II and III studies was 26.

Six of the studies[24,29–33] started intervention during the first 4 months of life with infants at high risk of CP, and the remaining four studies[26,28,34,35] enrolled participants who were at least 12 months of age and with a confirmed diagnosis of CP. Only one study[36] had a diverse age group and enrolled children between 6 months and 2 years with a formal diagnosis of CP. The rate of confirmed diagnosis of CP at the final assessment point ranged from 22% (Hielkema et al.[24]) to 77% (Morgan et al.[32]). One study did not report the number of infants with CP, as infants were only 6 months corrected age at the conclusion of the study.[33]

Both duration and intensity of intervention were variable across the studies. Duration of intervention ranged from 6 weeks[34] to 12 months.[26,29,30,35] Intensity of intervention ranged from monthly home visits over 12 months[31] to intensive inpatient rehabilitation provided 6 days per week for 6 weeks.[34] Most studies provided weekly or fortnightly sessions.

Neurodevelopmental therapy (NDT) was the most commonly studied intervention either as the experimental or control assignment. Four studies[24,26,35,36] compared NDT with another intervention, and one compared NDT plus electrical stimulation with NDT alone.[34] One study[28] compared two different intensities of NDT, and one study[29] compared early NDT with late NDT. One study[30] compared a curriculum-based early intervention programme (Curriculum and Monitoring System) with standard care, and one study[32] compared an early intervention programme based on the Neurobehavioral Assessment Scale with standard care. The study by Campbell et al.[31] compared a kicking and treadmill intervention with standard care, and the study by Morgan et al.[32] compared an environmental enrichment intervention, 'Goals, Activity and Motor Enrichment' (GAME), with standard care.

The interventions described within the studies were diverse and multifaceted. Table I lists the components of the interventions as described in the level II, III, and IV studies, and categorizes them according to the ICF. The components are defined in the legend of the table, and were identified by descriptions of the intervention within each paper, and author group consensus of the appropriate classification in the table. The most frequently listed component was parent education, listed in eight out of the 11 level II/III studies. No studies listed a component that could be classified at the ICF participation level.

Outcomes were assessed across the other domains of the ICF, with measures of activity most commonly assessed. All studies evaluated motor outcomes but different measures were used. The psychomotor scales of the Bayley Scales of Infant Development were used in three studies.[26,30,33] A further three studies used the criterion-referenced Gross Motor Function Measure as the motor measure.[28,34,36] The Alberta Infant Motor Scale and the Peabody Developmental Motor Scales were each reported in two studies.[25,31,32,35] The Griffiths Developmental Assessment and the Infant Motor Profile were each used in one study.[24,29] Five studies assessed infant cognition using either the Bayley Scales of Infant Development or the Griffiths Developmental Assessment.[25,26,29,30,33] Goal-setting tools, including the Canadian Occupational Performance Measure, were only used in one study,[32] and one study[25]

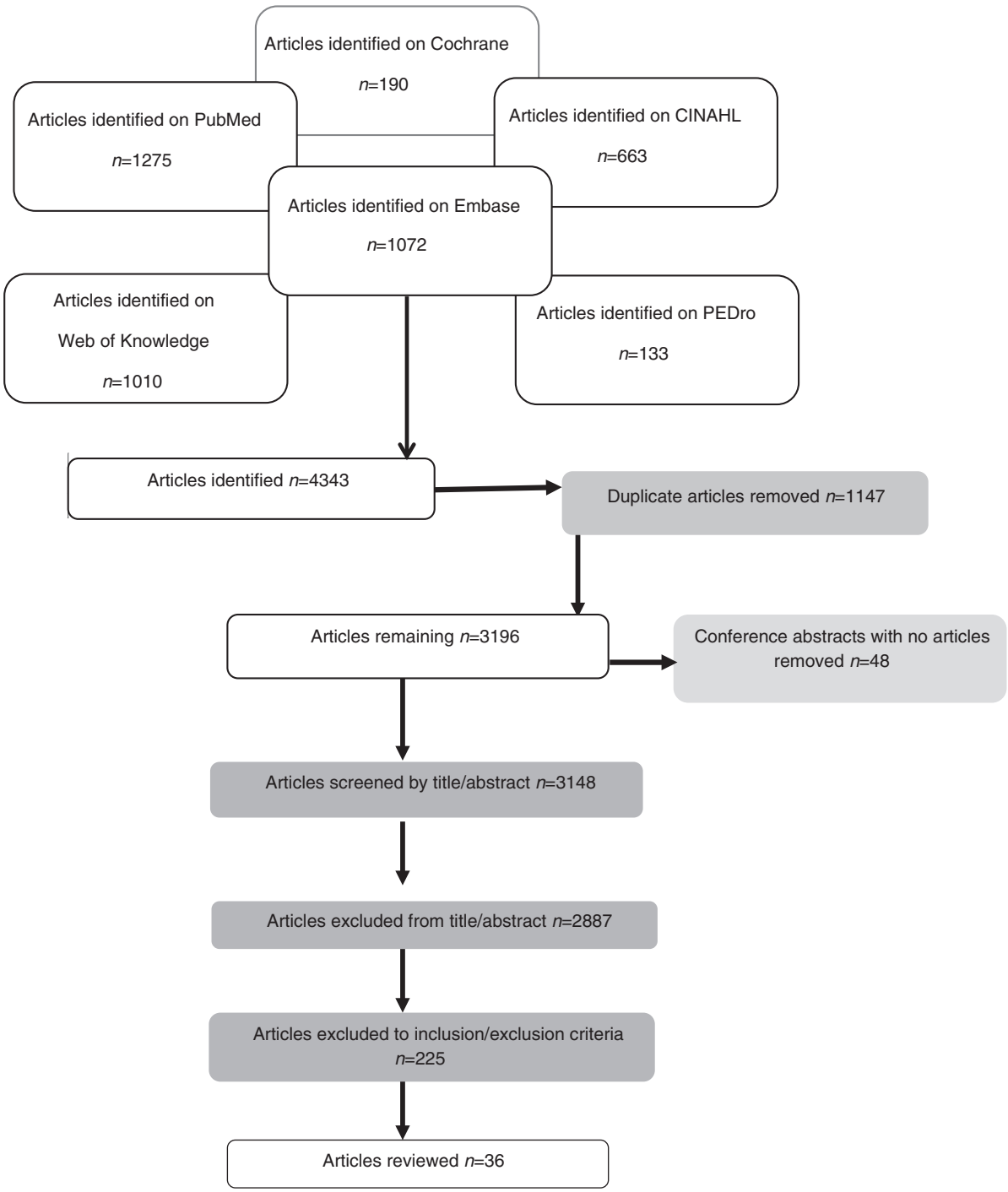

Figure 1: Flow diagram of search and extraction of studies.

used the Pediatric Evaluation of Disability Inventory to evaluate child functional ability.

Measures of contextual factors were included in four studies.[27,30,32,33] Two studies[27,32] assessed the quality of the home environment using the Home Observation Measurement of the Environment, and three[30,32,33] assessed aspects of parent well-being including measures of stress and anxiety. Only one study[27] assessed adaptive behaviour and used the Vineland Scales for this purpose.

Effects of intervention: motor: The level II studies were considered too heterogeneous to combine into a meta-analysis. There were four studies[26,32,34,36] that reported statistically significant between-group differences in motor outcomes at the end of the intervention period

Table I: Components of interventions

ICF	Body structure/function		Body structure/function/activity	Activity				Participation	Context		
Therapeutic component	Inhibit abnormal movement pattern	Facilitate normal movement pattern	Physical guidance	Child-initiated movement	Task-specific training	Developmental progression	Motor exploration/ variability		Parent education	Environment modification	Social scaffolding
Level II and III studies											
CAMS[30]					✓	✓			✓		
COPCA[24,25]				✓			✓		✓		
Developmental skills[36]					✓	✓			✓		
EIP (NBAS+NDT)[33]	✓	✓	✓						✓	✓	
E-stim+NDT[34]	✓	✓	✓								
GAME[32]				✓	✓		✓		✓	✓	✓
Kicking+treadmill[31]				✓	✓				✓	✓	
Learningames[26,27]				✓	✓	✓			✓	✓	
NDT[24–26,28,29,34–36]	✓	✓	✓		✓[32]				✓[24,32]		
NFDR[36]	✓	✓	✓			✓	✓				
Level IV studies											
Casting: weight bearing[41,47]	✓	✓	✓								
CIMT[37,38,42–44]				✓	✓	✓	✓		✓[35,42]	✓[42]	✓
Mobility training[45]				✓	✓		✓				
NDT[41,47,48]	✓	✓	✓								
Neurobehavioural intervention[39]		✓	✓			✓					
Physiotherapy[49]					✓	✓			✓		
Treadmill[46]		✓	✓		✓						
Vojta[40]	✓	✓	✓						✓		

Parent education: parents are trained in the provision of activities to progress the child in motor abilities. Environmental modification: changing the surroundings of the child to elicit new movements/increase motor behaviours. Social scaffolding: providing social modelling or social reinforcement to increase a motor behaviour. Inhibit abnormal motor patterns: physically guiding or restricting movement that is considered abnormal. Facilitate normal motor pattern: physically guide a movement such that the body segments are normally aligned for the specified activity. Physical guidance: assist a functional movement such that the function is accomplished, without regard to the motor solution. Child-initiated movement: child initiates movement without guidance and encouragement of trial and error. Specific task training: movement task(s) defined by the protocol, with intervention focused on the skills needed for the specific task(s). Developmental progression: approach follows hierarchical pattern in attempt to mimic typical sequence of acquisition of motor milestones. Constraint induced: constraint of the non-impaired arm. Motor exploration/variability: increase the motor repertoire for a motor goal. CAMS, Curriculum and Monitoring system; COPCA, COPing with and CAring for Infants with Special Needs; EIP, Early Intervention Program; ICF, International Classification of Functioning, Disability and Health; NBAS, Neurobehavioral Assessment Scale; NDT, neurodevelopmental therapy; E-stim, electrical stimulation; GAME, Goals, Activity and Motor Enrichment; NFDR, Neurofacilitation of development reaction; CIMT, constraint-induced movement therapy.

(Table SIII). Two of the studies were scored as low quality,[34,36] and two were of moderate to high quality.[26,32] (Appendix S4 contains individual quality scores for each study). Effect size ranged from 0.14 (small) to 0.75 (moderate to high). A positive effect size was demonstrated for the comparison group in three studies,[24,26,30] and a positive effect size for the experimental group in five studies.[29,31–34]

Effects of intervention on non-motor outcomes: Five studies[25,26,29,30,33] measured cognitive outcomes but only the study by Palmer et al.[26] demonstrated significant between-group differences in favour of the *Learningames* intervention after 6 months. Parent well-being outcomes were assessed in three studies, with only one study demonstrating benefit of the early intervention programme on parent anxiety and confidence.[33] One study found a short-term benefit of the early intervention programme on the quality of mother–infant interaction during feeding.[30]

Level IV and V included studies

The 13 level IV studies included three cohort and 10 single-subject designs. There was a total of 130 participants, ranging in age from 5 to 24 months. The most common intervention, used in five studies, was constraint-induced movement therapy (CIMT),[37,38,42–44] followed by three studies that used NDT,[41,47,48] one that used the Vojta approach,[40] one treadmill training,[46] one mobility training,[45] one a developmental programme,[39] and one intensive 'physiotherapy' defined as an eclectic mix of concepts.[49]

All studies reported positive results (Table SII), with the exception of Kinghorn and Roberts,[41] but causal inferences in these cases must be treated with caution because of the lack of comparison with a control, lack of statistical analysis in some studies, and the lack of rigorous measurement tools in many studies to document outcomes.

The 10 level V studies included a total of 24 participants, ranging in age from 3 to 21 months. Five studies examined CIMT,[51–55] two studies were of treadmill training,[50,59] one study examined the Vojta approach,[58] one used intensive motor-learning therapy for infants with CP at GMFCS level V,[56] and one used a ride-on car for early power mobility.[57] All studies reported positive results, but causal inferences in these cases must be treated with caution because of the lack of comparison with a control, and often the lack of valid outcome measures.

DISCUSSION

Overall we found only 34 studies of motor interventions in children below the age of 2 years with or at risk of CP. Of these studies, none were level I, and just 10 were level II. Thus, recommendations for clinical practice are weak. Below we summarize the level II and III studies and describe the intervention approaches that appear most promising and merit further evaluation. We then provide suggestions for future research to disentangle many of the confounding variables identified in this review.

Summary of the evidence from level II and III studies

The body of literature evaluating motor interventions for infants and young children 2 years of age and younger at high risk of or diagnosed with CP is sparse considering the clinical and research interest in early identification and intervention for this population.[3,4,15] Using the GRADE system, the body of evidence was graded as low quality. This means that further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.[23] Although there were 10 RCTs identified, the overall quality of the evidence was downgraded from moderate to low because of methodological flaws in many of the studies. The results of this review are influenced by the heterogeneity among the studies in the descriptions of important variables such as sample characteristics, intervention approaches and parameters, the outcomes evaluated, and the outcome measures used.

Sample characteristics

No study in this review achieved a level I evidence rating, primarily because of small sample sizes, a persistent problem in clinical research in CP.[60,61] Multi-site clinical trials are one solution to this problem.[62] Comparative effectiveness research studies, in which common data elements from many clinical sites are systematically collected, are appearing in CP research and could offer another solution to the methodological challenge of small sample sizes.[63] Other important sample characteristics, such as the ages when infants were recruited, ages at final assessment, and accurate identification of infants with CP, varied considerably among the studies, which made it challenging to compare results across studies.

A particular strength of our review is the stringent inclusion criteria used to define 'high risk of CP' status; many studies that used less predictive and less objective criteria to define 'high risk' status were excluded from this review. The inclusion criteria decreased the probability of including infants initially identified as 'high risk of CP' who had a high likelihood of 'self-righting' and not resulting in an outcome of CP. This group of infants presents a challenge for interpreting intervention studies with positive results because it cannot be determined if the participants' final classification is due to the intervention, the misclassification of initial developmental status of the infants, or a self-righting of their development. Despite the rigorous criteria, most studies in this review that included high-risk infants reported that less than half of the sample eventually received a diagnosis of CP. A multidisciplinary, international panel of researchers, parents, and expert clinicians is currently developing clinical guidelines to standardize the neurological assessment of at-risk infants to more accurately identify infants younger than 2 years of age who are at high risk or who have CP. The use of common guidelines such as this will ensure that intervention studies are evaluating samples of infants with similar characteristics.[64] In addition, more accurate and earlier diagnosis should enable infants at the highest risk of CP to access diagnosis-specific early intervention before severe motor delay is evident.

Interventions

Intervention approaches varied among the studies, even when the interventions were derived from the same conceptual framework. For example, seven studies[24,26,28,29,34–36] included NDT as either the experimental or control intervention, but the descriptions of the actual therapeutic components used in the studies varied (Table I). The challenge of a uniform definition of NDT has been identified previously[65] and complicates interpretation of its effectiveness. It also highlights the limitations of using acronyms such as NDT to describe an intervention without a detailed description of the intervention itself. Interventions need to be clearly described using contemporary terminology, and to include a theoretical or conceptual framework, and a description of the key ingredients of the approach that differentiate it from other interventions.

Most interventions in this body of research were not described in enough detail to ensure accurate replication in future research. Treatment frequency and duration were reported for all experimental interventions, but were absent for the comparison intervention in four studies.[29–31,34] The terms 'standard care' or 'usual care' were used to define the control intervention in four studies;[30–33] however, like NDT, components of 'standard care' and 'usual care' varied considerably among the studies and were often not described in enough detail to allow replication by other researchers.

Table I identifies the underlying components of the interventions described in the studies in this review. The two studies[26,32] with the largest effect sizes used similar intervention constructs that included child-initiated movement, task-specific training, and environmental modification. Their positive results merit further evaluation. These components of intervention have been supported in motor-learning research, specifically in research directed at determining the effects of rehabilitation in adults.[66] The study by Campbell et al.[31] also included these constructs, but treadmill training, another primary intervention component evaluated in this study, does not reflect child-initiated movement. The GAME[32] and *Learningames*[26] interventions both incorporated parent education, as did many other studies. Parent education can represent a range of concepts based on the perspective of the intervention. Interventions focused on child-initiated movement would be more likely to focus parent education on the importance of active movement, in contrast to approaches that emphasize facilitation and inhibition of a child's movement by a therapist or carer.

Lack of sufficient information to replicate intervention protocols is a long-standing methodological concern in rehabilitation.[65,67,68] It impedes future research designed to evaluate the same intervention. It also presents a knowledge translation barrier for clinicians wanting to adopt new intervention ideas into their clinical practice. An international panel of experts and stakeholders has developed a 'Template for Intervention Description and Replication' (TIDieR)[69] to address this replication challenge. The TIDieR checklist consists of 12 items to improve the replicability of interventions. Common use of a checklist such as TIDieR would ensure more accurate replication of studies and allow better identification of common intervention elements across different interventions. Two items in the TIDieR checklist refer to fidelity of treatment. Fidelity of treatment refers both to the degree to which treatment is provided as described and to the degree to which the control and experimental interventions differ in a study. It is an important methodological issue in clinical trials and no study in this review addressed the issue of how fidelity of treatment was ensured or evaluated. Campbell et al.[31] describe the lack of adherence to the intervention frequency as a possible reason for their lack of significant changes with their intervention.

Various intervention approaches were used in the studies. Most studies included therapeutic constructs derived from neuromaturational approaches, despite the lack of strong evidence supporting their effectiveness with older children.[9] This result is surprising considering the current interest in intervention approaches that emphasize functional, activity-based approaches.[9] There may be an assumption, based on tenets of neuroplasticity, that interventions aimed at remediating impairment issues (e.g. muscle tone, reflexes, postural reactions) are more appropriate for infants and more likely to 'normalize' their development. The results of this review do not support this assumption.

However, limited empirical evidence exists to support interventions based on functional, motor-learning approaches for this young population. The interventions described in the four studies reporting significant findings in this group varied in theoretical backgrounds: two[26,32] of moderate to high quality were based on enriched, activity-based approaches; while two[34,36] emphasized neurodevelopmental, postural correction approaches and were of lower methodological quality. The seminal study by Palmer et al.[26] suggests that a developmental learning programme may improve motor function more than NDT. In contrast, Hielkema et al.[24,25] found no differences between traditional infant therapy that included NDT concepts and their child-active COPing with and CAring for Infants with Special Needs (COPCA) programme, which is based on enhancing family participation and encouraging motor development using constructs derived from neuronal group selection theory.

The pilot study by Morgan et al.[32] evaluating the effect of a goal-focused, activity-based environmental enrichment programme reported an improvement of motor function compared with standard care. An enrichment paradigm for infant rehabilitation after brain injury has been advocated by Kolb et al. on the basis of their enrichment studies.[70] Kolb et al. suggest that results from their animal work generalize to some extent to the human infant, and enrichment concepts warrant further investigation in human studies. The absence of level II and III studies evaluating CIMT interventions with this age group is disappointing

considering the documented success of these types of intervention with older children[71] and the current interest in 'baby CIMT'.[72] A 'weak positive'[23] clinical recommendation from the evidence is to continue early motor interventions based on the emerging neuroscience knowledge, our knowledge of intervention effects with older children, and the positive outcomes and trends revealed in this review. The potential benefits of early motor intervention far outweigh the negligible risk of harm.

Outcomes and outcome measures

Outcomes measured were diverse across studies, and all authors used validated measures, although there was not one motor measure common to all studies. Even though family-centred philosophy and the ICF model both espouse the importance of understanding the interactions among developmental domains within a child and the effect of contextual factors on development, only four studies[27,30,32,33] evaluated outcomes representing the ICF components of environmental factors, and none evaluated participation outcomes such as play.

Responsiveness, the ability to detect a minimally important clinical change, was not addressed in any of the studies, and published information about responsiveness with this young age group is not available for any of the motor measures. Clinically important differences that can be attributed to intervention are challenging to determine in infants and young children because of developmental maturation that may be nonlinear. Research evaluating changes in motor scores over time is needed with both high-risk and low-risk groups of infants to aid in interpreting change scores in intervention studies.

Other risks of bias were present in the reviewed studies. All of the studies failed to ensure masking both of participants and of interventionists. The therapist–family–child relationship imperative in most interventions with young infants makes this risk criterion difficult to control and it may be an unrealistic expectation when evaluating the quality of studies assessing motor interventions with this population. Despite the increased availability and knowledge of RCT guidelines such as the Consolidated Standards of Reporting Trials,[73] risk biases such as lack of statistical precision (e.g. confidence intervals, power calculations) and confounding of different doses of intervention frequency and intensity between the experimental and control intervention were identified in this systematic review.

Trends identified from level IV studies

The 10 single-subject design studies varied in terms of interventions evaluated, dosage, and sample sizes. The measures mainly targeted the ICF component of activity. Most studies did not address reliability within all phases. The single-subject design was accurately described in most studies and the dependent variables were operationally well defined. However, many threats to validity remained in most studies, such as use of measures that had not been validated, as well as poorly described interventions. For validated measures, most children improved over baseline, and two studies cited improvement more than expected developmentally. Many studies had unique and individualized measures (e.g. rating of hand position) that were not validated.

By definition, the single-subject design studies do not provide strong levels of evidence in support of efficacy. However, some approaches such as CIMT were adaptations of successful therapies used in older children.[9] The positive outcomes in these studies have provided the basis for larger RCTs currently underway. For example, three studies are listed as 'currently recruiting' for CIMT trials on www.clinicaltrials.gov (two in the USA, one in Sweden[73]), and one trial is listed as active on www.anzctr.org.au in Australia. The mobility-training single-subject design study[45] led to a larger study funded by National Institute on Disability and Rehabilitation Research, which is currently underway. Consistent with the approaches found to be efficacious across all age groups of individuals with CP,[9] the evidence from these single-subject design studies points to the importance of active movement by the participant (task-oriented or motor-learning-based approaches) with high intensity of training. These studies have led to clearly testable hypotheses that can be further evaluated using more rigorous designs.

CONCLUSION

Considering the small sample sizes and the heterogeneity identified in intervention approaches, length of interventions, ages of evaluations, and outcome measures in the studies reviewed, recommendations for clinical practice are weak at best. Intervention approaches that appear promising and merit further evaluation are child-initiated movement, task specificity, and environmental modification. Large RCT or comparative effectiveness study designs with clear replicable descriptions both of experimental and of control interventions are essential to disentangle many of the confounding variables identified in this review.

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The authors have stated that they had no interests that might be perceived as posing a conflict or bias.

SUPPORTING INFORMATION

The following additional material may be found online:

Appendix S1: Search terms by database.

Appendix S2: Quality appraisal form for group studies

Appendix S3: Quality appraisal form for single subject studies.

Appendix S4: Level intervention (group) studies (from AACPDM).

Appendix S5: Level single-subject design studies (from AACPDM).

Appendix S6: Extraction form categories.

Table SI: Characteristics of level II and III studies.

Table SII: Characteristics of level IV and V studies.

Table SIII: Results of level II and III studies.

REFERENCES

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