Efecto de la terapia neonatal en el desarrollo motor, cognitivo y conductual de los recién nacidos prematuros: una revisión sistemática.

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OBJETIVO: Sintetizar la literatura existente y determinar la eficacia de la terapia neonatal, comenzando en la unidad de cuidados intensivos neonatales (UCIN), en los resultados motores, cognitivos y conductuales de los recién nacidos prematuros.

MÉTODO: Se realizaron búsquedas en las bases de datos de ensayos controlados aleatorios o ensayos controlados cuasialeatorios de intervención temprana de terapia directa para lactantes con una edad gestacional de menos de 37 semanas, iniciados en la UCIN y entregados por un terapeuta o padre con apoyo del terapeuta. La calidad se evaluó utilizando la herramienta de evaluación estandarizada de riesgo de sesgo de Cochrane. Las recomendaciones se hicieron utilizando el enfoque de Calificación de Recomendaciones, Evaluación, Desarrollo y Evaluaciones.

Resultados: Quince estudios cumplieron los criterios de inclusión. Los estudios se clasificaron en cuatro categorías de intervención: (1) intervención motora entregada por los padres (PDMI); (2) intervención de control postural administrada por el terapeuta (TDPCI); (3) cuidado del desarrollo; y (4) intervención oromotora. El riesgo de sesgo varió de bajo (10 estudios) a alto (tres estudios) o no estaba claro (dos estudios).

INTERPRETACIÓN: El soporte preliminar indica que el PDMI diario mejora los resultados motores y cognitivos a corto y posiblemente a largo plazo. TDPCI es eficaz para promover ganancias a corto plazo en el desarrollo motor. Los programas de atención del desarrollo diseñados por un terapeuta neonatal parecen ser efectivos para mejorar el comportamiento a corto plazo pero no son concluyentes para los resultados motores y cognitivos o los resultados conductuales a largo plazo. Con respecto a las intervenciones oromotoras, no hay suficiente investigación para confiar en su eficacia para mejorar los resultados del desarrollo.

LO QUE AGREGA ESTE DOCUMENTO: Las intervenciones motoras entregadas por los padres (PDMI) son más efectivas para mejorar los resultados motores y cognitivos que otras intervenciones. El soporte preliminar indica que el PDMI diario mejora los resultados motores y cognitivos a corto y posiblemente a largo plazo. Las intervenciones de control postural administradas por el terapeuta son efectivas para promover ganancias a corto plazo en el desarrollo motor. Los programas de atención del desarrollo diseñados por un terapeuta neonatal son efectivos para mejorar el comportamiento a corto plazo de los recién nacidos prematuros. Se encontró que las intervenciones motoras orales no tienen ningún efecto en la mejora de los resultados del desarrollo

Effect of neonatal therapy on the motor, cognitive, and behavioral development of infants born preterm: a systematic review

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ABBREVIATIONS

CGA	Corrected gestational age
NICU	Neonatal intensive care unit
PDMI	Parent-delivered motor intervention
RCT	Randomized controlled trial
TDPCI	Therapist-delivered postural control intervention

AIM To synthesize the existing literature and determine the efficacy of neonatal therapy, starting in the neonatal intensive care unit (NICU), on the motor, cognitive, and behavioral outcomes of infants born preterm.
METHOD Databases were searched for randomized controlled trials or quasi-randomized controlled trials of direct therapy early intervention for infants with a gestational age of less than 37 weeks, initiated in the NICU and delivered by a therapist or parent with therapist support. Quality was evaluated using the Cochrane standardized risk of bias assessment tool. Recommendations were made using the Grading of Recommendations, Assessment, Development and Evaluations approach.
RESULTS Fifteen studies met the inclusion criteria. Studies were categorized into four intervention categories: (1) parent-delivered motor intervention (PDMI); (2) therapist-delivered postural control intervention (TDPCI); (3) developmental care; and (4) oromotor intervention. Risk of bias varied from low (10 studies) to high (three studies) or was unclear (two studies).
INTERPRETATION Preliminary support indicates that daily PDMI improves motor and cognitive outcomes in the short-term and possibly long-term. TDPCI is effective in promoting short-term gains in motor development. Developmental care programs designed by a neonatal therapist appear to be effective in improving short-term behavior but are inconclusive for motor and cognitive outcomes or long-term behavioral outcomes. Regarding oromotor interventions, there is insufficient research to be confident in their efficacy on improving developmental outcomes.

Preterm birth is a global public health concern with 10% of all births being classified as preterm.[1] Children born preterm, before 37 weeks of completed gestation, are at higher risk of motor, cognitive, and behavioral problems compared to children who are born at term.[2–4] Although advancement in technology has led to an increase in the rate of survival, the rate of disability has been a major challenge with 50% of these infants exhibiting developmental delays in the motor, cognitive, and behavioral domains and diagnoses including cerebral palsy, autism, attention-deficit/hyperactive disorder, blindness, and deafness.[5]

Infants born preterm are also at risk of having developmental coordination disorder, language impairments, problems with social/emotional development, impaired executive functions, and a limited attention span.[6] The risk of developmental impairment in children born preterm increases with decreasing gestational age.[2] Impairments are complex and diverse and impact multiple domains; thus, they restrict participation in the home environment, at school, and in community activities, and ultimately affect overall quality of life.[5]

Basic science and animal research support the need for providing interventions as early as possible to harness the benefits of neuroplasticity.[7,8] Consistent with this goal, part C of the Individuals with Disabilities Education Improvement Act in the USA requires that early intervention services be provided to infants and children with established developmental disabilities from birth to the age of 3 years; in some USA states, it includes children at risk for developmental disabilities.[9] The interventions discussed in this systematic review are provided early, in the neonatal intensive care unit (NICU), and are not covered by the Individuals with Disabilities Education Improvement Act[9] since they are provided under a medical model of intervention. Therefore, we refer to the interventions reviewed as neonatal therapy.

In this review, neonatal therapy is defined as intervention provided by a physical, occupational, or speech

therapist or intervention delivered by a parent guided by a therapist (Table 1). The professional associations for physical therapy, occupational therapy, and speech-language pathology in the USA support that intervention with fragile and highly vulnerable infants in the NICU is a complex area of practice that should be preceded by advanced training.[10–12] Neonatal therapy is typically implemented using dynamic systems theory, synactive theory of development, international classification of functioning and disability, and a family-centered model of care in pediatric rehabilitation.[10,13] These advanced practice areas began to emerge during the early 1970s with the establishment of NICUs, specialized hospital intensive care units designed to support infants born preterm, or those born with birth conditions requiring support beyond what can be provided in the typical hospital nursery.[14,15]

Neonatal therapy interventions are highly specialized and individualized, with attention to promoting long-term development across developmental domains, preventing adverse sequelae, and nurturing the infant–family dyad.[13] Physical, occupational, and speech therapists are part of the multidisciplinary team and are typically involved in the assessment and intervention of infants born preterm and critically ill infants in the NICU.[16–18] Based on the laws and practice acts within each country, referral of infants to neonatal therapy services may be automatic or may need to be made by physicians or other team members. Multiple factors, such as complicated prenatal and birth history, birthweight less than 1500g, lower gestational age at birth, abnormal tone or posturing, congenital malformations, feeding difficulties, sensory impairments, seizures, or prolonged stay in the NICU are deciding factors for initiating referrals to therapy services.[19] However, the delivery of these services depends on the availability of skilled therapists trained in the care of neonates and varies from hospital to hospital based on philosophy, resources, national practice acts, and other considerations.[20]

The rationale for providing neonatal therapy is supported by three ideas:[21] (1) protection of the neonatal brain; (2) optimization of the environment and intervention to promote better developmental outcomes; and (3) support for parents to cope with the challenges of preterm birth and prepare to support infants at risk for developmental delays. First, Protection of the neonatal brain is important because preterm birth may result in direct or indirect brain insult sustained during the prenatal, perinatal, or neonatal period. Direct insult includes an injury to the central nervous system leading to periventricular leukomalacia or cortical lesion, increasing the chances of cerebral palsy. Indirect insult includes hypoxic brain injury, postnatal stroke, and other brain injuries that occur after delivery because of physiological instability. This instability is associated with exposure of the neonatal brain to a stressful environment, pain, position changes, and multiple episodes of handling during a long NICU stay.

Second, optimizing the environment and intervention enhances the ability of the neonatal brain to overcome the brain injury. The period when most infants are in the NICU, 22 to 40 weeks of gestation, is a period of rapid neuroplastic change. Exposure to noxious stimuli and atypical movements likely supports the strengthening of neurological pathways for these behaviors. In contrast, positive neuroplasticity or limiting these negative neuroplastic changes could occur with the support of calming strategies and movements simulating the intrauterine environment. This support may strengthen neuropathways for calming, midline motor patterns, and self-generated movements, which increase the likelihood of average developmental outcomes.[22]

Third, neonatal therapy services can provide support to parents and help them in navigating through the challenges of the unexpected arrival of their child before term,

What this paper adds

- Parent-delivered motor interventions (PDMIs) are more effective in improving motor and cognitive outcomes than other interventions.
- Preliminary support indicates that daily PDMI improves motor and cognitive outcomes in the short- and possibly long-term.
- Therapist-delivered postural control interventions are effective in promoting short-term gains in motor development.
- Developmental care programs designed by a neonatal therapist are effective in improving the short-term behavior of infants born preterm.
- Oral motor interventions were found to have no effect on improving developmental outcomes.

Table 1: Operational definitions

Neonatal therapy	Intervention provided by a physical, occupational, or speech therapist or delivered by parents guided by a therapist
PDMI	PDMI includes teaching a parent or caregiver to provide postural support and opportunities for movement with support during a parent–infant interaction with the goal of increasing infant movement quality and quantity. These interventions are individualized for each infant with the support of a therapist and delivered through a parent–therapist collaboration. It is theoretically based on action perception and dynamic systems theory
TDPCI	TDPCI includes providing postural support and moving the infant in different positions to provide sensory or motor input. These interventions often involve facilitation of movement by incorporating inputs from tactile, vestibular, and somatosensory receptors within the body. Those included in this review are based on NDT/Bobath concept
Developmental care	Developmental care consists of child- and parent-focused interventions that include regulating the environment and activities the infant is exposed to during general caregiving. While developmental care is often considered an NICU-wide framework, in this review developmental care was coordinated or provided by a therapist, meeting the inclusion criteria for this review. Developmental care is based on concepts of synactive theory and family-centered care
Oromotor intervention	Oromotor intervention is used to improve oral feeding in infants born preterm and consists of non-nutritive sucking, oral stimulation, and oral support designed and/or implemented by a therapist

PDMI, parent-delivered motor intervention; TDPCI, therapist-delivered postural control intervention; NICU, neonatal intensive care unit; NDT, neurodevelopmental therapy.

adjusting to the NICU environment, a long-term hospital stay, and the probability of risk of developmental delays. Supporting and engaging parents in the implementation of an intervention program empowers them, which leads to an increase in self-efficacy and a decrease in anxiety and depressive symptoms that have been associated with better developmental outcomes of at-risk infants.[23,24] A Cochrane review on the efficacy of early intervention programs provided in the first year of life concluded that interventions focused on parent–child collaboration had better developmental outcomes compared to when the intervention was solely focused on either parent or infant.[5] Thus, it is imperative to involve parents early on and explain that a developmentally appropriate home environment and sensitive parent–infant relationship can positively impact the infant's ongoing learning experiences and development.[25,26]

There is much variability in neonatal therapy, with models of intervention having a different focus, such as prevention, remediation, or treatment of a specific disability.[27] Heterogeneity also exists in the dose and timing of intervention. Some interventions start as early as a few weeks after birth, while still in the NICU, and continue after discharge,[5] whereas other studies provide intervention only in the NICU. In addition to heterogeneity, a lack of clarity in neonatal therapy research makes synthesizing the findings difficult. The key principles and efficacy of neonatal therapy, specifically provided by physical therapists, occupational therapists, or speech-language pathologists, has not been quantified in a systematic fashion.[5,23,28] Thus, the purpose of this review was to identify and evaluate studies where neonatal therapy was initiated in the NICU, as provided or designed by a physical, occupational, or speech therapist, and report the effect of the intervention on the motor, cognitive and behavioral outcomes.

METHOD

Search strategy

For this systematic review, we followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses[29] (PRISMA) guidelines. The review question and search strategy were based on the Population, Intervention, Comparison, Outcome (PICO) format.[30,31] All clinical trials published in English before 26th February 2018, which included human participants and fitted the inclusion criteria based on population, type of intervention, and reported outcomes, were included in this review. The population was limited to infants born preterm (<37wks' gestation), who received intervention that was initiated in the NICU. Intervention was either delivered directly by a therapist (physical, occupational, or speech-language pathology therapist), or designed by a therapist and delivered by the parent under the supervision of a therapist. Intervention may have been ongoing in the NICU or initiated just before discharge and continued at home or in the community. Studies that reported outcomes of behavior, motor development, and/or cognitive development using standardized assessments, were included. Studies were excluded if 50% of participants were not born preterm; studies were also excluded if they were not available in the English language, did not present the results of original research (e.g. case studies, reviews/commentary), did not include the intervention provided in the NICU, or the study was not a clinical trial or had no comparison group. Studies were also excluded if there was no developmental outcome reported, that is, they reported only biological outcomes such as heart rate, oxygen saturation, weight gain, and length of stay. Studies were excluded if the intervention consisted of only environmental modifications, such as light and sound modifications, multisensory intervention (without active motor engagement), massage, skin-to-skin care, music therapy, use of maternal voice, positioning, or the Newborn Individualized Developmental Care and Assessment Program model of care. These interventions were excluded because they are typically provided using a team approach that is part of routine care. While therapists may support these approaches, they are rarely able to document their participation as a direct service for a specific infant. In addition, drug therapy, genetics, cardiac and chest physiotherapy, interventions focused on breastfeeding, bottle feeding, nutritional or diet therapies, were excluded. Finally, all non-human studies were excluded.

Study selection

Consistent with the PRISMA guidelines, two reviewers independently completed the title and abstract screening based on the inclusion and exclusion criteria. Abstracts were retained for full-text review if the study could not be excluded, appeared to meet the inclusion criteria, or if more information was required to make a decision. Full-text articles were reviewed independently by two reviewers. Disagreements at any stage (title and abstract or full-text screening) were resolved by mutual discussion between reviewers. If the disagreement persisted, a third reviewer resolved the disagreement.

Data extraction

Two reviewers independently extracted data from the studies included after the full-text review. Data extracted from each study included: author(s); year of study; country/region; study design; sample size; participant inclusion/exclusion criteria; gestational age; birthweight; sex; days in the NICU; any brain injury; and parent educational level. Intervention details extracted included: key principles or theoretical background of the experimental and control intervention; personnel delivering the intervention; total number of sessions (in the NICU and at home); frequency; duration of session; period of intervention; adherence; and parental compliance. Outcome information extracted included: outcome measures used; age and time postintervention; and blinding of the examiner. The type of statistical analysis, mean/median (final or change scores), standard error of the mean, SD, confidence intervals, and sample sizes were extracted from each study. Effect size, if

presented, was extracted from the studies; otherwise, Cohen's *d* effect size of the intervention was calculated whenever possible.[32] Studies were categorized as having small ($d \leq 0.2$), moderate ($d \leq 0.5$), or large ($d \geq 0.80$) effect sizes based on Cohen's *d*.[33]

Because of high variability in the type, intensity, duration, and frequency of intervention, and developmental outcome measures, it was not meaningful to perform a meta-analysis. Therefore, the extracted data were synthesized narratively according to the main objective of the review. The studies were grouped into four categories (Table 1) based on the primary conceptual framework of the implemented neonatal therapy. The four categories were identified by the research team after all data were extracted to allow for detailed review and comparison. Through consensus, reviewers identified the primary principles of the neonatal therapy. Studies that included multiple principles were assigned to a category based on the primary focus of the intervention. The data extracted from each individual study were summarized in tabular format for review with general study description (Table S1, online supporting information) and data extracted (Table S2, online supporting information).

Quality assessment

The Cochrane standardized risk of bias assessment tool[34] was used to assess the quality of the studies retrieved. The tool, which is used to assess risk of bias in randomized trials, allows the reviewer to rate the quality of a study by using the ratings of high, low, or unclear to indicate risk of bias in the following seven categories: (1) sequence generation; (2) allocation concealment; (3) blinding of participants and personnel; (4) blinding of outcome assessors; (5) incomplete outcome data; (6) selective outcome reporting; and (7) other sources of bias. Two reviewers independently rated the quality of studies and any disagreements were resolved by mutual discussion or the expert opinion of a third reviewer. Consistent with the requirements of this tool, all categories were rated for each study (Table S3, online supporting information).

Grading of Recommendations, Assessment, Development and Evaluations

The Grading of Recommendations, Assessment, Development and Evaluations (GRADE)[35] system is a criterion standard, evidence-grading tool endorsed by the World Health Organization, which is used to rate both the quality of evidence and the strength of the recommendation for clinical use. The state of evidence for each category was evaluated using the GRADE guidelines (Table 2). The color-coding system used reflects a combination of effect sizes, significant group differences, design and quality of each study, and the strengths or limitations of each study. Like previous research, a stop light color system was used to demarcate the grade rating for each of the categories of intervention.[7] Green was used to identify moderate-to-large effect in studies with low/unclear risk of bias, yellow was used to identify studies with small effect and a low risk of bias or moderate/large effect with a high risk of bias, and red was used to identify studies with no or a negative effect (Table 3).

RESULTS

The initial database searches retrieved 9999 individual papers, 9836 of which were excluded by the title and abstract review. Of the remaining 163 studies used for the full-text review, 15 met the inclusion criteria and 148 were excluded (Fig. S1, online supporting information). Thirteen studies were randomized controlled trials (RCTs), one study was a cluster RCT, and one was a prospective cohort study (Table S1). The studies included in the review were completed in a variety of locations: three from Taiwan;[36–38] three from the Netherlands;[39–41] two from the UK;[42,43] two from the USA;[23,44] and one each from Korea,[45] Japan,[46] Australia,[47] Canada,[48] and Norway.[49] Sample sizes were highly variable across studies ranging from $n=14$ to $n=251$ (Table S1).

Parent-delivered motor intervention

Two studies[23,49] were included in this category; both were RCTs. The main similarity between the studies was the

Table 2: GRADE recommendations for different interventions

PDMI	Conditional recommendation
PDMI may improve motor and cognitive outcomes. It needs to include: 1. child-initiated active movements; 2. active parental participation and implementation at regular intervals; 3. an engaging environment	It is based on limited evidence of moderate quality
TDPCI	Conditional recommendation
TDPCI in the NICU may have a short-term effect on motor development; however, the benefits are not seen if the intervention is primarily provided after discharge	It is based on limited evidence of moderate quality
Developmental care	Conditional recommendation
Developmental care influences short-term behavioral outcomes. There is inconclusive evidence for motor and cognitive development	It is based on limited evidence of moderate quality
Oromotor intervention	There is no adequate evidence to make a recommendation
There is only limited evidence to draw any conclusions	

GRADE, Grading of Recommendations, Assessment, Development and Evaluations; PDMI, parent-delivered motor intervention; TDPCI, therapist-delivered postural control intervention; NICU, neonatal intensive care unit.

Table 3: Overall evidence of the effect of intervention

Intervention type	Risk of bias	Behavior 40–44wks	Behavior 6mo	Behavior 12mo	Behavior 24mo	Motor NICU discharge	Motor ≤6mo	Motor ≥12mo	Motor ≥24mo	Motor 44mo	Cognition NICU dis-char-ge	Cognition 6mo	Cognition ≥12mo	Cognition 24mo	Cognition 44mo
PDMI	Unclear[23]					1.04 [green]	1.2 [green]	1.0 [green]				0.8 [green]	1.0 [green]		
	Low[49]					0.40 [yellow]									
TDPCI	Low[42]						[red]								
	Unclear[44]	[red]				1.43 [green]									
	High[45]					1.47–2.42 [yellow]									
	Low[43]							[red]	[red]						
Developmental care	Low[37]	0.30 [yellow]													
	High[46]	0.7 [yellow]					[red]								
	Low[36,38]	[red]							[red]					0.50 [green]	
	Low[39–41]		0.45 [yellow]		[red]		0.39 [yellow]		0.14 [yellow]	[red]		0.35 [yellow]		[red]	[red]
	High[47]							0.70 [yellow]					0.70 [yellow]		
Oromotor	Low[48]					[red]									

Green, moderate-to-large effect in a low/unclear risk of bias study; yellow, small effect and low risk of bias or moderate/large effect with high risk of bias; red, no effect. NICU, neonatal intensive care unit; PDMI, parent-delivered motor intervention; Blank space, not reported; TDPCI, therapist-delivered postural control intervention.

collaboration between therapist and parent resulting in the parent being actively engaged in providing the intervention. Although the exact activities varied, both included support of midline positioning and active infant movement. Interventions were implemented based on the concept described separately in each paper: Supporting Play Exploration and Early Developmental Intervention;[23] and Mother–Infant Transaction Program and family-centered practice.[49]

The timing and dose of the interventions varied. The Supporting Play Exploration and Early Developmental Intervention[23] was initiated in the NICU with five sessions in the first 21 days of the study. This was followed by phase 2, when parents provided opportunities for the infants for 20 minutes per day, 5 days per week, for 3 months with the ongoing support of a therapist. The intervention focused on promoting motor control through a high dose of practice of infant-directed exploratory behaviors.[23] A Norwegian study evaluated the Mother–Infant Transaction Program and family-centered practice,[49] which is a variation of a neonatal developmental program with a focus on improving parent–infant interactions using postural support and facilitation to promote head control, midline orientation, and muscle balance and activity. Parents were trained during three consultation sessions to implement the intervention for 10 minutes, twice a day, for 3 weeks. The outcome measures employed in these studies included the Test of Infant Motor Performance, Bayley Scales of Infant and Toddler Development, Third Edition, or the Early Problem Solving Indicator.

Two studies[23,49] reported the positive effects of parent-delivered motor intervention (PDMI) on motor outcomes at term, 6 months, and 12 months of corrected gestational age (CGA) with effect sizes ranging from 0.40 to 1.04. One study[23] reported the positive effect of an intervention on problem-solving behavior (cognitive and language development) with a moderate-to-large effect size (0.6–1.3) at 6 and 12 months.

Therapist-delivered postural control intervention

Four studies[42–45] were included in this category. Three studies were RCTs and one study was a prospective cohort study. All four studies employed interventions such as positioning, postural supports, and active and passive movement toward midline. The interventions were therapist-delivered and parents were not actively involved in delivering the intervention or were only minimally involved. The exact timing and dose of intervention varied between the studies. Two studies[44,45] implemented hospital-based interventions, which were discontinued at discharge. In the other two studies,[42,43] the intervention started at the hospital and was continued after discharge. In the study by Weindling et al.,[43] infants were seen by the physiotherapist just before leaving the hospital and the follow-up intervention was carried out by a community physical therapist once a week for 6 months, followed by monthly visits for 3 months, and finally once a month until 1 year of corrected age. In the study by Cameron et al.,[42] the intervention was

provided in the NICU during weekdays by the physical therapist. Parents were involved in weekly meetings and were educated on postural support, behavioral states, and in administering the developmental protocol based on neurodevelopmental therapy (NDT)/Bobath concept. However, no information was provided about the number of sessions completed in the NICU. The follow-up intervention was provided by a primary researcher or community physical therapist based on the individualized needs of the child and parents. Parents were also advised to perform play activities with their child based on the infant's progress and developmental needs. The theoretical approach was based on NDT/Bobath concept and most of the intervention was delivered by the physical therapist during home visits, which is consistent with the other interventions in this category.

One study[44] used the Neonatal Behavioral Assessment Scale and reported no effect on behavioral performance. The two studies that implemented all their care in the NICU[44,45] found significant differences on motor scores of the intervention group at term age, with effect sizes ranging from 1.4 to 2.4. Neither study with intervention and assessments taking place post-NICU discharge found significant differences in motor development at 4 months CGA[42] or 12 and 30 months CGA.[43]

Developmental care

Five studies, including four RCTs[36,37,40,46] and one cluster RCT,[47] were included in this category. The results of these five studies were published as eight papers, of which three[38,39,41] are follow-up studies from the same sample of infants. The studies were based on the concepts of the synactive model of developmental care and family-centered care. The intervention used in these studies was based on exploring the infant's and parent's strengths to encourage optimal behavior, environmental modification, postural control, midline orientation activities, and dyadic parent–infant interaction. While there was some variability in the frequency and duration of sessions, all five studies included a few visits in the NICU with some visits after discharge from the NICU.

Three studies[37,40,46] reported significant differences in behavioral outcomes from term to 6 months of age with effect sizes ranging from 0.30 to 0.72. Two studies did not find any effect on behavior at term[36] and at 24 months[39] of age. In this group of studies, mental development and psychomotor development indexes were reported at 6, 12, 24, and 44 months of age. Positive effects on the mental development and psychomotor development index scores were reported at 6[40] and 12 months[47] of age, with effect sizes ranging from 0.35 to 0.70. No effect was found at 6 months in one study.[46] At 24 months, effects were inconsistent, with one study reporting improved cognitive, but not motor scores on the Bayley Scales of Infant and Toddler Development, Third Edition;[38] the other study[39] reported improved motor but not cognitive scores on the Bayley Scales of Infant Development, Second Edition. However, at 44 months no effect was found on mental development or psychomotor development index scores.[41]

Oromotor intervention

A single study[48] reported the effect of oromotor intervention on motor development. Oromotor intervention was provided by a therapist, twice a day for 10 days to observe the effect on the motor function of infants born preterm. The intervention showed no effect on motor performance measured using the Test of Infant Motor Performance.

Study quality

Risk of bias was low in 10,[36–43,48,49] unclear in two,[23,44] and high in three[45–47] studies (Appendix S1, online supporting information). Major sources of bias included no information regarding allocation, concealment, blinding of participants, and blinding of personnel. Most studies did not report the use of an intention-to-treat analysis. There was also inconsistency in the use of sequence generation. GRADE summaries are reported in Table 2.

DISCUSSION

To our knowledge, this is the first systematic review to evaluate the efficacy of neonatal therapy implemented or designed by a physical, occupational, or speech-language pathology therapist for a parent to deliver. The findings of the systematic review suggest that PDMI neonatal therapy may improve motor and cognitive outcomes in infants born preterm. Therapist-delivered postural control intervention (TDPCI) was found to have a short-term effect on motor development. However, the benefits were not seen if the intervention only had a few NICU visits, with most of the intervention provided after discharge. Developmental care also showed a positive effect on short-term behavioral outcomes but inconclusive evidence for motor and cognitive development. No conclusions can be drawn for oromotor interventions. The results of these four categories are discussed in detail in the following sections.

PDMI may improve motor and cognitive outcomes

Studies done in this category were good-quality studies with the risk of bias rated as low for one study and unclear for the others. Two studies reported positive outcomes on motor and cognitive development (using the Test of Infant Motor Performance and Bayley Scales of Infant and Toddler Development, Third Edition), and early exploratory behaviors. Effect sizes were moderate to high, which advocates the use of the key intervention principles involving parents in motor-based infant engagement to promote the development of infants born preterm. These results are consistent with the Cochrane systematic review by Spittle et al.[5] The results affirm that interventions based on motor learning, task-specific principles with active involvement of the child, parental education, and environmental modifications have a positive effect on motor development.[50] Taken together, this supports the notion that PDMI provided daily is likely to result in short-term gains in motor

development, as shown in green in Table 3. The preliminary efficacy of longer-term motor outcomes at 6 and 12 months was observed in one study,[23] but more long term studies are needed to confirm these findings. Moreover, these results need to be interpreted with caution given the small sample sizes and unclear risk of bias in one study. None of these PDMI studies addressed behavioral changes, thus leaving a gap in our understanding of the role of PDMI in supporting behavioral stability.

TDPCI

The one study of TDPCI[44] that assessed efficacy on behavioral outcomes showed no impact, suggesting the need for more assessment of these outcomes. Two trials[44,45] reported short-term effect on motor development; no long-term effect was observed. However, caution must be used when generalizing results. The trials included in this category had small sample sizes and an unclear-to-high risk of bias,[44,45] with extremely low methodological quality, such as a lack of blinding, intention-to-treat analysis, and concealed allocation. Summarizing evidence in this category suggests that TDPCI provided daily may result in short-term gains in motor development at NICU discharge with little to no gains post-NICU in very-high-risk infants.[21] Long-term data are either not available or suggest a lack of efficacy at 4, 6, and more than 12 months CGA. The results are in agreement with recent literature reporting a lack of efficacy for NDT-based interventions, as well as high ambiguity regarding the details of NDT intervention.[50,51]

Developmental care

Behavioral performance was positively impacted by developmental care interventions focused on parent–child interactions from term age to 6 months of CGA, as highlighted by three studies;[37,40,46] two studies reported no effect at term[36] or at 24 months of CGA.[39] The positive results on behavior can be attributed to parental involvement in the treatment plans, which resulted in improved parent–child interaction leading to better developmental outcomes.[5,52] Caution should be exercised in generalizing the results since there was much heterogeneity in the population and the outcome measures used to assess behavior. One study[46] had a high risk of bias and specifically included infants with brain injuries. Another study[36] did not report a positive effect, which may have been due to the treatment protocol already included in routine practice of care across the participating hospitals, resulting in no effect on behavior between groups. Five studies[37–40,47] examining the impact of developmental care interventions on cognitive and motor outcomes revealed conflicting results; they were of varying quality and associated risk of bias (high, low, and unclear). At 6 months of CGA, one study[40] found a positive effect, whereas another[46] reported that the intervention was not effective. At 12 months CGA, the intervention was found to be effective with a small-to-moderate effect size. Caution should be used in interpreting the positive finding at the 12-month CGA since the study included was a cluster RCT,[47] which is a lower quality of evidence. The overall risk of bias was high for this study, thereby reducing our confidence in the findings. Summarizing the evidence, we can postulate that developmental care programs designed by a neonatal therapist are likely to be effective in improving behavioral outcomes in the short-term, with limited evidence supporting a longer-term effect to 6 months CGA. Efficacy on motor and cognitive outcomes is variable, limiting our ability to draw any conclusion.

Oromotor intervention

The majority of oromotor studies were excluded during the screening process since reported short-term outcomes included frequency of suck, pressure of suck, sucking quality, and weight gain, rather than developmental outcomes. A single study[48] was included in this category and it reported no effect of the oromotor intervention on motor outcomes. Our inability to draw any conclusion can be attributed to the lack of studies of oromotor intervention. Thus, overall, there is limited evidence to draw any conclusion regarding the efficacy of oromotor interventions.

Clinical implications

Because of the limited number of studies included in the review, we could not carry out a meta-analysis to reach a definitive conclusion or provide strong recommendations regarding the effect of neonatal therapy on motor, cognitive and behavioral development. However, from the narrative synthesis, it is clear that neonatal therapy implemented in a way that invites active participation of the child, supported by parent engagement and an enriching environment, is more likely to bring about better developmental outcomes for at-risk infants. Likewise, interventions starting in the NICU and bridging to the community have the greatest, although still limited, research efficacy.

Based on these findings, NICU multidisciplinary teams are encouraged to work with community programs to develop intervention programs that begin in the NICU and continue to support parents and infants during the transition to home. Interventions should focus on providing active movement opportunities throughout the day, which requires parental engagement early. Neonatologists and pediatricians are encouraged to consider the developmental needs of infants born preterm in the first weeks and months of life and work with neonatal therapists to develop an evidence-based program. In areas where referral from a medical provider is needed for therapy services, we recommend that a standard be established for referral to therapy services 4 to 6 weeks before discharge, or earlier. Pediatricians caring for infants immediately after NICU discharge should consider referral to therapy services through early intervention or private therapy services to ensure continuation of therapy services from the NICU to home. While the results of this systematic review are not conclusive, there is adequate evidence to conclude that

intervention can improve the outcomes of infants born very preterm when started during the highly neuroplastic period in the NICU and continued in the first months of life, rather than using a wait-and-watch approach until delays are evident.

Limitations

The review was restricted to include studies that initiated intervention in the NICU/hospital. This was a deliberate choice since we were specifically interested in determining the effect of interventions initiated during this period of life, which is characterized by high neuroplasticity. Because of the heterogeneity of the studies, a meta-analysis could not be performed. The quality review required scoring on interventionist blinding; thus, all studies received a reduced score since it is not possible to blind the therapist to the intervention they were providing in a study. Not all studies included in this review were RCTs; one prospective cohort study and one cluster RCT were also included. Only articles published in English were included for the purpose of ease, which might have led to the inadvertent exclusion of relevant papers published in other languages.

Future recommendations

Future research should focus on additional high-quality RCTs with larger sample sizes in the category of collaborative parent–therapist interventions with focus on postural control, active play-based developmental stimulation, and environmental enrichment to confirm the results of this review. In this review, not all studies included were RCTs, which makes it very difficult to synthesize the findings and draw conclusions. We understand that infants born preterm are a highly vulnerable population and there are multiple challenges involved in conducting studies with this high-risk population. More studies are required to provide evidence about the effective dosing and intensity of neonatal interventions. To increase the state of evidence and provide strong recommendations, it is highly encouraged to conduct good-quality trials. Thus, it is important that researchers adhere to standardized guidelines while reporting their work so that findings can be employed to synthesize evidence and provide strong recommendations in this field where the need is critical. Ultimately, studies should track estimates of cost–benefit to allow for analysis and advocacy with policymakers and stakeholders.

CONCLUSION

The 15 studies analysed in the current review were mostly too small and heterogeneous, especially in the type, dosing, and outcome measures, to allow pertinent conclusions on the evidence of effects. However, the following conclusion can be drawn from the review: there is preliminary support that daily PDMI improves motor and cognitive outcomes in the short- and possibly long-term.

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SUPPORTING INFORMATION

The following additional material may be found online:

Table S1: General description of the studies included in the review.

Table S2: Data extraction from the studies included in the review.

Table S3: Risk of bias assessment table.

Figure S1: Flow diagram of the studies included in the review.

Appendix S1: Search terms and strategy.

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