

Virtual reality in motor rehabilitation for children with cerebral palsy: review of neurophysiological effects.

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ABSTRACT

Cerebral palsy affects movement and posture, resulting in multisystem impairments that limit functional independence and participation. Physical therapy plays a significant role in addressing these challenges, and virtual reality (VR) has emerged as a promising modality to improve motor control and support neuroplasticity. This systematic review aimed to determine the impact of virtual reality-based physical therapy interventions on motor function, gait, balance, and neuroplasticity mechanisms in children with cerebral palsy. Following PRISMA guidelines, nine studies were identified, critically appraised, and synthesized using a qualitative narrative approach. Virtual reality (VR)-based rehabilitation has emerged as an effective and engaging therapeutic modality for children with cerebral palsy. Evidence across diverse intervention formats demonstrates consistent improvements in upper-limb function, balance, gait performance, and overall motor abilities. Immersive and sensory-enriched VR systems enhance engagement, proprioceptive feedback, and sensorimotor integration. Although neurophysiological outcomes remain insufficiently investigated, preliminary findings suggest that multimodal VR, alone or combined with neuromodulation, may support neuroplasticity. Current evidence positions VR as a valuable adjunct to conventional pediatric therapy. Future research should prioritize standardized protocols, integration of neurophysiological measures, and large-scale randomized controlled trials to optimize clinical application.

Keywords: *Cerebral Palsy, Motor Skills, Neuroplasticity, Pediatric Physical Therapy, Rehabilitation, Virtual Reality.*

Realidad virtual en rehabilitación motora para niños con parálisis cerebral: revisión de los efectos neurofisiológicos.

RESUMEN:

La parálisis cerebral afecta al movimiento y la postura, provocando deterioros multisistémicos que limitan la independencia funcional y la participación. La fisioterapia desempeña un papel central en la afrontación de estos desafíos, y la realidad virtual (RV) ha surgido como una modalidad prometedora para mejorar el control motor y apoyar la neuroplasticidad. Esta revisión sistemática tuvo como objetivo determinar el impacto de las intervenciones de fisioterapia basadas en realidad virtual en la función motora, la marcha, el equilibrio y los mecanismos de neuroplasticidad en niños con parálisis cerebral. Siguiendo las directrices de PRISMA, se identificaron, evaluaron críticamente y sintetizaron nueve estudios utilizando un enfoque narrativo cualitativo. La rehabilitación basada en realidad virtual (RV) ha surgido como una modalidad terapéutica eficaz y atractiva para niños con parálisis cerebral. La evidencia en diversos formatos de intervención demuestra mejoras constantes en la función de las extremidades superiores, el equilibrio, el rendimiento de la marcha y las capacidades motoras generales. Los sistemas de RV inmersivos y enriquecidos sensorialmente parecen mejorar la implicación, la retroalimentación propioceptiva y la integración sensoriomotora. Aunque los resultados neurofisiológicos siguen siendo insuficientemente investigados, los hallazgos preliminares sugieren que la VR multimodal, sola o combinada con la neuromodulación, podría favorecer la neuroplasticidad. La evidencia actual posiciona a la RV como un complemento valioso de la terapia pediátrica convencional. La investigación futura debería priorizar protocolos estandarizados, la integración de medidas neurofisiológicas y ensayos controlados aleatorizados a gran escala para optimizar la aplicación clínica.

PALABRAS CLAVE: *Parálisis cerebral, habilidades motoras, neuroplasticidad, fisioterapia pediátrica, rehabilitación, realidad virtual.*

Introduction

Cerebral palsy is a disorder that affects movement and posture, often accompanied by additional conditions, Such as sensory, cognitive, communication, motor, epileptic, and musculoskeletal complications, all of which can restrict one's ability to manage routine activities and participate meaningfully in social or functional roles (Rosenbaum et al., 2007). The condition arises from abnormalities that may occur before, during, or shortly after birth and is categorized as a non-progressive brain injury occurring in early brain development or infancy (Bax et al., 2005).

From an etiological perspective, congenital causes include structural malformations during key developmental stages of the central nervous system—namely induction, proliferation, migration, and organization. Perinatal causes are frequently linked to prematurity, which increases the risk of intraventricular or periventricular hemorrhages, hypoxic events, ischemia, or blockage of the middle cerebral artery (Volpe, 2009). Postnatal causes may involve traumatic brain injuries, metabolic disorders, infections, or toxic exposures (Oskoui et al., 2013).

Cerebral palsy is classified by its topographic presentation into the following types: hemiplegia, diplegia,

tetraplegia, double hemiplegia, and monoplegia (Bax et al., 2005). The type of muscle tone and movement disorder observed depends on the nature of the brain lesion and may include spasticity, dystonia, or ataxia (Graham et al., 2016).

In physical therapy, interventions are tailored based on the lesion's origin and associated effects, addressing posture, gait, movement patterns, and upper limb function. Early intervention is emphasized to minimize long-term complications and support the child's functional development and participation in daily environments (Novak et al., 2013).

A wide range of therapeutic methods and interventions is available, with virtual reality emerging as an effective, evidence-based option. By creating interactive, immersive environments that mimic real-world scenarios through audio and visual feedback, virtual reality supports the development of body awareness and sensorimotor skills in children with cerebral palsy (Ravi et al., 2017).

These experiences enhance postural control, gait, and overall movement coordination during rehabilitation (Chen et al., 2018). That is why the purpose of this study is to determine the impact of virtual reality-based physical therapy interventions on motor function, gait, balance, and neuroplasticity mechanisms in children with cerebral palsy.

Methods

This systematic review will follow the PRISMA guidelines to ensure methodological transparency and quality. A systematic search will be conducted PubMed/MEDLINE, Scopus, Web of Science, Embase, and PEDro electronic databases. Studies published in English or Spanish will be included. The references for selected studies will also be manually reviewed.

Search Strategy

A comprehensive literature search was conducted following the PRISMA 2020 guidelines to identify studies investigating the effects of virtual reality-based physical therapy interventions on motor control and neurophysiological mechanisms in children with cerebral palsy. The search was performed in PubMed/MEDLINE, Scopus, Web of Science, Embase, and PEDro databases.

The search strategy combined Medical Subject Headings (MeSH) and free-text terms using Boolean operators (AND, OR). The following keywords and their variations were used:

("Cerebral Palsy"[Mesh] OR "spastic diplegia" OR "spastic quadriplegia" OR "children with cerebral palsy") AND ("Virtual Reality"[Mesh] OR "virtual reality exposure therapy" OR "immersive virtual environment" OR "interactive video

game" OR "VR-based rehabilitation" OR "exergames") AND ("Motor Skills"[Mesh] OR "Motor Activity"[Mesh] OR "motor control" OR "motor function" OR "motor learning" OR "motor planning" OR "motor execution") AND ("Neuroplasticity"[Mesh] OR "Brain Plasticity" OR "Cortical excitability"

Or"Electroencephalography"[Mesh] OR "Functional MRI" OR "Transcranial Magnetic Stimulation" OR "neurophysiological") AND ("Randomized Controlled Trial" OR "clinical trial" OR "intervention study" OR "systematic review")

The search was restricted to articles published between January 2019 and October 2025, in English or Spanish, involving participants aged 18 years or younger diagnosed with cerebral palsy.

Additionally, reference lists of relevant systematic reviews and meta-analyses were screened manually to identify any studies not captured by electronic search. Duplicates were removed using Mendeley Reference Manager before screening.

Only clinical trials, quasi-experimental studies, and systematic reviews evaluating the impact of virtual reality on motor performance or neurophysiological outcomes (e.g., EEG, EMG, fMRI, TMS) were included. Conference abstracts, narrative reviews, and case reports were excluded.

Study Selection Process

Study selection was conducted independently by two reviewers in two stages: first, by screening titles and abstracts, and second, through full-text evaluation.

Methodological Quality Assessment

For RCTs, the PEDro Scale was used. For non-randomized studies, the ROBINS-I tool was applied. Study quality was categorized as high, moderate, or low based on scoring.

Data Extraction and Analysis

Data extraction was performed independently by two reviewers using a standardized data collection form. Disagreements were resolved through discussion or consultation with a third reviewer.

The following data were extracted from each included study:

- General information: author, year, country, and study design.
- Participant characteristics: age, sex, type of cerebral palsy, GMFCS level, and sample size.
- Intervention details: type and modality of virtual reality (immersive/non-immersive), duration, frequency, session length, device, or platform used,

and therapeutic goals.

- Comparison intervention: description of conventional therapy or control condition.
- Outcome measures: assessment tools for motor function (e.g., GMFM-66, QUEST, AHA) and neurophysiological variables (e.g., EEG patterns, EMG activity, cortical reorganization on fMRI or TMS).
- Main findings: quantitative and qualitative results regarding motor control and neuroplasticity effects.

Whenever possible, effect sizes and confidence intervals were extracted or calculated to enable comparison across studies.

A narrative synthesis was performed to describe the characteristics and results of the interventions, and when sufficient homogeneity was found, data were considered for meta-analysis using standardized mean differences. The methodological quality of included studies was planned to be assessed using the PEDro scale or the ROBINS-I tool.

Use of artificial intelligence

In this manuscript, Open AI Chat GPT version GPT-5.1 was used to perform style corrections and adjustments according to the author's instructions established for the submission of articles to Cuidado & Ocupación Humana journal. All authors

declare that artificial intelligence was not used to provide false or non-existent data, and it can be verified that all sources of information provided in this article are accurate.

Results

Study selection followed the PRISMA 2020 recommendations. All retrieved records were exported into EndNote X9 for duplicate removal and subsequently screened using Rayyan QCRI. Two independent reviewers conducted title and abstract screening based on predefined eligibility criteria: (1) participants diagnosed with cerebral palsy aged 0–18 years; (2) interventions involving virtual reality–based physical therapy or motor rehabilitation; (3) outcomes related to motor control, neurophysiological processes, motor planning, or functional performance; and (4) original empirical research (experimental, quasi-experimental, or observational designs). Exclusion criteria included adult samples, mixed populations without disaggregated pediatric data, non-motor VR applications, case reports, conference abstracts, editorials, and all types of review articles.

A total of 1,236 records were identified through electronic database searches, and eighteen additional records were located through manual screening of

reference lists, yielding 1,254 total records. After removing 312 duplicates, 942 unique records were screened at the title and abstract level. Of these, 865 were excluded for not meeting inclusion criteria due to population mismatch, intervention irrelevance, absence of motor or neurophysiological outcomes, or incompatible study design.

A total of seventy-seven full-text articles were assessed for eligibility. Sixty-eight studies were excluded after full-text review for the following reasons: review or non-original manuscript ($n = 23$), adult or heterogeneous samples without extractable pediatric data ($n = 17$), VR not used as a therapeutic motor intervention ($n = 14$), absence of neurophysiological or motor-control-related outcomes ($n = 10$), or insufficient methodological detail/duplicate publication ($n = 4$). Ultimately, nine studies fulfilled all eligibility criteria and were included in the qualitative synthesis. Figure 1 shows PRISMA flow diagram for study selection process.

Figure 1. *PRISMA Flow Diagram for Study Selection Process*



Note. The PRISMA flow diagram summarizes the identification, screening, eligibility, and inclusion stages for studies evaluating virtual reality-based interventions in children with cerebral palsy.

A total of 1,246 records were identified through database searches and forty-two from other sources; after removing duplicates and exclusions, nine studies were included in the qualitative synthesis.

Study Characteristics

Nine studies met the inclusion criteria, representing six randomized controlled trials, one quasi-experimental study, one

pilot crossover trial, and two meta-analytic syntheses (Arnoni et al., 2019; Radwan et al., 2023; Bortone et al., 2020; Chang et al., 2020; Ghai & Ghai, 2019; Li et al., 2023; Menekşeoğlu et al., 2023; Aran et al., 2020; Ren & Wu, 2019). Samples included children with spastic hemiplegic, diplegic, or bilateral cerebral palsy, commonly within mild to moderate levels of motor impairment. The VR systems varied widely, ranging from non-immersive commercial gaming platforms (e.g., Nintendo Wii) to immersive head-mounted displays and hybrid systems integrating haptic feedback or neuromodulation.

Intervention Delivery and Dosage

Intervention dosages ranged from 20–60 minutes per session, delivered between two and five times weekly over 4–12 weeks. Immersive VR protocols frequently included real-time multisensory and biofeedback components (Bortone et al., 2020), while non-immersive systems emphasized functional task repetition and progressive training intensity (Chang et al., 2020; Aran et al., 2020). Combined approaches, such as VR paired with repetitive transcranial magnetic stimulation, were reported in protocol form and involved longer or multi-stage sessions (Li et al., 2023).

Motor Outcomes

Across studies, VR-based interventions produced clinically meaningful

improvements in motor performance, including upper-limb control, manual dexterity, postural stability, gait speed, and overall functional mobility. Upper-limb-focused programs demonstrated significant improvements in unilateral motor performance, particularly for children with hemiplegic cerebral palsy (Menekşeoğlu et al., 2023; Chang et al., 2020).

Balance- and gait-oriented VR training improved gait speed, cadence, and dynamic stability in children with bilateral or spastic presentations (Arnoni et al., 2019; Radwan et al., 2023).

Meta-analytic evidence supported these findings, indicating moderate to large, pooled effects for VR-mediated improvements in gait parameters and gross motor function (Ghai & Ghai, 2019; Ren & Wu, 2019).

Neurophysiological and Sensory Outcomes

Neurophysiological outcomes were less commonly reported. Among available evidence, immersive VR combined with wearable haptics enhanced sensory responsiveness, movement timing, and motor engagement (Bortone et al., 2020). Protocol-level evidence suggests potential synergistic effects of VR combined with neuromodulation strategies on neural plasticity, though

empirical findings are still emerging (Li et al., 2023).

Methodological Quality

Methodological quality varied across the included studies. Randomized trials demonstrated moderate quality, with PEDro scores ranging from 5/10 to 7/10 (Arnoni et al., 2019; Radwan et al., 2023; Menekşeoğlu et al., 2023; Aran et al., 2020). Frequent limitations included small sample sizes, incomplete blinding, and insufficient detail regarding allocation procedures. Non-randomized and synthesis studies demonstrated low-to-moderate risk of bias due to intervention heterogeneity and variability in outcome measurement (Ghai & Ghai, 2019; Ren & Wu, 2019). Table 1 summarizes the main outcomes of the included studies and shows the methodological quality assessment scores.

Table 1.*Summary of Included Studies on Virtual Reality-Based Motor Rehabilitation in Children with Cerebral Palsy*

Study	Year	Design	Sample / CP Type	Intervention	Outcomes	PEDro Score	ROBINS-I	Notes
Menekşeoğlu et al.	2023	Randomized Controlled Trial	Children with hemiplegic CP	Gamified VR upper-limb program	Upper limb motor function improvements	7/10	N/A	Limited assessor blinding
Chang et al.	2020	Quasi-experimental	Children with CP	VR-based UE rehabilitation	Motor function, dexterity	N/A	Moderate risk	Risk of confounding; no randomization
Aran et al.	2020	Randomized Controlled Trial	Unilateral spastic CP	VR vs traditional therapy	Motor functions, ADLs	6/10	N/A	Allocation concealment unclear
Arnoni et al.	2019	Randomized Controlled Trial	Children with CP	VR balance/motor training	Body oscillation, motor performance	6/10	N/A	Small sample; limited blinding
Ghai & Ghai	2019	Meta-analysis	Children with CP	VR gait training	Gait speed, cadence, balance	N/A	Low risk	High-quality synthesis
Bortone et al.	2020	Randomized Crossover Pilot Trial	Children with neuromotor impairment	Immersive VR + haptic wearable	Motor performance, engagement	5/10	N/A	Pilot trial; small sample
Li et al.	2023	RCT Protocol	Children with spastic CP	VR + rTMS	Motor development, pain (planned)	N/A	Low risk (planned)	Protocol only
Ren & Wu	2019	Meta-analysis	Children with CP	VR game-based training	Gross motor skills	N/A	Moderate risk	Heterogeneity across trials
Radwan et al.	2023	Randomized Clinical Trial	Bilateral spastic CP	VR vs tDCS	Gait performance	7/10	N/A	Good assessor blinding; small sample

Note. CP = Cerebral Palsy; VR = Virtual Reality (Menekşeoğlu et al., 2020).

Key Observations

VR interventions consistently improved motor outcomes across

- studies: across the nine included studies, VR-based rehabilitation produced measurable improvements in upper-limb function, gait performance, balance, and global motor function (Arnoni et al., 2019; Radwan et al., 2023; Chang et al., 2020; Menekşeoğlu et al., 2023; Aran et

- Upper-limb VR training demonstrated statistically significant gains in dexterity and functional use in children with hemiplegic CP (Menekşeoğlu et al., 2023; Chang et al., 2020).
- Gait-focused VR interventions showed significant improvements in gait speed and cadence (Arnoni et al., 2019; Radwan et al., 2023).
- Meta-analytic evidence confirmed moderate-to-large, pooled effects

favoring VR for gross motor outcomes (Ghai & Ghai, 2019; Ren & Wu, 2019).

- Immersive VR and multisensory systems enhanced engagement and sensorimotor integration: studies using immersive VR or wearable haptics reported improvements in movement timing, motor engagement, and responsiveness to sensory cues (Bortone et al., 2020). Bortone et al. documented significant within-group improvements in motor performance after immersive VR + haptic training, highlighting the importance of multisensory inputs.
- Upper-limb improvements were particularly robust in hemiplegic CP: Children with unilateral CP demonstrated greater upper-limb gains when VR was used as the primary training modality (Menekşeoğlu et al., 2023; Chang et al., 2020). Both studies found statistically significant pre-post differences in functional upper-limb performance metrics.
- VR gait and balance interventions improved locomotor parameters VR-based balance and gait training resulted in improvements in gait speed, Cadence, Stride regularity, postural stability (Arnoni et al.,

2019; Radwan et al., 2023; Ren & Wu, 2019). Radwan et al. (2023) reported significant between-group differences favoring VR over tDCS for gait performance. Arnoni et al. (2019) also reported significant reductions in body oscillation after VR training.

- Meta-analytic evidence supports a dose-response pattern: two meta-analyses demonstrated that VR interventions achieve consistent improvements across pooled trials (Ghai & Ghai, 2019; Ren & Wu, 2019). Both meta-analyses reported statistically significant aggregated effects, supporting the idea that higher training volume is associated with greater functional gain.
- Neurophysiological outcomes remain underreported: Only a subset of studies addressed neurophysiology directly, yet findings suggest that immersive VR and haptics may positively influence sensorimotor activity (Bortone et al., 2020). Li et al. (2023) proposed VR + rTMS as a mechanism to enhance corticospinal plasticity but reported no statistical results (protocol only).
- Methodological quality was moderate across studies:

Randomized trials scored between 5/10 and 7/10 on PEDro, indicating moderate methodological rigor (Arnoni et al., 2019; Radwan et al., 2023; Menekşeoğlu et al., 2023; Aran et al., 2020). Common weaknesses included small sample sizes, incomplete blinding, and inconsistent reporting of randomization procedures. Non-randomized and synthesis studies demonstrated low-to-moderate ROBINS-I risk, due to heterogeneity across trial designs (Ghai & Ghai, 2019; Ren & Wu, 2019).

- High heterogeneity exists in VR protocols, dosage, and hardware: studies differed in immersion level (non-immersive vs. immersive), session duration (20–60 minutes), frequency (2–5 sessions/week), total duration (4–12 weeks), outcome measures and domains assessed.
- Such variability limits the comparability of results and reduces the precision of pooled estimates (Ren & Wu, 2019; Ghai & Ghai, 2019).

Discussion

This review highlights the growing evidence supporting VR-based rehabilitation as a feasible and effective approach to enhancing motor performance in children with cerebral palsy. Across diverse VR platforms, consistent improvements were observed in upper-limb coordination, gait parameters, balance control, and overall motor performance (Menekşeoğlu et al., 2023; Chang et al., 2020; Aran et al., 2020; Arnoni et al., 2019; Radwan et al., 2023).

These findings align with contemporary neurorehabilitation principles emphasizing repetition, task-specific engagement, and multisensory enrichment—domains where VR offers clear advantages over conventional therapy environments.

A recurring trend across the studies included was the strong engagement elicited by immersive VR systems. Immersive environments amplify user attention, enhance proprioceptive feedback, and increase motivation, all of which may contribute to improved movement timing and motor planning (Bortone et al., 2020). Wearable haptics and enriched feedback systems further supported sensorimotor integration, suggesting that multisensory layering may

offer an additional therapeutic advantage.

Meta-analytic evidence reinforced these observations, showing that VR interventions contribute to improvements in gait speed, cadence, and gross motor function across multiple trials (Ghai & Ghai, 2019; Ren & Wu, 2019). Moreover, VR-based upper-limb training produced gains in unilateral dexterity and functional arm use, particularly among children with hemiplegic presentations (Menekşeoğlu et al., 2023; Chang et al., 2020).

Despite promising findings, several methodological issues limit the strength of current evidence. Many trials employed small samples, restricting generalizability (Arnoni et al., 2019; Bortone et al., 2020). Blinding was often incomplete or infeasible due to the nature of VR interventions (Aran et al., 2020). Significant variability in intervention dosage, VR systems, and outcome measures contributed to heterogeneity and limited comparisons across studies (Ghai & Ghai, 2019; Ren & Wu, 2019). Neurophysiological outcomes were underreported, although emerging protocols suggest potential for VR combined with neuromodulation to influence corticospinal plasticity (Li et al., 2023).

Future research should prioritize larger controlled trials with standardized outcome measures and detailed neurophysiological assessment to clarify underlying mechanisms of motor improvement. Comparative trials between immersive and non-immersive systems and between VR-only and VR-plus adjunct modalities may help identify optimal therapeutic strategies.

Conclusion

The findings of this review demonstrate that virtual reality (VR)-based rehabilitation is an effective and engaging therapeutic modality for improving motor outcomes in children with cerebral palsy. Across diverse intervention formats, VR consistently enhanced upper-limb function, balance, gait performance, and overall motor abilities (Arnoni et al., 2019; Radwan et al., 2023; Chang et al., 2020; Menekşeoğlu et al., 2023; Aran et al., 2020). Meta-analytic evidence further supports these improvements, indicating significant pooled effects for gait and gross motor function (Ghai & Ghai, 2019; Ren & Wu, 2019). Immersive and sensory-enriched VR systems may offer additional benefits related to engagement, proprioceptive feedback, and sensorimotor integration (Bortone et al., 2020).

Although neurophysiological outcomes remain insufficiently explored, preliminary evidence suggests that multimodal VR systems—and possibly VR paired with neuromodulation—may influence sensorimotor pathways and support neuroplasticity (Bortone et al., 2020; Li et al., 2023). Overall, the existing evidence supports VR as a valuable adjunct to conventional pediatric therapy. Standardizing protocols, incorporating neurophysiological metrics, and conducting larger randomized controlled trials will be essential to strengthening the evidence base and optimizing clinical application.

Limitations

Several limitations must be considered when interpreting these findings. First, the methodological quality of the included studies was moderate, with randomized trials scoring between 5/10 and 7/10 on the PEDro scale (Arnoni et al., 2019; Radwan et al., 2023; Menekşeoglu et al., 2023; Aran et al., 2020). Common methodological weaknesses included small sample sizes, limited assessor blinding, and insufficient reporting of allocation and concealment procedures. These issues increase the risk of bias and limit the strength of conclusions.

Second, considerable heterogeneity existed in intervention protocols, VR hardware, session duration, training intensity, and outcome measures (Ghai & Ghai, 2019; Ren & Wu, 2019). This variability restricts comparability across studies and reduces clarity regarding the optimal dosage and type of VR intervention for specific motor outcomes. Third, very few studies included neurophysiological assessments, preventing definitive conclusions regarding the neural mechanisms underlying VR-driven improvements (Bortone et al., 2020; Li et al., 2023).

Finally, long-term follow-up data were largely absent, limiting understanding of whether gains achieved through VR training are maintained over time. More robust and longitudinal research is needed to evaluate durability, generalization to daily activities, and the cost-effectiveness of VR interventions in pediatric rehabilitation.

Clinical Relevance Statement

Across the included studies, VR interventions consistently improved motor outcomes, including upper-limb dexterity, gait speed, balance, and overall motor performance. Immersive and multisensory VR systems enhanced engagement,

attentional focus, and sensorimotor integration, with particularly robust gains observed in children with hemiplegic cerebral palsy. Gait- and balance-focused VR programs demonstrated improvements in stride regularity, postural stability, and locomotor coordination. Although several studies suggested potential neurophysiological benefits, such as enhanced sensorimotor responsiveness, direct measures of neuroplasticity were limited. Methodological quality across trials was moderate, with small sample sizes, limited blinding, and considerable variability in VR hardware, training dosage, and immersion level. Overall, VR represents a promising adjunct to pediatric rehabilitation, offering meaningful motor improvements. Further research should establish standardized protocols and clarify neurophysiological mechanisms.

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