Towards functional improvement of motor disorders associated with cerebral palsy

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Cerebral palsy is a lifelong neurodevelopmental condition arising from non-progressive disorders occurring in the fetal or infant brain. Cerebral palsy has long been categorised into discrete motor types based on the predominance of spasticity, dyskinesia, or ataxia. However, these motor disorders, muscle weakness, hypotonia, and impaired selective movements should also be discriminated across the range of presentations and along the lifespan. Although cerebral palsy is permanent, function changes across the lifespan, indicating the importance of interventions to improve outcomes in motor disorders associated with the condition. Mounting evidence exists for the inclusion of several interventions, including active surveillance, adapted physical activity, and nutrition, to prevent secondary and tertiary complications. Avenues for future research include the development of evidence-based recommendations, low-cost and high-quality alternatives to existing therapies to ensure universal access, standardised cerebral palsy registers to harmonise epidemiological and clinical information, improved adult screening and check-up programmes to facilitate positive lived experiences, and phase 3 trials for new interventions.

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Introduction

Cerebral palsy is an umbrella term describing "a group of permanent disorders of the development of movement and posture, causing activity limitation, that are attributed to non-progressive disturbances that occurred in the developing fetal or infant brain. The motor disorders of cerebral palsy are often accompanied by disturbances of sensation, perception, cognition, communication and behaviour, by epilepsy, and by secondary musculoskeletal problems."[1] Cerebral palsy is a lifelong condition characterised by changes in function across the lifespan; hence, the importance of interventions to improve outcomes in motor disorders associated with the condition.

In the past 5 years, evidence elucidating the underlying pathophysiology, developments in early detection and technology, and shifts towards lifelong and global perspectives have contributed to new understanding of cerebral palsy. For example, accruing epidemiological data from high-income countries (chiefly Australia and countries in Europe) have suggested decreasing incidence of cerebral palsy since the mid-2000s.[2] Moreover, for the first time, registry studies and population-based studies have provided epidemiological information for low-income countries, highlighting priority needs in these settings.[2] Progress in pathophysiology with respect to inflammatory responses is elucidating potential targets for future treatment, and new clinical and neuroimaging data are supporting early detection, which might lead to earlier intervention than currently available. Awareness of vulnerabilities and specificities from a global perspective has grown because of international collaborative research projects. Furthermore, evidence is mounting on the usefulness of several technologies for diagnosis and intervention, including technologies based on telemedicine, which was enhanced during the COVID-19 pandemic, and robotics.

In this Review, we provide a critical summary of the literature from the past 5 years, with a focus on improving outcomes in movement disorders associated with cerebral palsy. We provide an update on movement disorder management and emerging therapeutic approaches, taking into account the WHO International Classification of Functioning, Disability and Health[3] biopsychosocial framework, which emphasises functioning and disability as multidimensional constructs related to body function and structure, activity and participation, and contextual factors.[3] We start with evidence on rehabilitation therapy because most people with cerebral palsy receive this treatment. We further discuss other interventions, such as pharmacological, neurosurgical, and orthopaedic interventions, which are typically given together with rehabilitation therapy. Our approach reflects the shift in attention from clinical outcomes at the level of body function and structure to functional outcomes related to activities of daily living, societal participation, and quality of life. Functional outcomes include skills and behaviours that enable the individual to achieve goals that are meaningful to them and their families. We reviewed all aspects related to improving outcomes of movement disorders associated with cerebral palsy, but we discuss only topics with sufficient evidence, highlighting the gaps in knowledge. Regardless of treatment goals and geographical location, management of people with cerebral palsy should be strictly guided by the bioethical principles of non-maleficence and beneficence.[4]

Epidemiology

The global birth prevalence of cerebral palsy ranges from 1·6 to 3·4 per 1000 livebirths, making cerebral palsy the most important cause of major motor impairment in childhood.[2] The range in prevalence reflects the differences between high-income countries and low-income and middle-income countries. Most population-based registers in high-income countries (mainly Australia and countries in Europe) have reported a decline in birth prevalence since the mid-2000s, which probably relates to improvements in public health and prenatal and perinatal care.[2]

Panel 1: Causal pathways of cerebral palsy

The aetiology of cerebral palsy is complex, multifactorial, and heterogenous; it is associated with early brain injury or maldevelopment (ie, brain dysplasia).

In high-income countries, more than 80% of children with cerebral palsy have atypical brain features seen with MRI that can disclose the pathogenic pattern and suggest the timing of the injury on the basis of maturational vulnerability.[8]

White matter injury (found in about 49% of children with cerebral palsy) predominates, followed by grey matter injury (21%).[8] Maldevelopments (11%) and several miscellaneous findings (eg, intracranial haemorrhages and calcifications; 9%) are also reported. Brain MRI shows no malformity in approximately 11% of children with cerebral palsy, underlining that pathology cannot be fully understood solely by the use of MRI.

MRI patterns are mainly lesional in children with unilateral spastic cerebral palsy (observed in 77% of cases), bilateral spastic cerebral palsy (71%), and dyskinetic cerebral palsy (59%), whereas ataxic cerebral palsy is mostly associated with maldevelopments (25% of cases), miscellaneous findings (21%), or normal findings (ie, no brain lesions identified; 32%).[8]

For many people with cerebral palsy, the full aetiological pathway remains unclear. On the basis of the timing of occurrence, risk factors for cerebral palsy are categorised into prenatal, perinatal, and postnatal (up to age 1 year).

The most prominent risk factor in high-income regions is gestational age, with preterm birth accounting for a third to half of all cases and the risk being higher the shorter the gestational age.[9] The relative importance of risk factors and causal pathways varies from region to region.

In low-income and middle-income countries, hypoxic ischaemic encephalopathy,[10] sentinel events,[10] obstructed labour,[10] infections,[10] kernicterus,[11] and, in some regions, consanguinity[12] are more common than in high-income countries.

Cerebral palsy or a high risk of cerebral palsy can be accurately diagnosed or predicted before the corrected age at 6 months (ie, a premature baby's chronological age minus the number of weeks the baby was born early before 40 weeks of gestation) by an experienced clinical team using standardised assessments. A clinical diagnosis of cerebral palsy or high risk of cerebral palsy should be followed by a referral for the infant to receive early interventions.[13]

Early interventions are crucial in maximising neuroplasticity and minimising irreversible changes to muscle and bone growth, and overall development. Further delineation of cerebral palsy type and topography is important to ensure timely management and to reach the desired outcomes.[13]

The prevalence reported in low-income and middle-income countries is higher than that in high-income countries. Existing reports of approximately 2·3–3·4 per 1000 livebirths might be an underestimate because of survival bias (ie, high mortality of infants) and difficulties in identifying children with mild cerebral palsy (ie, with mild motor impairment), especially where registers do not exist or are in early development.[2] The Australian and European cerebral palsy registers report a substantial decline in singletons[5] and twins,[6] but not in the very small proportion of higher-order multiples.[6] Conversely, a systematic review of studies done in China reported an increase in prevalence in the past three decades, with marked differences between regions and between rural and urban settings.[7] Causal pathways of cerebral palsy are discussed in panel 1.

Classification and clinical phenomena

The categorisation based on the predominant motor disorders of spasticity, dystonia, choreoathetosis, or ataxia includes clinical and physiological features like atypical muscle tone, involuntary movements, posture deformities, simultaneous activation of agonistic and antagonistic muscles, muscle weakness, and impaired coordination and selectivity (panel 2).[1] Spasticity (83–88% of cases) is the most common motor disorder, whereas dyskinetic cerebral palsy (8–12%) and ataxia (3–4%) are rarer.[24,25] Mixed presentation of motor disorders is common, particularly the presence of spasticity in people with dyskinetic cerebral palsy and of dystonia in people with spastic cerebral palsy.[26,27] On the basis of the topography of spasticity, spastic cerebral palsy is further subdivided into unilateral (occurring in about 38% of cases) and bilateral spastic cerebral palsy (62%).[24] In clinical practice and research, individuals can be classified in five levels (I, II, III, IV, or V), according to functioning in the domains of gross motor abilities (Gross Motor Function Classification System [GMFCS]),[28] manual abilities (Manual Ability Classification System [MACS]),[29] communication (Communication Function Classification System),[30] speech (Viking Speech Scale),[31] eating and drinking (Eating and Drinking Ability Classification System),[32] and vision (Visual Function Classification System;[33] table 1).

Proper recognition and discrimination of motor disorders are necessary for precise diagnosis, prognosis, follow-up, and tailored management. Consensual definitions have been widely used for spasticity, dystonia, and choreoathetosis, in both clinical practice and research; they include those suggested by panels of international experts such as the Surveillance of Cerebral Palsy in Europe,[34,35] the Taskforce on Childhood Movement Disorders of the US National Institutes of Health,[18,36] and a European consensus for spasticity and hyper-resistance.[14]

Because spasticity, dystonia, and choreoathetosis are often present simultaneously, clinical discrimination can be challenging, especially between spasticity and dystonia, and between dystonia and choreoathetosis. Good knowledge of the hallmarks of motor disorders is essential. In muscles with spasticity, muscle tone and resistance to passive movement are velocity-dependent, increasing with increased velocity, and are felt by the examiner in response to an imposed joint movement applied to the relaxed passive muscle.[14] By contrast, in dystonia, the muscle tone is typically fluctuating. Choreoathetosis is distinguished from dystonia on the basis of the observed movement characteristics, such as poor postures and lack of sustained muscle contractions.[17]

Weakness (ie, the inability to produce or maintain an intended amount of force) is a consistent clinical finding in people with cerebral palsy, arising from a combination of musculoskeletal and neural impairments.[20,37] Contributing factors to weakness vary largely among individuals. Besides the importance of muscle size to muscle strength, studies highlight the relation of

muscle weakness with patient-specific characteristics (eg, cognitive abilities and motivation) and treatment history (eg, physical therapy and injections).[37] In very young children with cerebral palsy, in whom testing for weakness is difficult, weakness could be a cause of hypotonia, which is often the most evident sign.[20] Axial or core hypotonia are often described in combination with hypertonic limbs. Hypotonic core muscles cause difficulties with postural alignment and stability that can result in developmental delay, spinal deformities, and pain. Neuroimaging patterns of motor and associated impairments in people with cerebral palsy are shown in the figure.

Natural history

Gross motor abilities are mostly stable at GMFCS levels II–IV in children aged 4 years or older.[39] However, reclassification can occur between age 2 years and 4 years. Walking ability can decline in adolescence and adulthood,[40,41] but this deterioration is more prevalent in people with dyskinetic cerebral palsy and bilateral spastic cerebral palsy than in individuals with unilateral spastic cerebral palsy.[41] Bimanual performance improves with age in most children, reaching a maximum performance by age 3–8 years.[42] Around half of children with manual abilities in MACS levels III or IV are reclassified to lower or higher levels after age 4 years, indicating that MACS is less stable than GMFCS (ie, children remain less time at the same level of manual ability than at the same level of gross motor function).[39] Around 66% of adults with cerebral palsy are classified at MACS levels I or II.[40] A Ugandan study reported that during a 4-year follow-up, more than a third of children and adolescents with cerebral palsy exhibited changes in GMFCS and MACS levels.[43] This finding indicates that classification systems might be less stable in cohorts from low-income countries (a finding mainly attributed to slower rate of motor development because of limited access to health-care and rehabilitation services), thereby impeding their crucial attribute to predict functional development over time and assist with timely interventions.[43] Compared with their peers from high-income countries, children and adolescents in Uganda attained lower scores in functional skills and had slower developmental rates in gross motor function and mobility.[43]

Motor deterioration can be secondary to musculoskeletal problems or, less commonly, to spinal cord compression. More than 90% of adults with dyskinetic cerebral palsy show progressive disc degeneration,[44] mainly attributed to atypical cervical motion due to involuntary movements.[45] Symptomatic cervical spinal stenosis is identified in about 8% of adults with spastic cerebral palsy across all GMFCS levels, with upper extremity symptoms (eg, numbness and muscle weakness), a decline in walking ability, neck pain, and incontinence.[45] Additionally, microstructural changes in the spinal cord have been reported in adults with cerebral palsy, possibly causing reduced hand dexterity, sensorimotor deficits, and increased spasticity.[46]

Panel 2: Motor disorders in cerebral palsy

In spastic cerebral palsy, spasticity refers to involuntary, stretch-velocity induced muscle activity as part of the neural contributions to hyper-resistance.[14] European experts warn that the term spasticity might not cover all aspects of perceived resistance (ie, neural and non-neural) and should be used only when clearly defined and together with the term stretch hyper-reflexia.[14] Spasticity is associated with functional impairments, such as impairments in reaching and grasping, and in distinctive gait like limited dorsiflexion during swing and at initial contact, scissoring, or excessive hip and knee flexion. Spasticity is hypothesised to result from upper motor neuron lesions that cause the loss of inhibitory descending input to the low motor neurons that keep the stretch reflex in the peripheral neuromuscular system from being overactive.[15]

In dyskinetic cerebral palsy, dystonia and choreoathetosis are predominant.[16] Both occur independently, with a predominance of dystonia in most cases.[16] Dystonia in people with cerebral palsy refers to poor postures, involuntary twisting, and repetitive movements due to sustained or intermittent muscle contractions, whereas choreoathetosis is characterised by hyperkinesia and muscle tone fluctuation.[17] Dystonia is a particularly challenging motor disorder and is often classified as a hypertonic and hyperkinetic motor disorder.[18] Dystonia in people with cerebral palsy is often more noticeable and has a higher impact on motor functioning than choreoathetosis, with higher severity in the upper limbs than in the lower limbs. Both disorders substantially increase with activity.[16] Dystonia has a major negative impact on activities of daily living, societal participation, and quality of life.[19] The pathophysiology underlining dystonia and choreoathetosis remains unclear; emerging hypotheses highlight loss of inhibition, sensory dysfunction, and impaired plasticity in basal ganglia circuits.[17]

Ataxic cerebral palsy is dominated by ataxia, which is defined as an inability to generate a voluntary movement trajectory that cannot be attributed to weakness or involuntary muscle activity in the affected joints.[20] Ataxic cerebral palsy is characterised by loss of muscular coordination so that movements are done with reduced force, rhythm, and accuracy. Trunk balance is disturbed; gait is broad-based, staggering (dysrhythmic), and unstable; and arm function is decreased by overshooting and undershooting of goal-directed movements.[21] Associations between clinical and neuroimaging features in individuals with ataxic cerebral palsy have been far less documented than in individuals with spastic or dyskinetic cerebral palsy. Ataxia in individuals with cerebral palsy is often associated with maldevelopment of, or injury to, the cerebellum (or its inflow or outflow tracts).[20,22] The implications of an ataxic cerebral palsy diagnosis are far less documented than for other types of cerebral palsy, and future studies should clarify its prevention and management.[23]

Management to optimise and maintain outcomes

Rehabilitation therapy

Rehabilitation therapy can be provided by physical, occupational, and speech language therapists. Its aim is to maintain or increase function and participation while reducing the impact of musculoskeletal deterioration associated with ageing (table 2). Functional approaches are based on the principles of motor learning; the individual is actively engaged and task practice is done in real-life settings, with emphasis on family and personal goals. This approach is more effective than impairment-based passive therapy in improving motor function.[47] Furthermore, the bioethical principle of autonomy, which refers to the individual's right to make their own choices and be actively involved in their treatment decisions and participation preferences, is particularly important when setting rehabilitation goals.

	Mobility; GMFCS (age 6–12 years)*	Manual ability; MACS (age ≥4 years)	Communication; CFCS (age >4 years)	Speech; VSS (age >4 years)	Eating and drinking; EDACS (age ≥3 years)	Vision; VFCS (age ≥1 years)
I	Child walks at home, school, outdoors, and in the community; can climb stairs without the use of a railing	Child handles objects easily and successfully	Child independently alternates between sender and receiver roles with most people in most environments	Speech is not affected by a motor disorder	Child eats and drinks safely and efficiently	Child uses visual function easily and successfully in vision-related activities
II	Child walks in most settings and climbs stairs holding onto a railing; might walk with physical assistance, a hand-held mobility device, or use wheeled mobility when travelling long distances	Child handles most objects but with partly reduced quality or speed of achievement, or both	Child independently alternates between sender and receiver roles with most people in most environments, but the conversational pace is slow and might make the interaction difficult	Speech is imprecise but usually understandable to unfamiliar listeners	Child eats and drinks safely but with some limitations to efficiency	Child uses visual function successfully but needs self-initiated compensatory strategies
III	Child walks using a hand-held mobility device in most indoor settings; uses wheeled mobility when travelling long distances and might self-propel (ie, move a manual wheelchair independently) for shorter distances	Child handles objects with difficulty; help is needed to prepare or modify activities	Child alternates between sender and receiver roles with familiar (but not unfamiliar) conversational partners in most environments	Speech is unclear and not usually understandable to unfamiliar listeners if out of context	Child eats and drinks with some limitations to safety; there might be limitations to efficiency	Child uses visual function but needs some adaptations
IV	Child uses methods of mobility that require physical assistance or powered mobility in most settings	Child handles a limited selection of easily managed objects and always requires some help from others	Child does not consistently alternate between sender and receiver roles; communication is sometimes effective with familiar conversational partners	No understandable speech	Child eats and drinks with substantial limitations to safety and efficiency	Child uses visual function in very adapted environments but only does parts of the vision-related activities
V	Child is transported in a manual wheelchair in all settings	Child is not able to handle objects or complete even simple actions with their hands	Child poorly alternates between sender and receiver roles; communication is rarely effective even with familiar conversational partners	NA	Child is unable to eat or drink safely and efficiently; tube feeding might be considered to provide nutrition	Child does not use visual function even in very adapted environments

GMFCS=Gross Motor Function Classification System. MACS=Manual Ability Classification System. CFCS=Communication Function Classification System. VSS=Viking Speech Scale. EDACS=Eating and Drinking Ability Classification System. VFCS=Vision Function Classification System. NA=not applicable. *Different descriptors are available for additional age groups.

Table 1: **Functional classification of cerebral palsy**

Overground gait training,[48] strength training[49] and functional power training,[50] constraint-induced movement therapy and bimanual therapy,[51] action observation therapy,[52] Hand–Arm Bimanual Intensive Training Including Lower Extremity,[53] and goal-directed training[47] are functional, activity-based programmes that are feasible, safe, and effective in improving functional outcomes. Most of these approaches are most effective in children with GMFCS levels I–III, although their effectiveness in children with GMFCS levels IV or V and in adults with cerebral palsy is vastly understudied.

Some adjunct therapy modalities include neuromuscular electrostimulation,[54] extracorporeal shockwave therapy,[55] and transcranial magnetic stimulation.[56] These approaches have been shown to reduce spasticity or dystonia, but their effectiveness in improving functional outcomes has not been shown.

Rehabilitation technology

The use of technology to support functional outcomes is not new. Simple technology includes assistive devices (eg, customised cutlery), mobility aids (eg, crutches and rollators), or communication boards. In the past 10 years, the evidence that supports the use of advanced rehabilitation technologies to improve motor and functional outcomes in individuals with cerebral palsy has increased (table 3).[57]

Mobility robotics assist people with functional movements by providing better control of the movement, sensory feedback, and information processing.[57] Arm robotic-assisted therapy is understudied compared with lower limb robotics; however, superior effects to conventional physical therapy in reducing spasticity and improving the quality of movement have been reported in children with unilateral spastic cerebral palsy.[58] Robotic-assisted gait training appears ineffective in improving walking speed and endurance or gross motor function in children and adolescents with spastic cerebral palsy (GMFCS levels I–IV).[59] By contrast, wearable exoskeletons have shown positive results in improving spatiotemporal gait parameters in individuals with cerebral palsy.[60] Treadmill gait training yields higher effects in improving gait speed and endurance than conventional therapy or overground gait training, probably because of the controlled speed and intensity of stepping cycles.[48,61]

Virtual reality and video games drive interest and engagement, which encourage individuals to actively participate in their rehabilitation programme through play. Overall, the quality of evidence supporting the use of virtual reality systems (alone or in combination with conventional therapy) to improve general motor function, upper limb function, gait kinematics, postural control, and balance is low and the use of these systems has

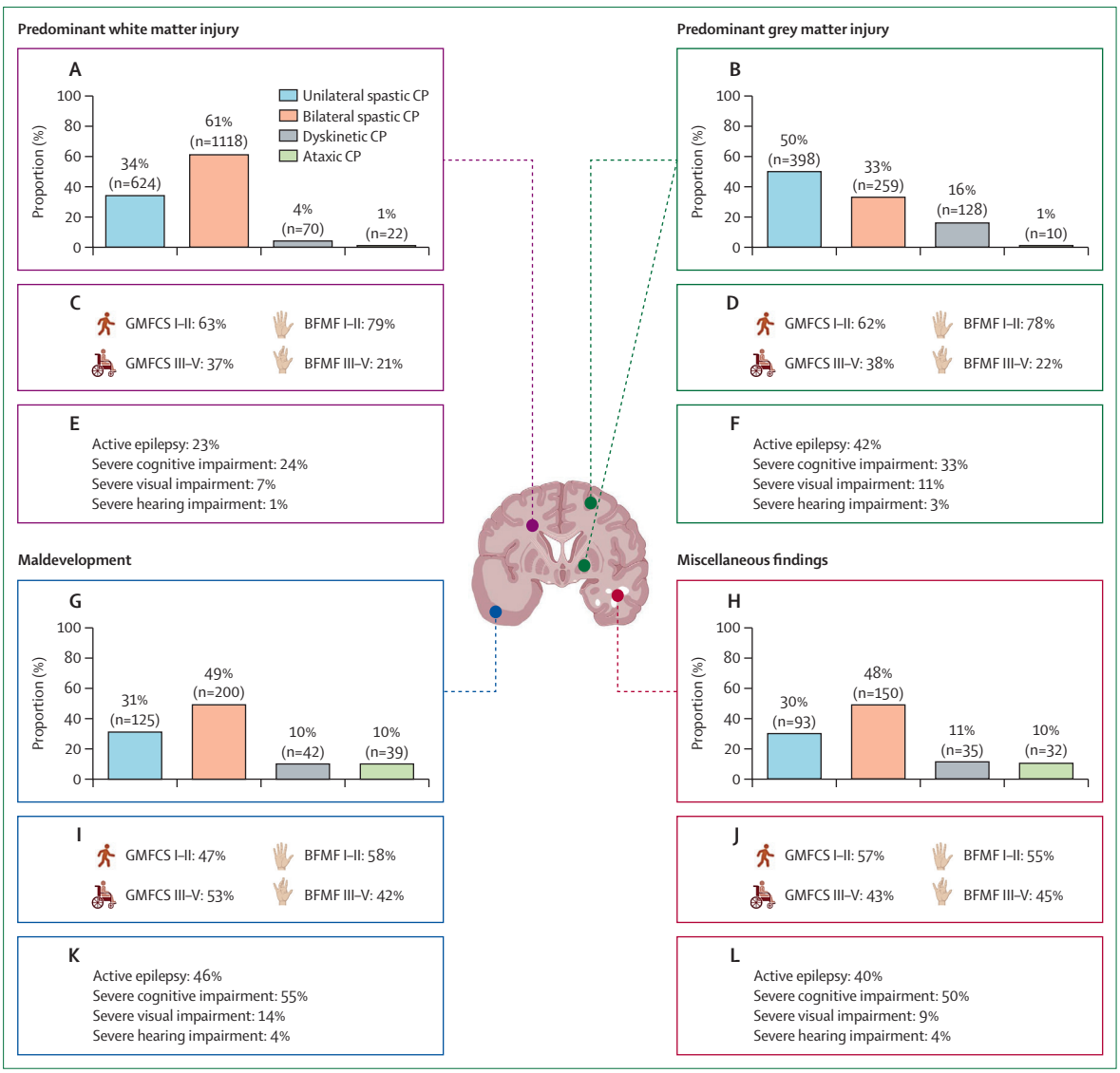

***Figure*: Neuroimaging patterns associated with motor and other impairments in people with cerebral palsy**

(A, C, and E) Children with predominant white matter injury. (A) Distribution of cerebral palsy by type: about 95% of children have spastic cerebral palsy, of which 61% have bilateral involvement. (C) Motor functioning: the majority of children are independent walkers (63%) and have good manual abilities (79%). (E) Associated impairments: 23% of children have active epilepsy and 24% have severe cognitive impairments; other associated impairments are less prevalent. (B, D, and F) Children with predominant grey matter injury. (B) Distribution of cerebral palsy by type: about 83% of children have spastic cerebral palsy, of which 50% have unilateral involvement; the largest group of children with dyskinetic cerebral palsy has predominant grey matter injury. (D) Motor functioning: most children are independent walkers (62%) and have good manual abilities (78%). (F) Associated impairments: 42% of children have active epilepsy and 33% have severe cognitive impairments. (G, I, and K) Children with maldevelopment. (G) Distribution of cerebral palsy by type: about 80% of children have spastic cerebral palsy, of which 49% have bilateral involvement. (I) Motor functioning: similar distribution between the severity of gross motor functions and manual abilities. (K) Associated impairments: 46% of children have active epilepsy and 55% have severe cognitive impairments. (H, J, and L) Children with miscellaneous findings. (H) Distribution of cerebral palsy by type: about 78% of children have spastic cerebral palsy, of which 48% have bilateral involvement; percentages in (H) do not add up to 100% due to rounding. (J) Motor functioning: similar distribution between the severity of gross motor functions and manual abilities. (L) Associated impairments: 40% of children have active epilepsy and 50% have severe cognitive impairments. Percentage values reproduced from Himmelmann et al.[38] Figure created with BioRender.com. BFMF=Bimanual Fine Motor Function. CP=cerebral palsy. GMFCS=Gross Motor Function Classification System.

unclear benefits.[62] Serious games (ie, digital games developed with specific goals to facilitate learning and training) for rehabilitative purposes accompany other rehabilitation technologies or conventional therapy. The improved motor outcomes in both ambulatory and non-ambulatory individuals with cerebral palsy are mainly linked to increased motivation and engagement during therapy, warranting their use as complementary and not as a substitute to other therapies.[63] In children with spastic cerebral palsy with GMFCS levels III or IV, a combination of conventional therapy and serious games has been shown to lead to the achievement of individual

	Definition	Motor outcome	Comments
Goal-directed training[47]*	Active practice of an individual goal or task until the desired functional outcome is achieved	Improved upper and lower limb functioning, including handwriting, bimanual function, and walking	For skills to be effectively transferred to everyday life, the practice of the goal should be done in a real-world context
Overground gait training[48]†	Active practice of walking to improve walking ability, involving overground gait training or treadmill-based gait training	Improved walking speed, walking endurance, and gait-related gross motor function	Feasible, safe, and more effective in improving walking speed compared with conventional physical therapy
Strength training[49]† and functional power training[50]‡	Strength training consists of exercises that involve the child's own bodyweight or equipment to increase muscle mass, endurance, and strength; functional power training consists of loaded functional exercises (eg, walking, running, and climbing stairs) done at high-movement velocities	Strength training: increased lower limb muscle strength, improved standing balance, increased walking speed, improved multiple dimensions (standing, walking, running, and jumping) of the gross motor function measure, and no adverse effects on spasticity; functional power training: improved walking and sprinting performance, and increased isometric and dynamic lower limb muscle strength	More research is needed to explore strength training and functional power training in non-ambulant people with cerebral palsy; insufficient evidence regarding dyskinetic cerebral palsy
Constraint-induced movement therapy,[51]§ bimanual therapy,[51]§ and action observation therapy[52]†	Constraint-induced movement therapy: upper extremity rehabilitation therapy to improve the function of the most affected hand by constraining the use of the least affected hand; bimanual therapy: repeated practice of two-handed (bimanual) activities; action observation therapy (based on the mirror neuron system): video observation of meaningful actions with the intent of imitating and doing the same actions	Improved unimanual (dissociated movements, grasp, weight-bearing, and protective extension) and bimanual performance in unilateral cerebral palsy	Constraint-induced movement therapy combined with action observation therapy leads to higher functional gains than constraint-induced movement therapy alone; upper limb therapy shows better results when implemented at a very early age and in children with poor hand function
Hand–Arm Bimanual Intensive Training Including Lower Extremity[53]¶	A functional, activity-based intensive training with simultaneous involvement of both upper and lower limbs to improve performance tasks of daily living	Improved manual abilities, simulated activities of daily living, and achievement of functional goals	Can be adapted for children with bilateral spastic cerebral palsy to improve their upper and lower limb function and their balance
Neuromuscular electrostimulation[54]†	Electrical current with sufficient intensity to produce muscle contraction by depolarising local motor nerves to facilitate the muscle strength and reduce spasticity	Improved walking speed and multiple dimensions (standing, walking, running, and jumping) of the gross motor function measure in children with spastic cerebral palsy	Neuromuscular electrostimulation combined with conventional physical therapy is more effective than physical therapy alone; neuromuscular electrostimulation might be more beneficial in young children (mean age 4 years)
Extracorporeal shockwave therapy[55]‖	Electric shocks of varying frequencies to relieve spastic muscle pain	Reduced spasticity with short-term efficacy duration and a potential to improve gross motor functioning	No improvements were reported in balance or gait outcomes in children with bilateral spastic cerebral palsy with GMFCS levels I or II after extracorporeal shockwave therapy combined with physical training
Transcranial magnetic stimulation[56]‖	Non-invasive technique where a focused magnetic pulse is delivered into the brain tissue (ie, motor cortex) with a coil; the therapeutic effect is based on altered cortical excitability, intracortical inhibition, and cortical plasticity	Reduced upper limb spasticity, reduced dystonia, improved upper limb passive range of motion, and improved static balance and gait velocity	Transcranial magnetic stimulation might be used as adjunct therapy to treadmill, gait, or virtual reality training; however, future large-scale longitudinal studies are needed

The presented examples were selected because they are rehabilitation therapies that are commonly used in clinical practice, with updated evidence in the past 5 years. These examples focus on upper and lower limbs, a combination of both, or involve modalities such as electrical currents and magnetic pulses. GMFCS=Gross Motor Function Classification System. *Clinical practice guidelines[47] provide evidence of goal-directed training. †Systematic reviews and meta-analyses[48,49,52,54] provide evidence of overground gait training, strength training, activation observation therapy, and neuromuscular electrostimulation. ‡An intervention study[50] provides evidence of functional power training. §A Cochrane systematic review[51] provides evidence of constraint-induced movement therapy and bimanual therapy. ¶A retrospective study[53] provides evidence of Hand–Arm Bimanual Intensive Training Including Lower Extremity. ‖Systematic reviews[55,56] provide evidence of extracorporeal shockwave therapy and transcranial magnetic stimulation.

Table 2: **Rehabilitation therapies to improve motor outcomes in individuals with cerebral palsy**

functional goals; however, boosts of therapy are necessary to maintain effects in the long term.[64]

Wheelchair mobility promotes overall development and increased levels of activity and participation. Intensive training in manual and powered wheelchair skills improves skills that are retained in the long term in individuals with GMFCS levels III–V, including a 70% achievement of individually set functional goals, such as exploration of surroundings and social interactions.[65,66]

Independent communication and access to computers for educational and leisure purposes are key to improved outcomes throughout the lifespan. Intensive augmentative and alternative communication interventions, such as use of eye-tracking technology in children with dyskinetic cerebral palsy,[67] can lead to the acquisition of operational competencies that optimise ease of use and interaction with the device.

Although technology appears promising for improving motor and functional outcomes, especially for individuals with GMFCS levels IV or V who would otherwise have low possibilities to independently participate in activities of daily living, the prohibitive cost of most of the devices makes them available only to a minority of users. Low-cost, three-dimensional printing techniques to produce patient-specific devices, such as orthoses or components of mobility devices; low-cost mobile applications;

	Mechanism	Motor outcome	Comments
Robotics and exoskeletons[57]*			
Upper limb robotics[58]†	Repetitive and task-specific upper limb movements to enhance neuronal plasticity and improve motor function and the quality of movement	Reduced upper limb spasticity and improved motor function (dissociated movement, grasp, weight-bearing, and protective extension) compared with conventional physical therapy	Evidence on robotics and exoskeletons is limited, warranting future larger-scale clinical trials; their effectiveness should also be explored in all types of cerebral palsy, particularly GMFCS levels IV and V
Robotic-assisted gait training[59]‡	Electromechanical device that assists stepping cycles by use of high-dosage, repetitive movements that imitate walking, while supporting bodyweight	Compared with non-robotic gait training, robotic-assisted gait training appears to have no effect on improvement of gross motor function, walking speed, and endurance in individuals with spastic cerebral palsy	Evidence on robotics and exoskeletons is limited, warranting future larger-scale clinical trials; their effectiveness should also be explored in all types of cerebral palsy, particularly GMFCS levels IV and V
Wearable exoskeletons[60]§	Wearable units that are controlled by a microprocessor with the purpose of supporting movements	Improved gait spatiotemporal parameters	Evidence on robotics and exoskeletons is limited, warranting future larger-scale clinical trials; their effectiveness should also be explored in all types of cerebral palsy, particularly GMFCS levels IV and V
Treadmill training[48,61]†‡			
Treadmill gait training[48]	Repeated weight loading on individual's lower limbs aiming at improving gait parameters and gait function	Improved gait walking speed, walking endurance, and knee flexor and extensor muscle strength, increased step length, and improved gross motor function	Treadmill gait training is more effective than overground gait training, possibly because of the controlled repetition gait cycles
Partial bodyweight support treadmill training[61]	Support of bodyweight with a chest corset that has straps positioned around the proximal legs aiming at reducing weight-riding in the lower extremities to provide symmetrical walking pattern	Improved gross motor function (standing, walking, running, and jumping)	Partial bodyweight support treadmill training is more effective than overground gait training, possibly because of the controlled repetition gait cycles and the postural control system consisting of a parachute assembly
Antigravity treadmill training[61]	Treadmill enclosed in an inflatable bag, providing the amount of bodyweight based on the air pressure of the bag, which creates lift force	Improved gait parameters (walking speed, stride length, cadence, and time spent in double-limb support), balance, fall risk, and gross motor function (standing, walking, running, and jumping)	Antigravity gait training might be a good option for children with high GMFCS levels (III or IV)
Virtual reality[57,62]*§	Computer-based stimulations of an environment that imitates a physical presence in the real or imagined world; virtual reality can be immersive (ie, head-mounted display) and non-immersive (ie, desktop display)	Low-to-very low quality of evidence that adding virtual reality to conventional physical therapy improves upper and lower limb function, postural control, and balance; virtual reality is effective in increasing motivation and engagement during therapy	The insufficient evidence of the effectiveness of virtual reality in improving motor and functional outcomes and their high purchasing costs warrant cautious use as an adjunct therapy
Serious games[63,64]§¶	Digital interactive rehabilitation games specifically used for a serious purpose (ie, to enhance motor function)	Home-based training: inconclusive results regarding improvement in motor function (upper and lower limb and balance); clinical-setting training: improved standing and dynamic sitting balance and postural control, inconclusive results on improved upper and lower limb function (walking, running, and jumping)	Gaming technology has a high purchasing cost, making its access impossible for children in poor-resource settings; future research should establish the effectiveness of the available free-to-low-cost games, because of their established potential to promote patients' motivation and engagement during therapy
Manual[65] and powered[66] wheelchairs‖	A chair fitted with wheels, manually operated or power-driven, designed to facilitate the mobility of individuals who are unable to walk independently	8-week manual wheelchair mobility skills training (combined with exercise training) leads to sustained improvements of physical activity, wheelchair mobility skills, and aerobic and anaerobic performance; 3-week intensive powered wheelchair skills training leads to sustained improvement of powered wheelchair skills, with 70% of individual functional goals achieved after intervention	Evidence on wheelchair mobility interventions in individuals with cerebral palsy with GMFCS levels III–V is mostly based on small-scale studies with low-quality evidence and high risk of bias; more robust research is necessary to explore motor and functional outcomes after wheelchair skill interventions

GMFCS=Gross Motor Function Classification System. *A narrative review[57] provides evidence of robotics and exoskeletons, and virtual reality. †Randomised controlled trials[58,61] provide evidence of upper limb robotics and treadmill training. ‡Systematic reviews and meta-analyses[48,59] provide evidence of treadmill training and robotic-assisted gait training. §Systematic reviews[60,62,63] provide evidence of wearable exoskeletons, virtual reality, and serious games. ¶A randomised crossover trial[64] provides evidence of serious games. ||Intervention studies[65,66] provide evidence of manual and powered wheelchairs.

Table 3: **Rehabilitation technology for cerebral palsy**

appropriate paper-based technology (ie, recycled materials converted into assistive devices); and do-it-yourself assistive technologies are emerging low-cost alternatives to rehabilitation technologies that should be considered in resource-poor settings.

Pharmacological management

Clinicians with expertise in cerebral palsy tend to use the same oral medications to reduce spasticity and dystonia, with higher effectiveness for the treatment of spasticity.[68] One study found that the most commonly used drugs are baclofen (administered to 39% of individuals with cerebral palsy), trihexyphenidyl (20%, for treatment of dystonia only), gabapentin (19%), diazepam (13%), and clonidine (10%).[69] Data on efficacy in tone reduction are scarce and adverse events limit clinical use (table 4). Effects of these drugs on body structure and function, such as range of motion and muscle strength, are understudied. Oral levetiracetam has also been used to reduce choreoathetosis.[72]

Botulinum neurotoxin A (BoNT-A) is mainly injected in large spastic lower limb muscle groups, aiming at reducing muscle tone to improve gross motor function, or at reducing pain.[70,73] Treatment success after

BoNT-A injections varies widely, with conflicting results on gait improvements and gross motor function.[73,74] Treatment is most effective when combined with physiotherapy and adapted orthoses and should not be used as a stand-alone therapy.[75] Therefore, better characterisation of treatment response predictors is needed.[75] The first two injections relieve spasticity and improve fine and gross motor activities.[76] Moreover, some evidence suggests that too frequent BoNT-A injections might cause permanent changes in the injected muscle, such as muscle atrophy and fibrosis,[73] and no clinical benefit exists in reinjecting before 6 months from the first injection.[77] The use of BoNT-A in the spastic upper limb muscles can decrease spasticity and avoid or delay contractures, thus improving upper limb function, speed and performance of alternating tasks, and quality of upper limb movement; however, evidence for fine manual abilities is scarce.[73,78] In individuals with dyskinetic cerebral palsy, BoNT-A is used to decrease dystonia and reduce pain; however, evidence is insufficient to affirm its effectiveness in improving motor function.[71] Systemic adverse events after a BoNT-A injection can occur, and they are more likely to occur if gross motor functions are severely impaired, if there is a history of dysphagia or aspiration pneumonia, or if the BoNT-A dose is increased.[79] In cases of resistance to BoNT-A, BoNT-B can be considered to improve muscle tone; however, its duration of action is shorter and its potency is 40 times lower than BoNT-A,[93] with a higher incidence of adverse events.[73]

	Targeted motor disorders	Mechanism of action	Motor outcome	Adverse events	Comments
Pharmacological management					
α-2 agonists (clonidine and tinazidine)[70,71]*†	Spasticity and dystonia	Increasing presynaptic inhibition of motor neurons	Reduced spasticity and improved dystonia	Sedation, cognitive effects, dizziness, hypotension, and bradycardia	Adverse events limit the use of these drugs
Anticholinergics (trihexyphenidyl and benzatropine)[71,72]†‡	Dystonia	Inhibition of acetylcholine action with antispasmodic effects on the muscle	Reduced dystonia	Worsening of chorea, agitation, confusion, dizziness, drowsiness, constipation, urinary retention, tachycardia, and blurred vision	Possibly ineffective in reducing dystonia; alternatives should be considered
Benzodiazepine receptor agonists (diazepam and clonazepam)[70,72]*‡	Spasticity and dystonia	Activation of $GABA_A$ receptors in motor neurons in the spinal cord to produce muscle relaxant effects	Reduced spasticity	Drowsiness, weakness, behavioural changes, constipation, headache, nausea, and paraesthesia	Evidence for spasticity but not for dystonia; use is limited by daytime sedation and pharmacological tolerance
Botulinum neurotoxin A[70,71,73-79]*†‡§¶	Spasticity and dystonia	Reversible blockage of acetylcholine release at the neuromuscular junction	Reduced localised spasticity and increased range of motion in the upper and lower limbs (decreased equinus, and improved gait and gross motor function)	Upper respiratory tract infections, generalised weakness, dysphagia, pharyngitis, and pyrexia	Injections should not occur more frequently than every 3–6 months; repeated injections can lead to antibody resistance
Dantrolene[70]*	Spasticity	Calcium inhibition in the sarcoplasmic reticulum of muscles resulting in muscle relaxation	Improved muscle tone, increased passive range of motion, and increased muscle strength	Diffuse weakness, possible hepatoxicity, anorexia, diarrhoea, and vomiting	Possibly ineffective; alternatives should be considered
Gabapentin[17,72]*‡	Spasticity and dystonia	Disrupts calcium signalling involved in neurotransmitter release	Limited evidence for reduced spasticity or dystonia	Dizziness, drowsiness, sedation, fever, fatigue, nystagmus, viral infection, and ataxia	Might be considered when hypertonia is associated with pain
Levetiracetam[17,72]*‡	Chorea	Inhibits presynaptic calcium channels, reducing neurotransmitter release and acting as neuromodulator	Reduced chorea	Dizziness, somnolence, headache, decreased energy, and mild ataxia	Limited evidence for efficacy
Levodopa[71,72]†‡	Dystonia	Enhances the activity of dopamine	Reduced dystonia	Orthostatic hypotension, nausea, and constipation	Limited efficacy; marked improvement might signal other diagnoses (eg, dopa-responsive dystonia)
Oral baclofen[68,70]*	Spasticity and dystonia	Activates $GABA_B$ receptors, thereby inhibiting both monosynaptic and polysynaptic reflexes at the spinal cord level, resulting in reduction of muscle spasticity	Reduced severity of muscle spasticity and dystonia	Gastrointestinal symptoms, somnolence, hypotonia, nausea, vomiting, lethargy, constipation, drowsiness, poor appetite, headache, and physical dependence	Limited ability to cross the blood–brain barrier; efficacy lower than with intrathecal administration; low efficacy for dystonia
Phenol and ethyl alcohol[68,70]*	Spasticity	Chemical neurolysis targeting α and γ motor neurons that acts non-specifically denaturating neural proteins and blocking efferent signals with a quick onset of action	Reduced localised spasticity and increased range of motion in upper and lower limbs	Pain in the injection site, skin irritation, anaesthesia-related complications, paraesthesia, and dysaesthesia	Long-lasting effect compared with other pharmacological options; technical difficulty and pain are important limitations
Tetrabenazine[72]‡	Dystonia	Depletion of presynaptic monoamines and prevention of dopamine release from vesicles	Reduced dystonia and improvement in hand function	Drowsiness, parkinsonism and rigidity, anxiety and depression, insomnia, and akathisia	Limited efficacy; adverse events limit the use of this drug

(Table 4 continues on next page)

	Targeted motor disorders	Mechanism of action	Motor outcome	Adverse events	Comments
(Continued from previous page)					
Neurosurgical management					
Deep brain stimulation[80-83]*†‖**	Dystonia	Electrodes emitting electrical pulses that modulate the basal ganglia and thalamocortical network	Reduced dystonia and improved motor function	Hardware problems, worsening of dystonia, worsening of chorea, CSF leakage, fever, respiratory distress, paraesthesia and sensory dysfunction, pneumonia, dysarthria, agitation, vertigo, seizure, and wound infection	Potential efficacious option for some children
Intrathecal baclofen[84-86]§**	Spasticity and dystonia	Activates $GABA_B$ receptors, thereby inhibiting both monosynaptic and polysynaptic reflexes at the spinal cord level, resulting in reduction of muscle spasticity	Reduced spasticity, reduced dystonia at rest, and improved upper and lower limb function	CSF leakage, site infection, pump failure, seizures, nausea, and vomiting	Reversible; efficacious option for some children and adults
Selective dorsal rhizotomy[87-92]‡§‖	Spasticity	Procedure in which lumbosacral dorsal nerve rootlets are selectively severed with preoperative electrophysiology on the basis of their presumed role in hyperexcitability	Reduced spasticity, increased muscle strength, and improved gross and fine motor function	Pulmonary complications, deep wound infections, dural CSF leaks, bladder and gastrointestinal dysfunction, hypersensitivity, numbness, paraesthesia, spinal deformity (lumbar lordosis, scoliosis, spinal stenosis, and spondylolisthesis), unmasking of weakness or dystonia (manifestations previously supressed by high levels of spasticity)	Irreversible; efficacious option for some children

*Narrative reviews[17,68,70,73,75,82] provide evidence of gabapentin, levetiracetam, oral baclofen, phenol and ethyl alcohol, botulinum neurotoxin A, α-2 agonists, benzodiazepine receptor agonists, dantrolene, and deep brain stimulation. †Systematic reviews and meta-analyses[71,81] provide evidence of α-2 agonists, anticholinergics, botulinum neurotoxin A, levodopa, and deep brain stimulation. ‡Systematic reviews[72,76,78,91] provide evidence of anticholinergics, benzodiazepine receptor agonists, botulinum neurotoxin A, gabapentin, levetiracetam, levodopa, tetrabenazine, and selective dorsal rhizotomy. §Observational studies[74,79,84,86,87,89,90] provide evidence of botulinum neurotoxin A, intrathecal baclofen, and selective dorsal rhizotomy. ¶An intervention study[77] provides evidence of botulinum neurotoxin A. ||Longitudinal studies[80,88,92] provide evidence of deep brain stimulation and selective dorsal rhizotomy. **Randomised controlled trials[83,85] provide evidence of deep brain stimulation and intrathecal baclofen.

Table 4: **Pharmacological and neurosurgical management of cerebral palsy**

Chemodenervation by the injection of neurolytic agents, such as phenol and ethyl alcohol, leads to reduced focal and regional spasticity and increased range of motion. These agents were widely used before BoNT-A was introduced.[70,73] Phenol injections can temporarily reduce tone in muscles selected for injection; however, its effect is inferior to BoNT-A and it is associated with a higher incidence of complications related to anaesthesia and injection.[70] Because of their reduced cost compared with BoNT-A, phenol injections are often a preferred choice in low-income and middle-income countries.

Neurosurgical interventions

Intrathecal baclofen treatment is used as an alternative to oral baclofen to reduce spasticity and dystonia, to improve function, and to prevent musculoskeletal deformities secondary to long-lasting hypertonia.[68] Because baclofen is delivered beyond the blood–brain barrier through an implanted pump, the dosage is much lower than oral baclofen, reducing the risk of adverse events. The majority of individuals with cerebral palsy who are treated with intrathecal baclofen are classified at GMFCS levels IV or V (approximately 95% of cases) and diagnosed with bilateral spastic cerebral palsy (approximately 82% of cases).[94] In Europe, 3·4% (varying between 0·4% and 4·7% depending on country) of children with cerebral palsy are treated with intrathecal baclofen; however, treatment access differs substantially depending on the country's gross domestic product.[94] In individuals with either spastic or dyskinetic cerebral palsy, treatment with intrathecal baclofen has a positive effect on the attainment of individual functional goals; a substantial decrease in spasticity and dystonia at rest; a decrease in chronic pain; improved mobility; improvements in the ease of changing position, sitting, and moving around; improved manual ability; decrease in dependence on caregiving by others; and increase in performance satisfaction.[84–86]

Selective dorsal rhizotomy is indicated only for treatment of spastic cerebral palsy and is another way of reducing spasticity. Selective dorsal rhizotomy is specifically used in individuals with bilateral spastic cerebral palsy and leads to reduced spasticity in both the upper and lower limbs, with an overall improvement of the upper limb dissociated movements, grasp, gross motor function, and quality of life.[87–90] The long-term effect of selective dorsal rhizotomy on spasticity is uncertain to date, with studies reporting the need for add-on treatments.[91] However, a slower decline in gross motor function, less dependence or need for daily assistance, lasting and stable levels of activities of daily living and social participation, and higher satisfaction have been reported in adults with cerebral palsy undergoing selective dorsal rhizotomy, compared with those who did not receive this treatment.[92]

Deep brain stimulation with implanted microelectrodes modulating the basal ganglia and the thalamocortical network is used to reduce dystonia and improve motor function.[80–82] Bilateral deep brain stimulation is most common, with better results from thalamic or globus pallidus pars interna stimulations than from globus pallidus pars externa stimulations.[82] Improvements in dystonia 1 year after deep brain stimulation are reported in about 27% of patients undergoing the procedure,[81] with a retained motor score improvement of 50% and a disability score improvement of 30% at a 5-year follow-up.[80] Deep brain stimulation shows a favourable effect on the attainment of individual goals, improved performance of daily-life activities (eg, sleeping, positioning, or dressing), and quality of life, even in patients without changes in dystonia severity.[83] All these neurosurgical interventions are listed in table 4.

Orthopaedic surgery

Orthopaedic surgery includes tendon lengthening to correct contractures; tendon transfers to re-establish muscle balance; rotational osteotomy for torsional bony deformities; and spine, hip, and foot stabilisation.[95] Single-event multilevel surgery (ie, separate orthopaedic procedures during one operative session) can lead to improvement of gait kinematics in children with bilateral spastic cerebral palsy, maintained during a 9-year follow-up in 77% of cases.[96] Similar improvements at a 9–10 year follow-up were also obtained in children with unilateral spastic cerebral palsy.[97] Surgery to correct scoliosis leads to deformity correction; however, the procedure is associated with a moderately high rate of complications (respiratory compromise and infection, wound infection, metalware complications, pseudo-arthrosis, etc), and evidence is insufficient in support of substantial improvements.[98] The presence of comorbidities (eg, hip subluxation or dislocation, spasticity, pulmonary function, seizures, gastrointestinal issues, poor nutritional status, and coagulopathy) might determine the risks of scoliosis surgery.[98] After equinus, hip displacement is reportedly the second most common orthopaedic issue in children with cerebral palsy, and is related to GMFCS level (with rates as high as 90% in children with GMFCS level V) but not to the type of movement disorder.[15] In children with GMFCS levels IV or V, non-surgical (eg, bracing, physical therapy, and BoNT-A injections) and neurosurgical approaches (eg, intrathecal baclofen or selective dorsal rhizotomy) do not prevent hip displacement but they might have other benefits related to muscle tone and pain.[99] Isolated soft-tissue surgeries do not prevent hip displacement but might postpone the need for a reconstructive surgery procedure. Reconstructive surgery is related to improved radiographic appearance, health-related quality of life, and pain-free transfers and activities of daily living.[99] National hip surveillance programmes are crucial to ensure early detection of hip displacement to enable timely referral to orthopaedic treatment. Orthopaedic surgery in individuals with dyskinetic cerebral palsy is less straightforward than in individuals with spastic cerebral palsy because of unpredictability in response outcomes and lack of clinical trials on its effectiveness.[100] In children with GMFCS levels I–III with mild dystonia, surgery of lower limbs resulted in preoperatively functional motor skills maintained in 14 (78%) of 18 cases and improved in only one (6%) case.[100] In children with GMFCS levels IV or V with severe dystonia, a linear increase of hip migration percentage was seen up to 21 months postoperatively; however, the outcome remained within the acceptable range of 30% or less.[100] Cervical laminoplasty to treat cervical myelopathy (mainly attributed to cervical muscle tone and involuntary movements) in adults with dyskinetic cerebral palsy seems effective in improving activities of daily living,[101] which were maintained at a 10-year follow-up.[44] A 10-year follow-up after laminoplasty showed substantial kyphosis correction and maintained cervical alignment, maintained walking ability in ambulatory patients, recovery of walking abilities in non-ambulatory patients, and improvement of sensory function.[44] Symptomatic cervical spinal stenosis is also present in adults with spastic cerebral palsy,[45] but to a much lesser extent than in adults with dyskinetic cerebral palsy.

Teleinterventions

Teleinterventions might improve access to health care and health outcomes cost-effectively, while addressing the unequal distribution of health-care services, especially in remote locations and in low-income and middle-income countries. Teleinterventions in people with cerebral palsy lead to overall substantial improvements in more than 50% of study outcomes, and an improvement on 23% of motor outcomes when the focus is on improving motor outcomes.[102] However, home-based interventions without videoconferencing show larger improvements (70%) than teleinterventions provided in real-time in both clinical and research settings (50%).[102] In children with unilateral cerebral palsy (GMFCS levels I or II and MACS levels I–III), teleinterventions substantially improved gait capacity and performance, occupational performance, dexterity, bimanual hand function, and lower limb function.[103]

Research on teleinterventions in individuals with cerebral palsy with high severity of motor impairments is scarce. The implementation of teleinterventions in low-income and middle-income countries is understudied. Poor internet connection, low availability of technology devices, and digital health illiteracy are barriers that should be addressed. The COVID-19 pandemic has rapidly increased the use of teleinterventions and has highlighted the role of telemedicine in providing continuity of care (eg, follow-up of adverse events and benefits of medication, adjustment of medication, orthopaedic monitoring, neurosurgical evaluations, and assessments of pain or range of motion); prevention of contractures and the development of deformities through routine telemonitoring; early detection of necessary interventions;

and support for patients and their caregivers regarding their questions and decision-making processes.[104] Lessons learned from these experiences are expected to lead to a better understanding of when and where teleinterventions should be used in clinical practice.

Secondary and tertiary prevention

Multimorbidity is highly prevalent in adults with cerebral palsy, with the most common comorbidities being cardiovascular diseases, respiratory diseases, dysphagia, fluid and electrolyte disorders, metabolic disorders, neurological-related disorders, gastrointestinal issues, and orthopaedic-related disorders,[105] most of which are associated with elevated mortality. Many of these comorbidities might be related to a sedentary lifestyle and restricted physical activity. Exercise interventions might be beneficial in increasing gait speed and muscle strength, but without any substantial effect on overall gross motor function.[106] Leisure-time physical activity interventions might lead to improved musculoskeletal health, cardiorespiratory fitness, and functional independence; however, more research is needed to enhance the reach and inclusion of non-ambulant individuals.[107]

Respiratory disease is the leading cause of mortality in individuals with cerebral palsy, with risk factors including mobility status, swallowing abilities, recurrent aspiration, impaired airway clearance, impaired lung function, seizures, poor nutritional status, and spinal and thoracic deformities.[108,109] Ongoing surveillance for the risk of respiratory diseases is crucial because most causes are manageable through non-invasive or invasive approaches.[108]

Because of feeding difficulties, people with cerebral palsy are at heightened risk of malnutrition and reduced growth.[110] 52–89% of children with cerebral palsy have moderate-to-severe undernutrition, associated with maternal education and the severity of the motor impairments (GMFCS levels III–V), particularly in resource-poor settings.[110] Infections pose one of the main threats to premature mortality in resource-poor countries, and are highly associated with undernourishment.[111] Nutrition-focused interventions, like dietary modifications and surgical interventions, might improve nutritional outcomes, thus calling for the development of best practice guidelines for the nutritional management of children with cerebral palsy in resource-poor settings.[112] Additionally, future research should explore any association between nutrition-focused interventions and motor and functional outcomes. Gastrostomy tube feeding can result in substantial weight gain and could be the only viable option to provide adequate nutrition to children with severe swallowing difficulties.[113] The risk of complications of gastronomy tube placement is high, requiring a close monitoring after placement; complications include functional tube and bowel problems, pulmonary aspiration, infections, and bleeding.[113] Skeletal fragility increases the risk of fractures across the lifespan, causing acquired disability, morbidity, lower quality of life, and early mortality.[114] Therefore, the optimisation of nutrient intake and weight-bearing is essential to improve bone health in individuals with cerebral palsy. Preventing the occurrence or progression of postural asymmetries decreases the likelihood of scoliosis, windswept hips, and flexion contractures in the hips and knees.[115]

Conclusions and future directions

A multidisciplinary and integrative approach that considers the inseparable link of motor behaviour with somatosensory impairments, cognition and learning, pain, mental health, social aspects, and quality of life is crucial in the management of people with cerebral palsy, ensuring meaningful outcomes throughout the lifespan. Cerebral palsy is a heterogeneous condition and clinical practice suggests that a universal approach is inadequate. People with cerebral palsy have individual needs and priorities, also depending on the stage of life. Therefore, treatment goals should always be tailored to address these needs and what individuals and their families deem relevant and meaningful. Regarding a family-centred approach to services, the most important aspects rated by parents are provision of specific information about their child's therapy and assessment results, and coordinated and comprehensive care for the child across services.[116] Tools like the WWW-roadmap digital tool (with the Ws standing for What do I want to know?, Where can I find information?, and Who can help me further to answer my questions?) have been developed to help caregivers explore the needs of both individuals with cerebral palsy and their family, find information, and prepare before consultations with professionals. These tools appear to show positive results in supporting parental involvement in decision-making processes.[117] Beside a family-centred approach to services, people with cerebral palsy and their families should guide research priorities and be actively involved in different phases of research projects that concern them. The Involvement Matrix is a tool that was developed to support the discussion between people with cerebral palsy, families, and researchers about their roles and expectations.[118] The Involvement Matrix could be used to enhance the quality of cerebral palsy research.

International, evidence-based recommendations to improve outcomes in cerebral palsy stem mainly from studies done in well-resourced settings with children with cerebral palsy who have access to early interventions, regular therapy, adaptive equipment, and pharmacological and neurosurgical interventions.[119] However, access to several treatment options with the recommended dosages or to rehabilitation and assistive technologies is very limited for individuals with cerebral palsy living in resource-poor countries.[119,120] Such inadequate access creates a disparity that makes international evidence-based recommendations not fully applicable worldwide. Future guidelines should consider studies done across all settings, involving people with cerebral palsy of all ages,

Search strategy and selection criteria

We identified references for this Review by searching Ovid MEDLINE, Allied and Complementary Medicine Database, Cochrane Reviews, Embase, Evidence-Based Medicine Reviews, ClinicalTrials.gov, and the WHO International Clinical Trials Registry Platform for publications between Jan 1, 2017, and Aug 13, 2022, without language restrictions and filtering for peer-reviewed articles. We hand-searched references of relevant articles. Search terms included "cerebral palsy", the different types of cerebral palsy ("spastic", "dyskinetic", and "ataxic") and motor disorders ("spasticity", "dystonia", "athetosis", "chorea", "choreoathetosis", "tremor", "ataxia", "hypotonia", "hypertonia", etc), a list of pharmacological, surgical, and therapeutic interventions ("baclofen", "trihexyphenidyl", "benzodiazepines", "botulinum toxin", "deep brain stimulation", "physical therapy", "functional gait training", etc), technology-based interventions ("robotics", "virtual reality", "exergames", "wheelchairs", etc), "telehealth", and "teleintervention". We prioritised studies with higher scientific rigour, including systematic reviews and meta-analyses, population-based studies, randomised controlled trials, and intervention studies with large sample sizes.

and including all functional classification levels.[119,120] Crucial steps forward to ensure universal and equal access to technology for greater functional independence might include developing innovative, low-cost, high-quality alternatives to the existing rehabilitation and assistive technologies; adapting certification of medical devices to consider low-tech and low-cost solutions for low-income and middle-income countries; improving access, dissemination, and reimbursement policies; and raising awareness. The bioethical principle of justice indicates the equal and fair distribution of care and resources, and it should guide the reorganisation of the health-care system and future disability policies to consider individuals' needs as challenges that concern not only the person with cerebral palsy but also the community they live in.[4] Sound, standardised cerebral palsy registers should be implemented in low-income and middle-income countries to expand the initiative of the Global LMIC CP Register to harmonise and share epidemiological and clinical information, with the aim of identifying modifiable risk factors and favouring early diagnosis and timely provision of interventions.

Cerebral palsy is a lifelong, changing condition and children require a transition to adult-oriented health services that address their preferred adult roles.[121] Compared with the general population, adults with cerebral palsy (particularly those with higher limitations in gross motor and cognitive functions) report reduced rates of employment, independent living, intimate and social relationships, participation rates, and overall quality of life.[40,122,123] Additionally, adults with cerebral palsy report high levels of pain and fatigue, and are at high risk of severe anxiety and depression.[124] Paediatric models of care do not address the needs of adults with cerebral palsy; therefore, improved screening and check-up programmes, accessibility to health care and service support, increased knowledge dissemination, and use of new technologies such as telemedicine are crucial to ensure positive lived experiences.[105,121] The evidence for the long-term effects of childhood interventions is insufficient. This gap in knowledge specifically calls for future research to inform therapy and practices—namely, choice of best treatment options and optimal dosage.

Furthermore, more research is needed on the effectiveness of therapeutic modalities in individuals with severe motor and non-motor impairments (eg, non-ambulant, non-verbal, and profound cognitive impairments). Telemedicine and home-based interventions can increase accessibility to consultations, treatments, and new interventions.[102] Emerging technologies (eg, eye-tracking technology, powered wheelchairs with unconventional interfaces, and adapted environmental control systems) hold the potential to unlock greater independence towards positive lived experiences.

New interventions during pregnancy and in the neonate are reducing the incidence and severity of brain injuries that cause cerebral palsy. Examples include cooling after neonatal encephalopathy and the use of magnesium sulphate for women going into very premature labour.[15] Some new therapies have been introduced in the management of cerebral palsy, including stem-cell therapy and medical cannabinoids;[15] however, their effectiveness remains uncertain to date, and large phase 3 trials are required.

This Review has highlighted the many options that are available, and more therapeutic and technological advancements are foreseen. At the same time, advocacy efforts are increasing to ensure that societal and access barriers are addressed. Nevertheless, despite the excitement about remarkable progress, decision making in clinical practice (ie, establishing which treatment, of all those available, is best for an individual with cerebral palsy) remains challenging. Ultimately, managing cerebral palsy should be aimed at achieving the best motor and functional outcomes that will support each individual achieve their goals throughout life.

Contributors

All authors conceptualised the Review. SB did the literature search and prepared the figure and tables. SB, EM, and BD drafted the first version of the manuscript. SM, GS, SRH, and NT contributed to the revision and editing of the manuscript. BD was responsible for the project administration. All authors had responsibility for the decision to submit for publication.

Declaration of interests

We declare no competing interests.

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