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Chapter 23

High-risk follow-up: Early intervention and rehabilitation

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Abstract

Early detection of childhood disability is possible using clinically available tools and procedures. Early detection of disability enables early intervention that maximizes the child's outcome, prevents the onset of complications, and supports parents. In this chapter, first we summarize the best-available tools for accurately predicting major childhood disabilities early, including autism spectrum disorder, cerebral palsy, developmental coordination disorder, fetal alcohol spectrum disorder, intellectual disability, hearing impairment, and visual impairment. Second, we provide an overview of the preclinical and clinical evidence for inducing neuroplasticity following brain injury. Third, we describe and appraise the evidence base for: (a) training-based interventions that induce neuroplasticity, (b) rehabilitation interventions not focused on inducing neuroplasticity, (c) complementary and alternative interventions, (d) environmental enrichment interventions in the neonatal intensive care and community settings, and (e) parent–child interaction interventions in the neonatal intensive care and community settings. Fourth, we explore emergent treatment options at clinical trial, designed to induce brain repair following injury. In conclusion, early diagnosis enables early intervention, which improves child and parent outcomes. We now know which interventions provide the biggest gains and the information can be used to help inform parental decision making when designing treatment plans for their children.

EMMA'S STORY

You are paged to the neonatal intensive care unit (NICU) to treat newborn Emma. Emma's start to life was uncertain and complex. Sophia was admitted for an emergency cesarean section with fetal maternal hemorrhage. After what seemed an eternity to new father Liam, he was ushered to a private room. The senior nurse communicated, "I am sorry, Liam, I have bad news; she has died." Not knowing he was having a daughter, Liam erroneously assumed his wife Sophia had died. His sorrow was tormenting. This was certainly not the day of joy Liam had been anticipating for 9 months. Liam's silence was eventually replaced by tears, as he cautiously asked "And my baby …?" Just as the assumption about Sophia was being corrected, the nurse was paged back to the emergency room. Within minutes, the nurse returned to Liam's side, to share more unexpected news: "We have her back!" At this moment, Liam assumed his daughter's miraculous recovery meant all was well.

You note that Emma had a low Apgar score, hypoxic ischemic encephalopathy (HIE) and multiorgan dysfunction. You treat Emma's seizures with phenobarbitone and therapeutic hypothermia is commenced within 3 h of life. You order a brain MRI at day 5 and observe there is increased T2 signal and diffusion restriction in the cerebral cortex and subcortical white matter bilaterally. There is also diffusion restriction in the basal ganglia and the posterior limb of the internal capsule bilaterally. Your role is to provide prognostic information to Sophia and Liam. You wonder if Liam can take the news. "I'm sorry. I have more bad news. Emma has suffered brain damage. She has

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moderate HIE." You notice that Liam and Sophia are now trembling with apprehension; they brace themselves and their questions flow: "What is HIE? What does this mean for her future? How bad is it?"

Beyond the NICU, many infants survive without disability, but it is important to identify those with disability. Hypoxic ischemic encephalopathy Sarnat 2 positions Emma deep with an uncomfortable gray zone for prognostication. You ask yourself: "Where does Emma's future lie? Will she have a lasting disability? Will she be my patient that recovers? Should I monitor and wait and see, or should I refer her to early intervention? What facts can I communicate to Liam and Sophia? How will they react? How can I do this well?"

Early detection of disability enables early intervention to improve outcomes. Early intervention enables prevention of complications. Therefore no matter how difficult the conversation with Liam and Sophie is, it is important that it is done well.

The focus of this chapter is to describe state-of-the-art: (a) early screening for detection of disability following prematurity, brain injury or genetic and/or social disruptions to development and (b) early interventions and rehabilitations that harness the infant's neuroplasticity and learning.

HIGH-RISK FOLLOW-UP

Rates of disability following prematurity, encephalopathy, and neonatal surgery are now well understood. Early detection of childhood disability such as cerebral palsy and sensory impairments (vision and hearing) is possible using clinically available tools and procedures (Morton and Nance, 2006; Novak et al., 2017). The purpose of high-risk developmental follow-up is to identify childhood disability early, to enable early intervention that maximizes the child's outcome and prevents the onset of complications. Early detection of disability can also provide an opportunity to establish early parental support, which is known to have a lasting positive impact on the parent's mental health (Spittle et al., 2016).

Not all infants discharged from the NICU have the same level of risk for long-term disability. Less than 10% of extremely preterm infants will go on to have cerebral palsy, for example, although a larger proportion will have cognitive and learning difficulties persisting into adolescence. Screening high-risk infants to more specifically identify the domains of risk is important, to optimize child outcomes and make best use of the health resources available. Evidence is now available about effective diagnostic-specific early interventions for children with disabilities such as cerebral palsy and autism. Therefore, it is important to differentiate not only levels of risk but also exactly what the infant is at risk of. "High risk for cerebral palsy" is different from "high risk of autism" vs "high social risk," and effective interventions for these conditions and contexts differ. Historically it has been difficult to identify and treat childhood disability early, because infants are preverbal, with a low motor repertoire and emergent cognitive skills. Now, psychometrically sound tests exist that enable early and accurate prediction of the risk for long-term disability.

From the child and family's perspective, it is important that comprehensive follow-up, screening, and intervention occur, especially when known risk factors for childhood disability exist. Who is responsible for coordinating follow-up? Responsibility for follow-up will vary depending on the country, funding available, medical training programs, and the service delivery model in the child's location. Care and follow-up might be coordinated by neonatal neurologists or neonatologists or child neurologists, or pediatricians. No matter who is responsible, it is important that follow-up be comprehensive, evidence based, and compassionate, without delay in diagnosis or gaps in continuity of care and intervention, while transitioning from neonatal intensive care into community-based follow-up.

We will now summarize best-available evidence for the tools that assist in early detection of major childhood disabilities following NICU admission or parent-identified developmental concerns (Fig. 23.1).

Autistic spectrum disorder early detection

Autism spectrum disorder (ASD) is disorder of social, communication, and cognitive skills that arises in the first years of life. The updated diagnostic criteria for ASD are defined in the DSM-5 (American Psychiatric Association, 2013). Universal screening for ASD has been recommended by the American Academy of Pediatrics (AAP) to ensure early detection and early evidence-based treatment (Johnson and Myers, 2007). Screening in universal and high-risk populations should be conducted using ASD-specific instruments at 18- and 24-months corrected age (corrected for prematurity), in conjunction with developmental surveillance (Johnson and Myers, 2007; Volkmar et al., 2014; Zwaigenbaum et al., 2015). A clinical guideline exists that summarizes best-available evidence about accurate early diagnosis and provides guidance about ASD-specific tool selection (Volkmar et al., 2014; Zwaigenbaum et al., 2015).

At 18–24-months corrected age, the most predictive tools for detecting risk of ASD are: (a) 10 Q-CHAT Quantitative Checklist for Autism in Toddlers, which is a 10-question parent-completed screening tool that detects the risk for ASD with 91% sensitivity in research conducted to date (Zwaigenbaum et al., 2015) and (b) the Modified Checklist for Autism in Toddlers (M-CHAT)

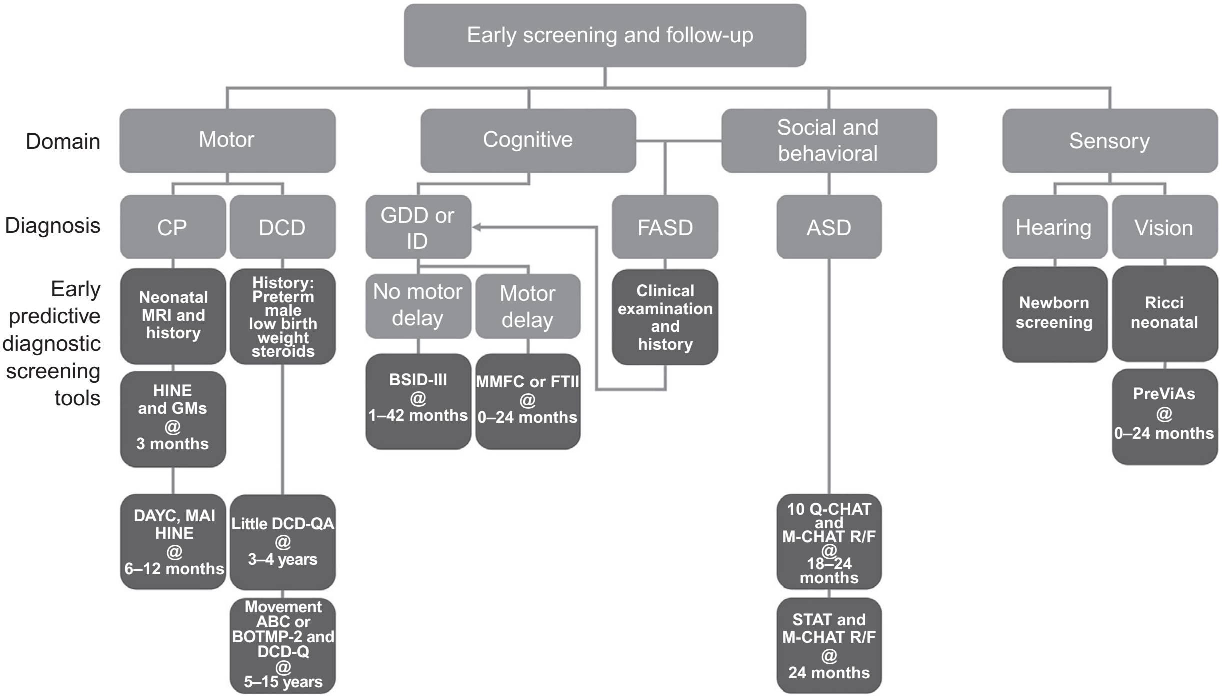

Fig. 23.1. Summary of tools for early detection of disability. *10 Q-CHAT*, Quantitative checklist for autism in toddlers; *ASD*, autism spectrum disorder; *BOTMP-2*, Bruininks–Oseretsky test of motor proficiency; *BSID-III*, Bayley scales of infant and toddler development, Third Edition; *CP*, cerebral palsy; *CVI*, cortical visual impairment; *DCD*, developmental coordination disorder; *DCD-Q*, developmental coordination disorder questionnaire; *FASD*, fetal alcohol spectrum disorder; *FTTI*, Fagan test infant intelligence; *GDD*, global developmental delay; *HINE*, Hammersmith infant neurological evaluation; *ID*, intellectual disability; *MAI*, motor assessment of infants; *M-CHAT R/F*, modified checklist for autism in toddlers revised with follow-up; *MMFC*, Mayes motor free compilation; *MRI*, magnetic resonance imaging; *PreViAs*, preverbal visual assessment; *STAT*, screening tool for autism in 2-year-olds.

Revised with Follow-up, which predicts risk for ASD in 54% of cases when the child's total score is initially greater than 3 and then greater than 2 at follow-up (Robins et al., 2014). Screening for ASD before 24 months is associated with higher false-positive rates than screening at 24 months but is still informative and worthwhile to enable early intervention (Zwaigenbaum et al., 2015). Screening is especially important when a sibling has the diagnosis of ASD (Zwaigenbaum et al., 2015). False positives occur because some behaviors of typically developing toddlers overlap with ASD symptoms (for example, repetitive behaviors like turning the lights on and off, and restricted interests with instance on routines). These behaviors may resolve with time (Zwaigenbaum et al., 2015).

At 24 months' corrected age, the most accurate tools for predicting the risk of ASD are: (a) the Screening Tool for Autism in Two-Year-Olds (STAT), which has 92% sensitivity for detecting risk of ASD and (b) Modified Checklist for Autism in Toddlers (M-CHAT) Revised with Follow-up, which predicts risk for ASD in 54% of cases when the child's total score is initially greater than 2 at follow-up (Robins et al., 2014).

The AAP recommends that children who screen positive on an ASD-specific screening tool should receive a comprehensive diagnostic work-up and concurrent referral to ASD-specific early intervention services with an emphasis on speech language pathology and early education (Johnson and Myers, 2007).

Cerebral palsy early detection

"Cerebral palsy describes 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" (Rosenbaum et al., 2007). Cerebral palsy is a clinical diagnosis, based on a combination of clinical signs, neurologic symptoms, and motor activity limitations, not a laboratory biomarker. The diagnosis of cerebral palsy can be accurately made before 6 months' corrected age, but it is more difficult with milder forms of cerebral palsy where the child may initially meet their motor milestones. A clinical guideline exists that summarizes best-available evidence and provides guidance (Novak et al., 2017). Early diagnosis begins with a medical history and involves using neuroimaging, standardized neurologic, and standardized motor assessments that indicate congruent abnormal findings indicative of cerebral palsy.

Before 5 months' corrected age, the most predictive tools for detecting risk of cerebral palsy are: (a) term-age MRI indicating brain abnormalities affecting the motor tracts, which has 86%–89% sensitivity for detecting risk of cerebral palsy; (b) Prechtl's Method on the Qualitative Assessment of General Movements, indicating "absent fidgety movements" equating to reduced quality of spontaneous movement, which has 98% sensitivity for detecting risk of cerebral palsy; and (c) the Hammersmith Infant Neurological Evaluation (HINE), where a score below 57 indicates neurologic signs likely to affect motor performance, which has 90% sensitivity for detecting risk of cerebral palsy (Novak et al., 2017).

After 5 months but before 24 months of corrected age, the most predictive tools for detecting risk of cerebral palsy are: (a) MRI where safe and feasible (which has 86%–89% sensitivity for detecting risk of cerebral palsy); (b) the HINE, where a score below 57 indicates neurologic signs likely to affect motor performance, which has 90% sensitivity for detecting risk of cerebral palsy; and (c) the parent report checklist known as the Developmental Assessment of Young Children (DAYC), which has an 83% C-index for detecting risk of cerebral palsy (Novak et al., 2017). Topography and severity of cerebral palsy are more difficult to ascertain in infancy; however, MRI and the Hammersmith may be helpful in assisting clinical decisions. There is a strong relationship between the Hammersmith scores and likelihood of later ambulation. Hammersmith scores below 40 indicate a low likelihood of ambulation, whereas scores above 40 indicate a high likelihood of ambulation.

Neurologists should understand the importance of prompt referral to diagnostic-specific early intervention to optimize infant motor and cognitive plasticity, prevent secondary complications, and optimize caregiver well-being (Novak et al., 2017).

Developmental coordination disorder early detection

Developmental coordination disorder (DCD) is a disorder of motor coordination that is not explainable by intellectual disability or any specific congenital or acquired neurologic condition, and the updated diagnostic criteria are defined in the DSM-5 (American Psychiatric Association, 2013). Approximately 5% of children have DCD, a disorder of praxis. Males born preterm with low birth weight are at high risk. A clinical guideline exists that defines the disorder, the diagnostic process, and recommended evidence-based treatments (Blank et al., 2012). In order to make the diagnosis of DCD, evidence from a standardized norm-referenced motor test is necessary to establish that the child's motor performance is substantially "below expected levels," combined with history taking, clinical examination, and validated questionnaires (Blank et al., 2012). Traditionally the diagnosis of DCD was made at 5 years of age, but research efforts are underway to identify methods of earlier detection.

At 3–4 years of age, the most predictive tool for detecting risk of DCD is the Little Developmental Coordination Disorder Questionnaire for Preschool Children (Wilson et al., 2015), which is a parent report checklist. More research is underway seeking to validate this tool in an even younger age group, which may lower the age at which it is possible to detect and treat DCD.

At 5 years of age and older, the most predictive tools for detecting risk of DCD are: (a) the Movement ABC and the Bruininks–Oseretsky Test of Motor Proficiency (BOTMP-2), which are both standardized movement assessments, where the child must score below the fifth-centile cut-off to be eligible for the diagnosis of DCD. The sensitivity of the Movement ABC is higher than the Bruininks–Oseretsky and it is therefore more strongly recommended and (b) the Developmental Coordination Disorder Questionnaire (DCD-Q), which is a parent-completed questionnaire of motor performance and functional skills (Blank et al., 2012).

Fetal alcohol spectrum disorder early detection

Fetal alcohol spectrum disorder (FASD) is a common but underrecognized cause of intellectual disability (Williams et al., 2015). The neurobehavioral problems resulting from prenatal alcohol exposure are lifelong, but early detection, diagnosis, and therapy improve outcomes (Williams et al., 2015). A clinical guideline exists that summarizes new nomenclature and categorization of the diagnosis into fetal alcohol spectrum disorder (Cook et al., 2016). Children with perinatal alcohol exposure may have a cluster of neurobehavioral symptoms present, with or without the sentinel facial features present (reduced palpebral fissure length, smooth philtrum, and thin upper vermillion lip border) (Cook et al., 2016). The guideline includes a diagnostic algorithm for classifying the various subtypes of FASD and risks for FASD (Cook et al., 2016).

Children with or suspected of FASD need to be diagnosed and managed by a team (Cook et al., 2016). The neurologist should refer children for psychometric testing of cognition and/or intelligence plus behavioral and motor testing to ensure the child receives the right family and learning supports.

Hearing impairment early detection

Clear evidence-based guidelines exist for newborn screening of hearing impairments (Joint Committee on Infant Hearing, 2007). The purpose of screening is to identify and correct hearing loss early, to promote literacy and speech development (Joint Committee on Infant Hearing, 2007). Assessment of hearing is an essential aspect of developmental follow-up, as critical periods exist for language development.

Intellectual disability or global developmental delay early detection

"Intellectual disability is characterized by significant limitations both in intellectual functioning and in adaptive behavior as expressed in conceptual, social, and practical adaptive skills" (Schalock et al., 2007). Global developmental delay (GDD) is the term used before 5 years of age for delay in 2 or more areas of development. The term GDD is used to allow for the scenario that the child may grow out of their delay. It is important for parents and school planning to confirm whether or not the cognitive delay is permanent and reclassify the condition as intellectual disability.

A clinical guideline exists summarizing the medical genetics diagnostic work-up for the diagnosis of intellectual disability (Moeschler and Shevell, 2014). The guideline recommends history taking, physical examination for dysmorphic features, followed by genetic testing when required. When a specific disorder is suspected, conduct single gene testing or chromosome microarray (CMA) as appropriate. When the diagnosis is unknown, (a) conduct CMA; then (b) screen for inborn errors of metabolism to identify any treatable metabolic conditions, followed by (c) fragile X genetic testing. When no diagnosis is established, test for: (a) X-linked conditions in males and (b) Rett syndrome in females. When head circumference is abnormal or intractable seizures exist, a brain MRI may be informative. Complete the diagnostic work-up by formulating a management plan with the family (Moeschler and Shevell, 2014). Genetic testing can clarify etiology, assist in determining prognosis, refine treatment options, and enable the family to receive genetic counseling and identify specific peer-based family support (Moeschler and Shevell, 2014). A diagnosis also validates the child's learning issues and helps the family and carers to develop realistic expectations (Moeschler and Shevell, 2014).

Screening for and quantifying cognitive delay is difficult, as most assessments have poor sensitivity in infancy for predicting intelligence over the long term. In addition, many tests are unsuitable for use with children with motor impairments (Lobo and Galloway, 2013). Moreover, some learning difficulties do not appear until school age, when literacy and graphomotor demands are higher. Below the age of 5 years, the Bayley Scales of Infant Development Version 3 (BSID-III) are the most commonly used standardized norm-referenced tool for identifying GDD. For infants less than 24 months old, with known motor delays or physical disability, the Bayley Scales may underestimate their cognitive skills, because of the physical abilities required to complete the testing, e.g., manipulation of blocks. For these infants, a systematic review recommends the use of the motor free tests, including the Mayes Motor Free Compilation or the Fagan Test of Infant Intelligence to produce more valid and accurate cognitive testing results (Morgan et al., 2018). In children over 5 years a range of robust intelligence tests exist, but in children with physical disabilities testing should be carried out by a clinical psychologist or neuropsychologist with expertise in adjusting and interpreting the test in such clinical scenarios.

Vision impairment early detection

The AAP recommends evaluation of the visual system in infancy and continuing at regular intervals throughout childhood, to identify children who may benefit from early interventions to correct or improve their vision (Committee on Practice and Ambulatory Medicine, 2015). Preterm infants should be screened for retinopathy of prematurity (ROP) and then referred to an ophthalmologist experienced in evaluating infants for a specialized eye examination (Committee on Practice and Ambulatory Medicine, 2015). Infants with a family history of eye disease should also be referred for specialized eye examinations (Committee on Practice and Ambulatory Medicine, 2015). In preverbal infants, the identification of eye health is more straightforward than the identification of abnormal visual behavior. Cerebral visual impairments (CVI) are common but underdiagnosed and undertreated in children with disabilities (Philip and Dutton, 2014). CVI can present in different ways, but the aim of management is to identify the child's individual problems and practical solutions to these to overcome these problems (Philip and Dutton, 2014). Management will need to involve a team approach, including the ophthalmologist, optometrist, orthoptist, pediatrician, occupational therapist, nurse, teachers, and caregivers (Philip and Dutton, 2014).

Children with or suspected of HIE, perinatal arterial ischemic stroke, hydrocephalus, hypoglycemia, or seizures, and/or cerebral palsy or ASD, should be comprehensively screened for CVI and visual field loss. Infants with HIE, with MRI findings in the parieto-occipital and parasagittal or watershed regions of the brain, are most at risk (Hoyt, 2003; Philip and Dutton, 2014). Infants with asymmetric myelination of the optic radiation evident on MRI and DTI, following perinatal arterial ischemic stroke, are at high risk for visual field deficits (Koenraads et al., 2016).

In infants less than 6 months of age, assessing whether the infant can track a high-contrast visual stimulus (e.g., black and white face) for a full 180-degree arc in both directions can be a useful blunt screening indicator for whether or not more specialist visual assessments are required.

The Ricci Assessment is a simple 5–10-min examination of visual function in the first days after birth at term. The test examines ocular movements, fixing, tracking, pursuit, discrimination, and attention at a distance (Ricci et al., 2011).

The PreViAs (preverbal visual assessment) parent report questionnaire can be used to assess visual behavior of infants under 24 months of age and to assess the normative outcomes at each age (García-Ormaechea et al., 2014). The PreViAs examine visual attention, visual communication, visual motor coordination, and visual processing (García-Ormaechea et al., 2014).

An essential part of follow-up is to communicate the findings of screenings to parents. They need to hear both the good and bad news. The way diagnostic and prognostic information is shared with parents will have a long-lasting impact on their trust in you and the healthcare system (Novak et al., 2016b). When sharing “bad news,” first gather information about the parent’s knowledge and readiness for the news. Next, provide clear information in a compassionate manner, minimizing the emotional impact and sense of isolation that can result from hearing this difficult news. Conclude with jointly planning a course of action and management that includes early intervention, as parents will want to help their child (Novak et al., 2016b).

KEY DRIVERS OF PLASTICITY AND LEARNING

Brain damage changes neurones, synapses, and neuronal networks and therefore can alter future learning processes (Kleim and Jones, 2008). In addition, some neonates will have genetic abnormalities on their causal pathway to brain injury, which may also interfere with subsequent learning (Kleim and Jones, 2008). Neuroplasticity is the basis for learning in the normal developing brain and relearning in the damaged brain through rehabilitation (Kleim and Jones, 2008). Regardless of how the brain was injured in the first place, all infant’s brains constantly remodel their neural circuitry to encode new experiences to develop adaptive behaviors (Kleim and Jones, 2008). The ultimate goal of rehabilitation therefore is to induce early neuroplasticity that restores the full potential of the injured brain.

Rehabilitation therefore must be individualized to the infant, their brain injury, and family circumstances, to harness drivers of plasticity and learning. Rehabilitation should also provide support and education to parents, because of their fundamental role in their child’s development. Key drivers of plasticity and learning are: (1) training-based interventions harnessing experience-dependent plasticity; (2) environmental enrichment; and (3) parent–child interactions (Fig. 23.2). Research is also underway to determine whether stem cells, novel pharmacologic agents, and neuromodulation might further enhance plasticity and even promote neuroregeneration (Novak et al., 2016a; Ismail et al., 2017).

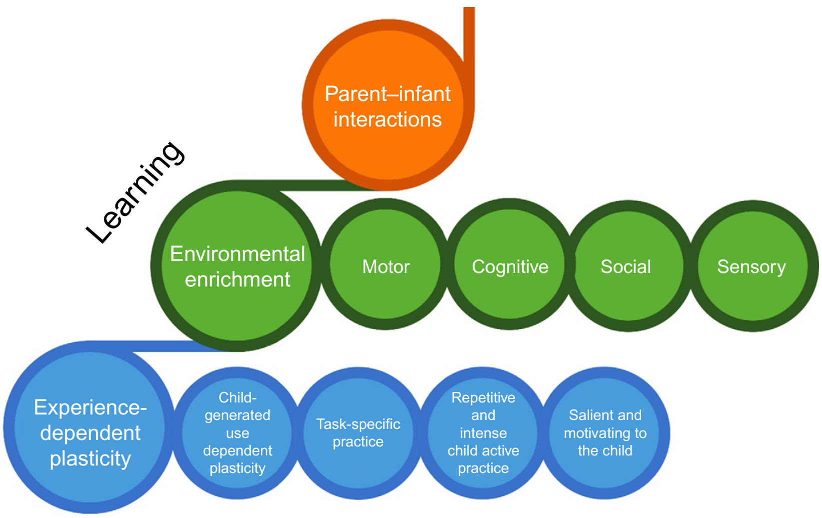

Fig. 23.2. Key drivers of plasticity and learning.

Training-based interventions harnessing experience-dependent plasticity

Infants have a remarkable capacity for learning and plasticity compared to adults, as evidenced by their ability to learn to speak multiple languages and to learn complex motor tasks such as walking or playing musical instruments (Ismail et al., 2017). The developing brain changes in response to learning experiences, parent–child interactions, stress, medication and drug exposure, hormones, diet, and brain injury (Kolb et al., 2013). It is the human infant's ability to learn that sets us apart from all other animal species, despite the noticeable biologic disadvantage of being unable to walk or talk at birth, owing to immature selective motor control and problem solving (Stewart, 2017).

Neuroscience preclinical data strongly support early training as an intervention for improving brain structure reorganization and functional outcomes after early brain damage. In preclinical studies, training induces: (a) reactive synaptic plasticity, dendritic growth and synaptogenesis; (b) major increases in cortical territory dedicated specifically to the trained skill; (c) lasting neural changes in synaptic strength, synapse numbers, and motor map reorganization; (d) long-term potentiation of motor-evoked synaptic responses; (e) elevation of neurotrophic factors and other plasticity-related molecules improving functional outcomes; and (f) sparing of neuron death and loss of neural connections after brain injury (Kleim and Jones, 2008; Kolb et al., 2013; Ismail et al., 2017).

Learning is not something that is done to an infant but is achieved through active involvement of the infant (Stewart, 2017). Children learn because they innately have an explanatory drive to make sense of their own experiences and attain mastery (Stewart, 2017). The role of early intervention and rehabilitation is to maximize children's self-efficacy through enriching their environments to "call forward the learning" and through promoting and scaffolding child-active and child-led learning of tasks and knowledge beyond their current skill-set and understanding (Morgan et al., 2013; Stewart, 2017). Experience-dependent plasticity can be harnessed to accelerate children's outcomes. From a rehabilitation perspective, this means using interventions that specifically train an infant to perform a skill (Kolb et al., 2013; Morgan et al., 2016a).

Parents often feel compelled to try everything for their child and may attempt multiple different treatment approaches simultaneously after leaving the NICU, initially with an aim of finding a cure. Parents will ask for advice about the most beneficial treatments for their child. Rehabilitation has changed substantially over the last decade, in line with current understandings of neurology, the effects of late phase injury, synaptogenesis, and experience-dependent plasticity. It can be helpful for parents to develop an understanding of the principles of neuroplasticity to use as a filtering mechanism when choosing treatments for their child, especially when reading uncurated sources of information from the internet. We will now describe the key features of interventions that induce neuroplasticity via a training approach.

Child-generated actions driving use-dependent plasticity

Preclinical data clearly demonstrate that neural circuitry not in use, either from environmental deprivations or brain injury, degrades over time, leading to permanent functional losses (Kleim and Jones, 2008). The converse is also true. Neuroplasticity can be induced within specific brain regions, through intense training, and these gains are maintained with regular use of these skills (Kleim and Jones, 2008). There is substantive human data to support the efficacy of training-based rehabilitation interventions for improving function after brain injury (Cramer et al., 2011; Novak et al., 2013; Smits-Engelsman et al., 2013). However, most of this data is in older children or adults, with very few infancy training trials ever conducted, because of the complexity of training preverbal infants (Novak et al., 2013; Morgan et al., 2016a). The issue of early training is further compounded by late diagnosis of childhood disability, such as cerebral palsy, affecting trial recruitment feasibility when aiming to test the efficacy of early interventions (Novak et al., 2013; Morgan et al., 2016a).

There is currently great momentum within the rehabilitation field to devise and empirically study infant-friendly training-based interventions, based on compelling human and preclinical neuroscience data indicating that better outcomes might be possible. For example, an elegant experiment in the feline model of hemiplegic cerebral palsy showed that nonuse postinjury led to no functional recovery, which is equivalent to late diagnosis and a "wait-and-see" approach to intervention in the human infant (Martin et al., 2011). On the other hand, when early training-based interventions that harness neuroplasticity principles coupled with environmental enrichment were used, functional recovery and restoration of corticospinal connectivity occurred. However, these same gains were not conferred if the intervention started late, after the corticospinal tract completed development, which is thought to be by 6 months of age in the human infant (Martin et al., 2011). This preclinical study provides the scientific imperative to study training-based interventions very early in infants.

Task-specific practice

Both preclinical and human studies indicate that specific neural plasticity and behavioral changes are dependent upon specific learning experiences (Kleim and Jones, 2008). The more specific the practice, the more neuroplasticity that is induced and cortical space dedicated to the task. The concept of task-specific plasticity has revolutionized rehabilitation and moved it away from generic interventions to very specific training of real-life tasks the infants need or want to perform. For example, more neuroplasticity will occur from an infant repeatedly practicing weight shift in prone and freeing one hand to obtain a wanted toy, than will occur from rehabilitation that elicits generic righting reactions over a therapy ball. The contingency of obtaining the toy generates positive reinforcement and thus the infant commits the successful movement strategy to memory.

Repetitive and intense child-active practice

Repetition of a newly learned behavior is required to induce lasting neuroplasticity changes. In addition to repetition, the intensity of the training also induces plasticity (Kleim and Jones, 2008). For the intervention to meet these neuroplasticity criteria, the child must actively practice the tasks repeatedly themselves. The intervention cannot be passively "done to the child" using a "hands-on" therapeutic approach from an adult or therapist, such as massage or stretching. In the rehabilitation literature, it has been suggested that 90 h of child-active training within 6 weeks is required to induce lasting neuroplasticity and functional changes (Sakzewski et al., 2014). Intense training with infants is complex to operationalize because infants require sleep during the day and fatigue quickly. Intervention will need to involve parents and repetition within the infant's daily routine and environment to achieve the recommended intensity (Morgan et al., 2013).

Salient and motivating to the child

Children will practice a task more often and more intensely when they are motivated by the task (Kleim and Jones, 2008). Motivation and attention are key modulators of neuroplasticity (Cramer et al., 2011). Rewarding an enjoyable activity engagement promotes repetitious practice and thus plasticity. Furthermore, if the task holds importance to the child, success is encoded more readily (Kleim and Jones, 2008). Rehabilitation with older children and adults begins with the adult or child's goals, because this is known to produce better outcomes. In the case of preverbal infants unable to articulate goals, rehabilitation begins by asking about the infant's interests and preferred toys and by developing an understanding of the parent's goals, to increase the family's motivation to structure the infant's practice.

We will now describe common rehabilitation interventions as well as complementary and alternative interventions, the supporting evidence, and their relationship to the principles of neuroplasticity (Table 23.1). The effectiveness of the interventions described in this chapter and the quality of the evidence base has been appraised using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework (Guyatt et al., 2011) and the Evidence Alert Traffic Light System (Novak and McIntyre, 2010). The GRADE framework rates both the quality of the evidence and the strength of the recommendation for use. Quality is rated where randomized trials = high, observational studies = low, and other levels of evidence = very low, but trials can be downgraded when methodological flaws exist. Recommendations for use consider benefits and harms, including quality, inconvenience, outcomes, magnitude and precision of effect, burdens, costs, and family values. The Evidence Alert Traffic Light System is a GRADE-complementary knowledge translation tool designed to assist clinicians to obtain easily readable, clinically useful answers quickly. In the Evidence Alert Traffic Light System, green signifies "go" because high-quality evidence indicates effectiveness; red signifies "stop" because high-quality evidence indicates harm or ineffectiveness; and yellow signifies "measure" because insufficient evidence exists to be certain about whether the child will benefit.

Rehabilitation interventions that fully harness neuroplasticity

Bimanual training (also known as HABIT): Bimanual training is a task-specific occupational therapy or physical therapy treatment approach designed to increase the use of both hands, when the child has asymmetrical hand use following a unilateral or asymmetrical brain injury. Therapy typically involves intensive practice of real-life functional tasks that require the use of two hands for successful task performance (e.g., removing a lid from a screw-top jar), to increase the child's practice with two hands. Clinical trials have shown the approach is effective (Dong et al., 2013; Novak et al., 2013), both in individual treatment sessions or in a group-based camp model of service. Clinical trials have also shown that bimanual training is equally as effective as constraint-induced movement therapy (CIMT), so either or both approaches can be used, guided by family preferences (Novak et al., 2013).

Cognitive orientation to occupational performance (CO-OP): CO-OP is task-based therapy designed to directly address goals set by the child. CO-OP first teaches children to problem solve an effective movement strategy to enable them to perform their desired task, which is a form of cognitive training. Once the child has identified a successful strategy, task-specific motor training occurs using the child's self-generated strategy. CO-OP uses the principles of neuroplasticity to promote

Table 23.1

Pediatric rehabilitation interventions evidence base and neuroplasticity features

Intervention	Neuroplasticity: Child-generated movement	Neuroplasticity: Task specific	Neuroplasticity: Repetitive child-active practice	Neuroplasticity: Salient to the child	Population	Evidence	Outcome	Evidence alert and GRADE
Rehabilitation interventions that fully harness neuroplasticity rehabilitation								
Bimanual training	✓	✓	✓	✓	Cerebral palsy (hemiplegic subtype)	Level 1: Systematic review | High quality (Dong et al., 2013; Novak et al., 2013)	SHORT-TERM: Improved bilateral hand function	Green STRONG + Do it
CO-OP (Cognitive orientation to occupational performance)	✓	✓	✓	✓	Developmental coordination disorder	Level 1: Systematic review | Moderate quality (Smits-Engelsman et al., 2013)	SHORT-TERM: Improved motor task performance Improved self-confidence	Green STRONG + Do it
					Cerebral palsy (All subtypes)	Level 2: RCT | Moderate quality (Cameron et al., 2017; Jackman et al., 2018)	SHORT-TERM: Improved motor task performance Improved self-confidence	Yellow WEAK + Probably do it
					Spina bifida	Level 4: Case series | Low quality (Peny-Dahlstrand et al., 2017)	SHORT-TERM: Improved motor task performance Improved self-confidence	Yellow WEAK + Probably do it
CIMT (Constraint-induced movement therapy)	✓	✓	✓	✓	Cerebral palsy (Hemiplegic subtype)	Level 1: Systematic review | High quality (Dong et al., 2013; Novak et al., 2013)	SHORT-TERM: Improved hand function	Green STRONG + Do it
Goal-directed/ Task-specific training	✓	✓	✓	✓	Developmental coordination disorder	Level 1: Systematic review | Moderate quality (Smits-Engelsman et al., 2013)	SHORT-TERM: Improved motor task performance	Green STRONG + Do it
					Cerebral palsy (All subtypes)	Level 1: Systematic review | High quality (Novak et al., 2013)	SHORT-TERM: Improved motor task performance	Green STRONG + Do it
GAME (Goal–activity–motor enrichment)	✓	✓	✓	✓	Cerebral palsy (All subtypes)	Level 2: RCT | Moderate quality (Morgan et al., 2016b). Note: Definitive RCT underway	SHORT-TERM: Improved motor task performance Improved cognition	Yellow WEAK + Probably do it
Learningames	✓	✓	✓	✓	Cerebral palsy (Diplegic subtype)	Level 1: Systematic review | Moderate–high quality (Morgan et al., 2016a)	SHORT-TERM: Improved motor task performance Improved cognition	Yellow WEAK + Probably do it
Motor imagery training	✓	✓	✓	✓	Cerebral palsy (Hemiplegic subtype)	Level 1: Systematic review | Low quality (Sakzewski et al., 2013)	SHORT-TERM: Improved motor task performance	Yellow WEAK + Probably do it
Perceptual motor therapy contemporary	✓	✓	✓	✓	Cerebral palsy (All subtypes)	Level 2: RCT | Moderate quality (Harbourne et al., 2010)	SHORT-TERM: Probably improved sitting skills	Yellow WEAK + Probably do it

Continued

Table 23.1

Continued

Intervention	Neuroplasticity: Child-generated movement	Neuroplasticity: Task specific	Neuroplasticity: Repetitive child-active practice	Neuroplasticity: Salient to the child	Population	Evidence	Outcome	Evidence alert and GRADE
Rehabilitation interventions not focused on neuroplasticity								
Anat Baniel method	×	×	✓	×	Cerebral palsy (All subtypes)	No published evidence (Baniel and Sharp, 2013)	SHORT-TERM: Unknown	Yellow WEAK + Probably do it
Context-focused therapy	×	✓	×	✓	Cerebral palsy (All subtypes)	Level 2: RCT | Moderate quality (Law et al., 2011)	SHORT-TERM: Improved function	Green STRONG + Do it
Developmental intervention approach	✓	×	×	×	Cerebral palsy (Diplegic subtype)	Level 1: Systematic review | Moderate–high quality (Morgan et al., 2016a)	SHORT-TERM: Gains are smaller than task-specific training	Yellow WEAK + Probably do it
Electrical stimulation	×	×	✓	×	Cerebral palsy (All subtypes)	Level 1: Systematic review | Low quality (Cauraugh et al., 2010)	SHORT-TERM: Probably improved strength	Yellow WEAK + Probably do it
Feldenkrais	✓	×	✓	×	Cerebral palsy	Level 1: Systematic review | No published evidence (Liptak, 2005)	SHORT-TERM: Unknown	Yellow WEAK + Probably do it
Hippotherapy	✓	×	✓	✓	Cerebral palsy (All subtypes)	Level 1: Systematic review | Low–moderate quality (Whalen and Case-Smith, 2012)	SHORT-TERM: Improved gross motor skills	Yellow WEAK + Probably do it
Hydrotherapy/Aquatic therapy	✓	×	✓	✓	Cerebral palsy (All subtypes)	Level 1: Systematic review | Low–moderate quality (Gorter and Currie, 2011)	SHORT-TERM: Improved gross motor skills	Yellow WEAK + Probably do it
Massage	×	×	×	×	Cerebral palsy (All subtypes)	Level 1: Systematic review | Low quality (Novak et al., 2013)	SHORT-TERM: Conflicting results. Some trials show pain and spasticity reduction; others do not	Yellow WEAK + Probably do it
Neurodevelopmental treatment (NDT) or Bobath (Traditional)	×	×	×	×	Cerebral palsy (All subtypes)	Level 1: Systematic review | Low quality (Brown and Burns, 2001; Butler and Darrah, 2001; Martin et al., 2010)	SHORT-TERM: No gains over controls	Red STRONG – Do not do it
Orthotics	×	×	✓	×	Cerebral palsy (All subtypes)	Ankle foot orthoses Level 1: Systematic review | Low quality (Figueiredo et al., 2008)	SHORT-TERM: Probably improved ankle range of motion, gait kinetics, and kinematics	Yellow WEAK + Probably do it
					Cerebral palsy (All subtypes) and brain injury	Hand splints Level 1: Systematic review | Low quality (Jackman et al., 2014)	SHORT-TERM: Probably improved hand function while wearing the orthotic	Yellow WEAK + Probably do it
Perceptual motor therapy traditional	✓	×	✓	×	Learning disability	Traditional Level 1: Systematic review | Moderate quality (Smits-Engelsman et al., 2013)	SHORT-TERM: Probably improved motor skills Gains are smaller than task-specific training	Yellow WEAK + Probably do it

Sensory approaches	×	×	×	×	Attention deficit hyperactivity disorder	Level 2: RCTs | Moderate quality (Lin et al., 2014; Fedewa et al., 2015)	SHORT-TERM: No benefits over controls	Yellow WEAK – Probably do not
					Autism spectrum disorder	Level 1: Systematic reviews | Moderate quality (Case-Smith et al., 2013; Tanner et al., 2015; Watling and Hauer, 2015)	SHORT-TERM: No benefits over controls for behavior Conflicting results for social skills	Behavior: Yellow WEAK – Social: Yellow WEAK+
					Cerebral palsy (All subtypes)	Level 1: Systematic reviews | Moderate quality (Steultjens et al., 2004)	SHORT-TERM: No benefits over controls	Yellow WEAK – Probably do not
					Developmental coordination disorder	Level 1: Systematic review | Moderate quality (Smits-Engelsman et al., 2013)	SHORT-TERM: Improved kinesthetic skills but gains are bigger from task-specific practice	Yellow WEAK – Probably do not
Sensory integration	×	×	×	×	Autism spectrum disorder	Level 1: Systematic review | Low quality (Case-Smith and Arbesman, 2008; Lang et al., 2012; Case-Smith et al., 2013; Watling and Hauer, 2015)	SHORT-TERM: Improved goal achievement but studies are biased worsened behavior and cannot be recommended	Red STRONG – Do not do it
					Cerebral palsy	Level 1: Systematic review | Low quality (Novak et al., 2013)	SHORT-TERM: Conflicting results Most studies show no benefits	Red STRONG – Do not do it
					Developmental coordination disorder	Level 1: Systematic review | Moderate quality (Smits-Engelsman et al., 2013)	SHORT-TERM: Conflicting results Some studies showed improved behavior, attention, and motor skills, but high risk of bias	Yellow WEAK – Probably do not
Spider cage therapy	✓	×	✓	×	Cerebral palsy	Level 2: RCT | Low quality (Kaushik and Kumar, 2016)	SHORT-TERM: Probably improved motor skills	Yellow WEAK+Probably do it
					Down syndrome	Level 2: RCT | Low quality (El-Meniawy et al., 2012)	SHORT-TERM: Probably improved motor skills	Yellow WEAK+Probably do it
Strength training	✓	×	✓	×	Cerebral palsy	Level 1: Systematic review | Moderate–high quality (Mockford and Caulton, 2008)	SHORT-TERM: Improved muscle strength but this does not necessarily improve function	Yellow WEAK+Probably do it
Stretching or range of motion	×	×	×	×	Cerebral palsy	Level 1: Systematic review | Low quality (Katalinic et al., 2010)	SHORT-TERM: Insufficient data. Ineffective in other neurologic conditions	Yellow WEAK – Probably do not
Therasuits/Adelisuits	✓	×	✓	×	Cerebral palsy	Level 1: Systematic review with metaanalysis | Low quality (Mockford and Caulton, 2008)	SHORT-TERM: Unclear conflicting results. Trials by originators show positive findings. Trials by independent researchers show no gains over controls	Yellow WEAK – Probably do not
Treadmill training	✓	×	✓	×	Cerebral palsy Down sydnrome Spinal cord injury Physical disability	Level 1: Systematic review | Moderate quality (Zwicker and Mayson, 2010)	SHORT-TERM: Improved weight bearing and walking on a treadmill. NOTE: Treadmill training improves neuroplasticity for stepping but research has not yet shown that these benefits transfer to improved walking on the ground because of the lack of task-specificity	Yellow WEAK + Probably do it
Whole body vibration	×	×	×	×	Physical disability	Level 1: Systematic review | Moderate quality (Matute-Llorente et al., 2014)	SHORT-TERM: Improved fitness	Yellow WEAK+ Probably do it
Yoga	✓	×	✓	×	Attention deficit hyperactivity disorder Intellectual disability	Level 1: Systematic review | Moderate quality (Galantino et al., 2008)	SHORT-TERM: Improved breathing	Yellow WEAK+ Probably do it

Continued

Table 23.1

Continued

Intervention	Neuroplasticity: Child-generated movement	Neuroplasticity: Task specific	Neuroplasticity: Repetitive child-active practice	Neuroplasticity: Salient to the child	Population	Evidence	Outcome	Evidence alert and GRADE
Complementary and alternative interventions								
Acupuncture	×	×	×	×	Cerebral palsy (All subtypes)	Level 1: Systematic review | Low quality (Zhang et al., 2010)	SHORT-TERM: Probably improved gross motor skills	Yellow WEAK – Probably do not
Chiropractic manipulation	×	×	×	×	Children	Level 1: Systematic review | Low quality (Vohra et al., 2007; Gotlib and Rupert, 2008)	SHORT-TERM: Unknown if benefits occur Risks for adverse events	Yellow WEAK – Probably do not
Conductive education	✓	×	✓	×	Cerebral palsy (All subtypes)	Level 1: Systematic review | Moderate quality (Tuersley-Dixon and Frederickson, 2010)	SHORT-TERM: Probably improved gross motor skills but gains are smaller than task-specific training	Yellow WEAK – Probably do not
Craniosacral/Cranial osteopathy	×	×	×	×	Cerebral palsy (All subtypes)	Level 2: RCT | Moderate quality (Wyatt et al., 2011)	SHORT-TERM: No benefits over controls	Red STRONG – Do not do it
Cuevas Medek exercise	×	×	×	×	Cerebral palsy (All subtypes)	No published evidence	SHORT-TERM: Unknown	Yellow WEAK – Probably do not
Doman Delecato	×	×	×	×	Cerebral palsy	Level 1: Systematic Review | No published evidence (Liptak, 2005)	SHORT-TERM: Unknown	Yellow WEAK – Probably do not
Homeopathy	×	×	×	×	Attention deficit hyperactivity disorder	Level 1: Systematic review | Low–moderate quality (Heirs and Dean, 2007)	SHORT-TERM: No benefits over controls	Yellow WEAK – Probably do not
					Children	No published evidence about efficacy, but safety data exists (Ernst, 2003)	SHORT-TERM: Unknown Risks for adverse events	Yellow WEAK – Probably do not
Hyperbaric oxygen	×	×	×	×	Cerebral palsy (All subtypes)	Level 1: Systematic review with metaanalysis | High quality (Novak and Badawi, 2013)	SHORT-TERM: No benefits over controls Risks for adverse events	Red STRONG – Do not do it
Reflexology	×	×	×	×	Cerebral palsy (All subtypes)	Level 1: Systematic review | No published evidence (Liptak, 2005)	SHORT-TERM: Unknown	Yellow WEAK – Probably do not
Votja	×	×	×	×	Cerebral palsy (All subtypes)	Level 1: Systematic review | Moderate quality (Novak et al., 2013)	SHORT-TERM: Gains reported but studies have high levels of bias Crying commonly occurs	Yellow WEAK – Probably do not

GREEN, "GO" because high-quality evidence indicates effectiveness; *RED*, "STOP" because high-quality evidence indicates harm or ineffectiveness; *YELLOW*, "MEASURE" because insufficient evidence exists to be certain about whether the child will benefit; *TICK*, Yes, treatment employs this neuroplasticity principle; *CROSS*, No, treatment does not employ this neuroplasticity principle.

both cognitive and motor learning. The intervention can be performed by an occupational therapist or physical therapist certified in the CO-OP approach. CO-OP was originally designed for children with developmental coordinator disorder who have executive function difficulties in planning movement. Emergent new clinical trial evidence suggests the approach might also work in children with cerebral palsy (Jackman et al., 2018) and spina bifida. The approach cannot be used with infants because it involves verbal reasoning.

CIMT: CIMT is a motor training intervention for children with asymmetrical hand use following a unilateral or asymmetrical brain injury. A mitt, sling, or cast is placed on the child's dominant hand to constrain its effective use. The constraint creates an environment where child-active practice of tasks or movements are more successful with the lesser-used hand and occur more often, and therefore this can also be categorized as an environmental enrichment intervention (Section "Community-based environmental enrichment interventions"). CIMT promotes neuroplasticity of movement and learning about the hand's usefulness. CIMT intervention can be performed by an occupational therapist or physical therapist. Numerous clinical trials have shown the approach is highly effective (Dong et al., 2013; Novak et al., 2013). CIMT is effective both in individual treatment sessions and in a group-based camp model of service. CIMT is equally effective with a mitt, sling, or cast, but children tend to prefer removable constraints such as mitts and slings. CIMT is equally as effective as bimanual training, so either approach can be used and family preferences can be sought (Novak et al., 2013).

Goal-directed or task-specific or functional training: Goal-directed training and task-specific or functional training are task-specific motor training approaches that aim to guide children to successfully perform a functional task that is meaningful to them. Goal-directed training begins by having the child set a desired goal to achieve. The therapist then identifies the goal limiting factors affecting performance, e.g., task knowledge, experience, fatigue, muscle strength for the task, etc., and then devises a treatment plan that addresses the goal limiting factors. The treatment also considers the child's stage of learning, e.g., new learner through to automated movement. Several clinical trials have shown the approach is effective for improving function (Novak et al., 2013; Smits-Engelsman et al., 2013). Goal-directed training and task-specific or functional training utilize all the features of neuroplasticity: child-generated movements, task-specific practice, repetition, and saliency.

Goals–activity–motor enrichment (GAME): GAME is an infant-friendly motor learning intervention that is a combination of task-specific training to reach parent-set goals about their infant's development (e.g., sitting independently), parent coaching to help parents learn to read and respond to their infant's cues (e.g., a small upward arm movement might be a sign of intent the child is trying to reach for a toy but the task is too difficult and requires adjusting), and enrichment of the child's home environment (Section "Community-based environmental enrichment interventions"). GAME is a new treatment approach, which in a small clinical trial appeared promising for improving the motor and cognitive skills of infants with cerebral palsy compared to controls (Morgan et al., 2016b). GAME is currently being tested in a large definitive clinical trial (ACTRN12617000006347). GAME harnesses all the features of neuroplasticity: child-generated movements, task-specific practice, repetition, and saliency.

Learningames: Learningames is a curriculum-based early intervention program that provides parents with enjoyable games to play with their infant to promote motor and cognitive development (Sparling and Lewis, 1979). The curriculum has been tested with infants with diplegic cerebral palsy in a small clinical trial and has been shown to produce better motor and cognitive effects than other physical therapy approaches (Palmer et al., 1988, 1993; Morgan et al., 2013). Learningames harnesses all the features of neuroplasticity: child-generated movements, task-specific practice, repetition, and saliency. Learningames can also be categorized as an environmental enrichment intervention (Section "Community-based environmental enrichment interventions").

Motor imagery training: Motor imagery training involves mental rehearsal of motor tasks but without performing the task. Mental rehearsal is widely used by athletes and musicians to enhance their performance. Neuroplasticity studies have described the process by which motor imagery training works, via the mirror neurone system, which activates the same circuits involved in performing the motor task by watching task performance (action observation) and thinking through task performance. The obvious benefit to children with physical disabilities is that mental rehearsal is less physically fatiguing, enabling longer and more intense practice. Motor imagery training is underresearched and underutilized in clinical practice. Low-quality evidence suggests it works in the hemiplegic cerebral palsy population (Sakzewski et al., 2013). More research is warranted. The approach cannot be used with infants because of the advanced cognitive skills required.

Perceptual motor therapy (Contemporary approach): In the contemporary era, perceptual motor therapy involves task-specific training to improve the motor skill of independent sitting. The physical therapy involves using child-initiated movements with environmental feedback to the child about their performance success. A small trial suggests efficacy for teaching sitting skills to children with cerebral palsy (Harbourne et al., 2010). More research is warranted.

Rehabilitation interventions not focused on neuroplasticity

Anat Baniel method: The Anat Baniel method is based upon Feldenkrais physical therapy. The physical therapist guides the child's movements and the child pays attention to what they feel during movement. The Anat Baniel method has not been studied empirically and the efficacy is therefore unknown. The approach cannot be used with infants because of the advanced cognitive skills required.

Context-focused therapy: In context-focused therapy the occupational therapist or physical therapist does not attempt to change the child (i.e., treat the child's symptoms such as weakness) but instead, using an entirely "hands-off" approach, adapts the task or environment so that the child succeeds (e.g., provides a bigger, lighter ball, so the child successfully catches a ball). The approach focuses on improving the child's independence by changing the environment in such a way that the task becomes possible for the child to perform. In a clinical trial that compared context-focused therapy head-to-head with therapy that involved treating the child, the approaches were equally effective, indicating that adapting the task or environment is worthwhile (Law et al., 2011).

Developmental interventions: In the developmental intervention approach, the parent and infant are asked to practice developmental milestones in sequential order, e.g., first tummy time is recommended and, once head control is acquired, sitting will be then recommended. The developmental approach does involve using child-generated movements, but a major limitation, due to the approach being delivered in a developmental sequence, is that the practice is underdosed and very delayed when compared to the natural window of child development. Children with disabilities do not necessarily learn in a standard developmental sequence and may never show "readiness," but may still respond to treatment. A systematic review of all the motor interventions for infants showed that, while the developmental approach probably works, the effect sizes are smaller than those seen when a comprehensive motor learning task-specific approach is employed (Morgan et al., 2016a).

Electrical stimulation: Electrical stimulation is a device-based treatment in which a muscle is stimulated through a skin electrode to induce passive muscle contractions with the aim of building muscle strength. In order to have a clinical gain in function, the child must be able to selectively control the muscle in the first place in order to be able to use this new muscle strength within task performance. Some e-stim devices can be set up to be activated only after the child initiates the muscle contraction in the first place, which leads to greater functional gains because the child's role in the learning, and thus plasticity, is greater. Often children with lower sensation tolerate e-stim treatment better than children with normal sensation, because they can tolerate the high threshold device-induced muscle contractions without pain or discomfort. Low-level evidence supports the approach for children with neurologic disorders, and the approach has been tested with infants and found to be feasible (Park et al., 2001; Cauraugh et al., 2010).

Feldenkrais: Feldenkrais is a physical therapy technique that is an educational approach to teaching the child to use movement and perception to foster functional movement. Feldenkrais has not been studied empirically for children with disabilities and the efficacy is therefore unknown (Liptak, 2005). For a child with cerebral palsy to make progress from Feldenkrais, they would need to have selective motor control in order to participate in the therapy.

Hippotherapy: Hippotherapy is therapeutic horseback riding. The original theoretical underpinnings of the approach were that, through riding, the rider's pelvis would experience anterior–posterior motion from the horse's movement and that this experience would translate into better gait. For the most part, hippotherapy improves a child's horseback riding skills (i.e., it is task-specific practice of horseback riding, not task-specific practice of walking on the ground). Low-quality evidence supports the use of hippotherapy for improving movement skills (Whalen and Case-Smith, 2012), and many children enjoy the approach and connection with the horse.

Hydrotherapy: Hydrotherapy is aquatic therapy or therapy conducted within a heated pool. Water exerts less gravitational force and therefore makes it easier to move, and yet the very resistance of the water helps build muscle strength. For the most part, hydrotherapy improves a child's movement skills in the pool (i.e., it is a task-specific practice of swimming or movement in water, not a task-specific practice of walking on land). Low-quality evidence supports the use of hydrotherapy for improving movement skills (Gorter and Currie, 2011).

Massage: Massage seeks to reduce pain and muscle tension. Massage is passively applied by a physical therapist or massage therapist to the child. The level of supporting evidence is low for improving movement skills (Novak et al., 2013). Massage does not involve any child-generated, task-specific, active movements necessary for learning movement skills, but may improve the child's comfort. In Section "NICU-based environmental enrichment interventions" we discuss the benefits of massage from an environmental enrichment perspective.

Neurodevelopmental treatment (NDT) or Bobath (Traditional approach): NDT or Bobath originally set out to normalize a child's movements and muscle tone via the therapist passively handling and guiding the child through normal movement patterns (e.g., moving the child from lying to sitting using a normal movement pattern). To use the approach, the physical therapist or occupational therapist should undertake certification courses. Clinical trials that have empirically evaluated the effectiveness of traditional NDT or Bobath show no gains in the acquisition of functional movement over-and-above controls (Brown and Burns, 2001; Butler and Darrah, 2001; Martin et al., 2010). NDT or Bobath in its traditional format did not involve any child-generated, task-specific, active movements necessary for learning movement skills. However, over time, some NDT and Bobath trained therapists have incorporated task-specific practice into their clinical practice, under the umbrella term of NDT and Bobath. In the contemporary era, because of the varied eclectic approaches used, it is not clear precisely what therapies are being provided to children and it is also difficult to understand the effectiveness of the total umbrella approach. Expert certified therapists claim NDT and Bobath are effective, but conclusive data are lacking and these therapists usually work in private practices or commercial entities selling NDT or Bobath education. A clinical trial that compared task-specific training head-to-head with NDT showed more favorable gains from task-specific training than NDT (Bar-Haim et al., 2010). An important study of NDT vs Learningames in infants with spastic diplegia showed infants had superior motor and cognitive gains as well as earlier onset of independent walking from Learningames over NDT (Palmer et al., 1988).

Orthotics: Orthotics or splints are removable external devices designed to support weak or ineffective joints or muscles. Ankle foot orthoses (AFOs) are designed to either immobilize the ankle in a neutral position (fixed AFO) or prevent unwanted plantar flexion (hinged AFO) so as to prevent contracture and toe-walking. Low-quality evidence supports the use of AFOs for minimizing contracture development and improving the appearance of walking, but not necessarily the efficiency of walking (Figueiredo et al., 2008). Hinged AFOs allow more ankle movement but cannot be made for small feet. Fixed AFOs interfere with the child's ability to feel the floor through their feet and may interfere with performance of transitional movements, such as moving from sitting to standing. Therefore, the benefits and harms need to be evaluated when the child is first learning to mobilize. Hand splints are very underresearched and not well tolerated by children. Low-quality evidence suggests dynamic hand splints may improve hand function while being worn, but the gains do not carry over when the splints are taken off (Jackman et al., 2014). Static night hand splints, designed to prevent wrist and finger contracture, are also supported by moderate-quality evidence (Jackman et al., 2014). Night splints interfere with sleep for some children, and careful clinical reasoning must be applied to evaluate the benefits and harms, especially in cases where the child's hypertonicity is lower during sleep.

Perceptual motor therapy (Traditional approach): In Section "Rehabilitation interventions that fully harness neuroplasticity" and Table 23.1 we describe the contemporary perceptual motor therapy, which is different from the traditional approach. Traditionally, perceptual motor therapy involved generic gross motor and fine motor skill training programs (e.g., running, jumping, skipping, painting, drawing, cutting with scissors). Moderate-quality evidence in the learning disability population shows that traditional perceptual motor therapy probably improves gross and fine motor skills, but the gains are smaller than from task-specific training (Smits-Engelsman et al., 2013). Task-specific training has higher specificity and thus more plasticity is harnessed.

Sensory approaches: Sensory approaches are adaptations of the sensory integration treatment approach. Sensory approaches include brushing, therapy balls, weighted vests, warm-ups, and sensory stimulation, with the aim of dampening overstimulation or excessive responses to sensory stimuli. The quality of the evidence is low in support of these approaches (Steultjens et al., 2004; Case-Smith et al., 2013; Smits-Engelsman et al., 2013; Lin et al., 2014; Fedewa et al., 2015; Tanner et al., 2015; Watling and Hauer, 2015).

Sensory integration: Historically, children with hypersensitivities to sensory information (e.g., light hypersensitivity, dislike of wearing textured clothing, or eating certain food textures) have been labeled as having sensory processing disorder and prescribed sensory integration therapy. The theoretical construct behind sensory integration was that if vestibular, proprioceptive, auditory, and tactile sensory input are provided, reorganization of the sensory system will occur, leading to improved movement and intellect. Sensory integration includes a variety of sensory techniques including: sensory diets, swinging, brushing, therapy balls, weighted vests, and body socks. Clinical trials in almost every diagnostic group have found no benefits over-and-above controls, with the exception of some recent small and biased trials in the autism spectrum population (Case-Smith and Arbesman, 2008; Lang et al., 2012; Case-Smith et al., 2013; Novak et al., 2013; Smits-Engelsman et al., 2013; Watling and Hauer, 2015). The AAP recommends that the diagnostic label sensory processing disorder should not be used because of the lack of a diagnostic framework and lack of evidence that symptoms are ameliorated by treatment (Zimmer et al., 2012). Given the lack of supporting evidence, the cost, the evidence that some children's behavior worsens, and the presence of effective alternatives, sensory integration intervention is not recommended.

Spider cage therapy: In spider cage therapy or suit therapy, the child is suspended inside a metal cage while wearing an elasticized suit designed to provide line of pull to make some movements easier and resistance to make some movements stronger. Low-quality evidence suggests spider cage therapy may improve gross motor skills (El-Meniawy et al., 2012; Kaushik and Kumar, 2016). Parents often report favoring the novelty, intensity, and expert nature of the intervention, and thus often become more motivated to encourage their child to practice motor skills both inside and outside the cage. Interpretation of the key features of the intervention therefore becomes difficult; is it the cage or the increased practice? From a neuroplasticity perspective, what the child practices after removing the suit outside the cage (i.e., task-specific practice), is probably more important than the cage itself.

Strength training: Strength training uses progressively more challenging resistance to muscular contraction to build muscle strength and anaerobic endurance. Historically, increased strength was theorized to increase unwanted hypertonicity, but clinical trials have since shown that this is not true. Rather, spastic muscles are weak and benefit from resistance training. Clinical trials show strength training builds muscle strength but does not carry over to increased function (Mockford and Caulton, 2008). If functional gains are sought, task-specific functional training should be used in combination with strength training. In infancy and early childhood, it is not easy to conduct strength training, because the concept of maximal voluntary contraction must be understood by the patient to be sure strength training is indeed progressive and offered at the right intensity.

Stretching or range of motion: The physical therapist or occupational therapist passively holds the child's muscle in a stretched position, so as to prevent contracture. Systematic reviews of neurologic conditions have shown that this is an ineffective manual treatment for preventing contracture, because the dose is too low, i.e., it is not possible to hold the muscle in a stretched position for long enough every day to have a clinical benefit (Katalinic et al., 2010). There is insufficient data in cerebral palsy to be certain if the effects of manual stretching are the same or different (Katalinic et al., 2010). However, most children experience pain and dislike the treatment, which can have a negative effect on parent–child interactions. The benefits and harms have to be weighed, given the lack of supporting conclusive evidence.

Therasuits/Adelisuits: Therasuits are dynamic, orthotic, full-body fabric suits, designed to improve the child's proprioception, reduce unwanted reflexes, and provide resistance to movements for building muscle strength. Given reflexes are not under voluntary control, it is hard to understand how this type of clinical gain might be possible. Clinical trials show conflicting results. Trials conducted by suit inventors show positive results, whereas independent trials comparing suits head-to-head with physical and occupational therapy without suits found no difference between the groups (Mockford and Caulton, 2008). A systematic review concluded that suits do not improve functional movement and that the inconveniences to the child and family need to be weighed against the lack of proven benefits (Wells et al., 2017). Suits are expensive and children grow quickly. In addition, suits are difficult to put on and hot to wear in warmer climates. Parents often report favoring the novelty, intensity, and expert nature of suit intervention, and thus often become more motivated to encourage their child to practice motor skills both with the suit on and off. Interpretation of the most important features of the intervention therefore becomes difficult; is it the suit or the increased practice?

Treadmill training: Treadmill training involves repetitive walking practice on a treadmill, which may include providing partial body support from a suspended harness to help keep the child in the upright position and to ensure safety. Moderate-quality evidence suggests treadmill training is effective for improving walking, especially in children who have the potential to walk, e.g., children with Down syndrome (Zwicker and Mayson, 2010). Treadmill training is useful for increasing the intensity of therapy; however, treadmill training is task-specific to the treadmill, not task-specific to walking on the ground. Children with Down syndrome who will walk earlier if treadmill training is applied (Zwicker and Mayson, 2010). Low-quality evidence also supports home-based treadmill training for accelerating walking and improving motor skills in young children with CP (Mattern-Baxter et al., 2013). Children with CP also require overground walking practice, for functional gains to be conferred.

Yoga: Yoga is a mind–body movement therapy, with a focus on stretching muscles and controlling postures. Moderate-quality evidence suggests yoga helps breath control in children with attention deficit hyperactivity disorder and intellectual disability (Galantino et al., 2008). More recently, the approach is also being tested in children with cerebral palsy, with similar effects.

Complementary and alternative interventions

Acupuncture: A trained acupuncturist passively applies electrostimulation to the scalp and body via needles and manual pressure. The approach is widely used within Eastern medicine but has low levels of supporting empirical evidence in the childhood disability population (Zhang et al., 2010). Experts claim the approach helps develop gross motor skills, even though the treatment does not involve any child-generated, task-specific, active movements.

Chiropractic manipulation: A chiropractor passively applies spinal manipulative therapy to physically adjust the musculoskeletal system into symmetrical anatomic alignment. Theoretically, correct alignment might make movement easier to perform and may reduce pain and secondary spasm. However, in children with brain injuries, the child may not have the selective motor control available to move or maintain the alignment. Furthermore, chiropractic treatment does not involve any child-generated task-specific movements likely to lead to improved neuroplasticity of movement skills. Adverse events including spinal cord injuries have occurred. Given the low quality of supporting evidence (Vohra et al., 2007; Gotlib and Rupert, 2008), the associated risks, the costs, and the existence of other interventions that deliver greater positive effects, the approach is not recommended.

Conductive education: Conductive education is a Hungarian educational classroom-based approach to teaching movement using rhythmic intention, routines, and groups. Conductive education is performed by a trained conductor. Conductive education uses a combination of approaches, for example: for teaching movement, the students practice rote classroom motor activities using specialized ladder-back chairs and rings, whereas, in contrast, conductors may use a task-specific educational approach to toilet training. Clinical trials show conflicting results. Trials conducted by private conductive education units show positive results, whereas an independent trial that compared conductive education head-to-head with task-specific physical and occupational therapy at the same intensity found the gains were three times larger from therapy (Tuersley-Dixon and Frederickson, 2010). Crying is a commonly cited reason for ceasing conductive education or dropping out of studies, which further biases the trial results. Moreover, if children are crying and stressed during treatment, their elevated cortisol levels may be causing further harm to their brain development. Parents report gains from the social interaction that occurs during classroom time, but social skills have not been studied empirically. Given the conflicting evidence (Tuersley-Dixon and Frederickson, 2010), that many children cry during intervention, the costs, and the existence of other interventions that deliver greater positive effects, the approach is not recommended for learning motor skills but may be helpful for promoting social skills.

CranioSacral therapy or cranial osteopathy: An osteopath or a physical therapist with certification in CranioSacral therapy passively provides physical palpation to ease musculoskeletal strain and treat the central nervous system. Akin to the theoretical thinking behind chiropractic treatment, the idea is that correct alignment makes movement easier to perform and may reduce pain and secondary spasm, although the treatment does not involve any child-generated, task-specific, active movements. A single clinical trial showed no benefit on children's movement over-and-above standard care, and risks for adverse events occur (Wyatt et al., 2011). On parent blog sites, some parents anecdotally report that their child receives a relief from their constipation. Given the lack of supporting evidence (Wyatt et al., 2011), the associated risks, the costs, and the existence of other interventions that deliver greater positive effects, the approach is not recommended.

Cuevas Medek exercises: Cuevas Medek exercises are a Spanish approach, in which the practitioner holds the child distally and passively moves the child into a position that challenges or "forces" the presentation of "non-obvious motor functions" (https://www.youtube.com/watch?v=C0jzNo3dQoU). The child is "forced" into making an automated righting response or postural adjustment to the practitioner's stimulus to try to stay upright against the force of gravity. For example, the practitioner might hold the child in midair in the upright standing position by the ankles, and because it is an unstable position the technique elicits a balance reaction from the child to prevent falling. Cuevas Medek exercises evoke practitioner-specific practice, not task-specific practice. Cuevas Medek exercises have not been studied empirically and the efficacy is therefore unknown. The most similar approaches from a theoretical point of view are early traditional forms of NDT and proprioceptive neuromuscular facilitation (PNF) that provoked righting reactions, which have not shown to improve movement skills.

Doman Delecato or Institute for Human Potential: In this treatment, four adults "pattern" (i.e., passively move) each of the child's limbs to simulate crawling movement. Patterning may occur on a downward ramp, so the child experiences forward locomotion. Experts claim the approach helps develop gross motor skills (first crawling, then walking), even though the treatment does not involve any child-generated, task-specific, active movements. The approach is expensive to use because four adults are required for each child treated. To overcome this cost barrier, some parents establish rosters of community volunteers to help carry out the treatment, which parent's anecdotally report elevates caregiving burden. The approach has not been empirically researched and therefore efficacy is unknown. Given the lack of supporting evidence, the costs, and the existence of other interventions that are known to deliver positive effects, the approach is not recommended.

Homeopathy: Homeopathic practitioners prepare special combinations of herbal substances, designed to enhance the body's ability to heal itself. Cochrane Reviews have failed to find evidence of the benefit of homeopathy over and above the placebo effect for children with attention deficit hyperactivity disorder (Heirs and Dean, 2007). Systematic reviews have also identified the risks of serious adverse events for children, because herbal medicines may contain heavy metals, plant-based poisons, and synthetic drugs including steroids (Ernst, 2003).

Hyperbaric oxygen: Hyperbaric oxygen is the provision of inhaled 100% oxygen inside a pressurized hyperbaric chamber. The theoretical construct behind this treatment is that increased oxygenation might improve or reverse the effects of a hypoxic brain injury in children with cerebral palsy. The trials have mostly been conducted by investigators with commercial involvement in hyperbaric chambers, but independent data also exists. A metaanalysis showed no gains to gross motor skills were conferred over-and-above control group treatment (Novak and Badawi, 2013), which is perhaps not surprising given that not all cerebral palsy arises from hypoxia and hyperbaric treatment does not involve any child-generated, task-specific, active movements. In addition, risks for serious adverse events, such as hearing loss, exist.

Reflexology: A reflexologist applies pressure to pressure points to release muscle tension and pain, induce relaxation, and induce healing. Reflexology has not been studied empirically, other than one Russian clinical trial where reflexology was combined with a neuroprotective medication, massage, and exercise for children with cerebral palsy, which makes interpretation of the findings difficult (Ukhanova and Gorbunov, 2012). Thus, the efficacy in isolation is unknown. Reflexology does not involve any child-generated, task-specific, active movements.

Vojta: Vojta is a German physical therapy technique in which pressure is applied to the body, so that the stimulus leads to the child making “automatic and involuntarily complex movement.” The research that has been conducted suggests positive effects on movement; however, all of these trials include high risks of bias (e.g., inclusion criteria that involves normal children, lack of controls to account for maturational effects), making interpretation of the findings difficult. Crying is a commonly cited reason for ceasing treatment or dropping out of studies, which further biases the trial results. Moreover, if children are crying and stressed during treatment, their elevated cortisol levels may be causing further harm to their brain development. Vojta does not involve any child-generated, task-specific, active movements. Given the biased supporting evidence, the pain caused to children, and the existence of other interventions that are known to deliver positive effects, the approach is not recommended.

ENVIRONMENTAL ENRICHMENT

Enriched environments promote brain recovery and learning. Substantial preclinical data exist to show that brain-injured animals have markedly better recovery and function if housed within enriched environments (Kolb et al., 2013). Enriched animal housing environments that include toys and exercise equipment promote voluntary, self-initiated actions and learning, with motivating but repetitive challenge. In other words, enriched environments promote experience-dependent learning. We know that environments also have a powerful effect on human development. For example: (a) institutionalized children experiencing environmental deprivation have 20-points lower IQ than children that live at home (Bakermans-Kranenburg et al., 2008); (b) disadvantaged children raised in poverty have worse health, delayed growth, and lower IQ (Bradley et al., 1994); and (c) if baby equipment is used that restricts movement or promotes learning from an atypical position, an infant’s rate of milestone acquisition is slowed down. For example, an infant that practices “walking” in a baby-walker walks later than normal, because they have been practicing while seated in a sling, using a different set of muscles, and there is no generalization to the actual skill of walking (Abbott and Bartlett, 2001).

Unlike animals, human infants cannot voluntarily access their environment at birth, because of delayed motor and vision maturation (Morgan et al., 2013). Infants require the help of their parents to set up and enrich their environment. Environmental enrichment interventions for infants with brain injury aim to enrich at least one of the motor, cognitive, social, or sensory aspects of the infant’s environment for the purposes of promoting learning (Morgan et al., 2013). We will now describe the environmental enrichment interventions that foster brain development in infants with brain injury. Table 23.2 contains information about the highest level of evidence for each intervention.

NICU-based environmental enrichment interventions

Within the intensive care environment, it is especially important to structure an environment that is conducive to child development. Infants can experience extraordinary levels of stress, caused by NICU noise, light, and procedural pain, elevating their cortisol levels, which can be harmful to brain development. Reducing sensory stimuli and the number of painful procedures helps promote infant well-being and development.

Facilitated tucking: Facilitated tucking is where the parent holds the child in a calming flexed position to help

Table 23.2

Environmental enrichment interventions evidence base

Intervention	Enrichment type	Population	Evidence	Outcome	Evidence alert and GRADE
Early childhood education	Cognitive and social	Typically developing infants	Level 1: Systematic review | High quality (Protzko et al., 2013)	SHORT-TERM: Improved cognition	Green STRONG + Do it
		Social disadvantage	Level 1: Systematic review | High quality (Anderson et al., 2003; Reynolds et al., 2011; Walker et al., 2011)	SHORT-TERM: Improved cognition LONG-TERM: Improved cognition Decreased criminal and violent behavior	Green STRONG + Do it
		Preterm infants after discharge	Level 1: Systematic review with metaanalysis | High quality (Spittle et al., 2015)	SHORT-TERM: Improved cognition	Green STRONG + Do it
Facilitated tucking	Sensory	Preterm infants in the NICU	Level 1: Systematic review | High quality (Cignacco et al., 2007)	SHORT-TERM: Reduced pain	Green STRONG + Do it
Home visiting	Cognitive and social	Social disadvantage	Level 1: Systematic review | High quality (Peacock et al., 2013)	SHORT-TERM: Improved cognition Improved communication Improved behavior Reduced family violence	Green STRONG + Do it
		Preterm infants after discharge	Level 1: Systematic review with metaanalysis | High quality (Spittle et al., 2015)	SHORT-TERM: Improved cognition	Green STRONG + Do it
		Fetal alcohol syndrome	Level 1: Systematic review | Moderate quality (Reid et al., 2015)	SHORT-TERM: Improved cognition LONG-TERM: Benefits not sustained	Yellow WEAK + Probably do it
Kangaroo mother care	Sensory	Preterm infants in the NICU	Level 1: Systematic review | Moderate quality (Athanasopoulou and Fox, 2014; Brouwer and van den Hoogen, 2015)	SHORT-TERM: Improved parent–child interactions Improved parent mood/mental health, e.g., lowered depression or anxiety	Green STRONG + Do it
Music	Sensory	Preterm infants in the NICU	Level 1: Systematic review | Low quality (Cignacco et al., 2007; Lubetzky et al., 2010; Standley, 2012)	SHORT-TERM: Improved respiration Reduced pain	Yellow WEAK + Probably do it
NIDCAP	Sensory	Infants in the NICU	Level 1: Systematic review with metaanalysis | Moderate–high quality (Blauw-Hospers and Hadders-Algra, 2005; Bonnier, 2008; Ohlsson and Jacobs, 2013)	SHORT-TERM: Improved parent–child interactions No change in medical status LONG-TERM: No reduction in the rate of survival without a disability	Green STRONG + Do it [Short-term] WEAK + [Long term]
Nonnutritive sucking	Sensory	Preterm infants in the NICU	Level 1: Systematic review | High quality (Cignacco et al., 2007; Pinelli and Symington, 2011)	SHORT-TERM: Improved self-regulation Reduced pain	Green STRONG + Do it
Nutritional supplements	Cognitive	Typically developing infants	Level 1: Systematic review | High quality (Protzko et al., 2013)	SHORT-TERM: Improved cognition	Green STRONG + Do it
Pain management	Sensory	Infants in the NICU	Consensus statement (Anand and The International Evidence-Based Group for Neonatal Pain, 2001)	SHORT-TERM: Improved pain control LONG-TERM: Prevention of neuropathic pain	Yellow WEAK + Probably do it
Prone positioning	Sensory and motor	Preterm infants in the NICU	Level 1: Systematic review | High quality (Cignacco et al., 2007)	SHORT-TERM: Improved head control Reduced pain	Green STRONG + Do it
Reading	Cognitive and social	Typically developing infants	Level 1: Systematic review with metaanalysis | High quality (Dunst et al., 2012; Protzko et al., 2013)	SHORT-TERM: Improved cognition Improved language Improved literacy	Green STRONG + Do it
Swaddling	Sensory	Preterm infants in the NICU	Level 1: Systematic review | High quality (Cignacco et al., 2007)	SHORT-TERM: Improved self-regulation Reduced pain	Green STRONG + Do it

GREEN, "GO" because high-quality evidence indicates effectiveness; *RED*, "STOP" because high-quality evidence indicates harm or ineffectiveness; *YELLOW*, "MEASURE" because insufficient evidence exists to be certain about whether the child will benefit.

reduce pain via a reduction in pulse rate and reduction in crying time. Facilitated tucking is supported by high-quality evidence (Cignacco et al., 2007).

Kangaroo mother care also known as skin-to-skin care: Kangaroo care fosters skin-to-skin contact between the parent and infant, by having the parent hold the infant against their chest, ideally accompanied by breastfeeding where safe and appropriate (Athanasopoulou and Fox, 2014; Brouwer and van den Hoogen, 2015).

Massage: For a description, refer to Section "Rehabilitation interventions not focused on neuroplasticity" and for a summary of the evidence refer to Table 23.1. Massage seeks to reduce pain by helping the infant to become calmer and more settled (Vickers et al., 2004) via provision of calming and environmentally enriching sensory stimuli. Massage has also been shown to improve visual acuity in preclinical and clinical studies of preterm infants and infants with Down syndrome (Guzzetta et al., 2011; Purpura et al., 2014).

Music: Music played for up to 15 min is provided to help the infant relax and better regulate their breathing, leading to pain reduction (Cignacco et al., 2007; Standley, 2012).

Newborn individualized developmental care and assessment program (NIDCAP): NIDCAP is a family centered developmental care program that includes parental training to improve parent–infant interaction and foster development, aiming to avoid developmental delays, especially in the cognitive domain (Blauw-Hospers and Hadders-Algra, 2005; Bonnier, 2008; Ohlsson and Jacobs, 2013).

Nonnutritive sucking: Nonnutritive sucking involves providing the infant with a pacifier (also known as a dummy) to suck without breast or formula milk to provide nutrition. Nonnutritive sucking seeks to reduce pain via helping infants becoming calmer and more attentive, coupled with a reduction in crying (Cignacco et al., 2007; Pinelli and Symington, 2011).

Parent-administered physical therapy: Teaching parents of medically stable preterm infants to provide early motor stimulation in midline orientation to promote head control leads to improved motor performance at term equivalent age (Ustad et al., 2016).

Prone positioning: Positioning the infant in prone is thought to provide abdominal counter pressure that relieves pain (Cignacco et al., 2007). The prone position also stimulates the motor task of head lifting. Prone positioning must be monitored carefully so as not to elevate the risk for sudden infant death syndrome (SIDS).

Swaddling: Swaddling involves wrapping the infant in a fabric cloth following a painful intervention to reduce pain via a reduction in pulse rate and is also used to promote self-soothing (Cignacco et al., 2007), but the risk for SIDS from hyperthermia and prone positioning must be monitored carefully.

Community-based environmental enrichment interventions

After an infant leaves the NICU, there are a number of environmental enrichment interventions that promote brain development. Children learn better in their natural home environment because they are familiar and comfortable in this setting. Improvements in functional outcomes in children with cerebral palsy, autism, and intellectual disability are even better when training interventions take place in their own home, because children learn best in supported natural settings, where training and learning is personalized to their enjoyment (Novak and Berry, 2014). Home-based practice also translates to more intense, specific, and relevant practice. A key part of intervention therefore is to enrich the home environment and parental knowledge to accelerate the child's learning (Adams and Tapia, 2013).

CIMT: For a definition refer to Section "Rehabilitation interventions that fully harness neuroplasticity" and for a summary of the evidence refer to Table 23.1. CIMT creates a change in the environment that encourages the child to actively practice movements with their nondominant hand. Provision of stimulating toys that evoke curiosity, play, and spontaneous use of the nondominant hand promotes experience-dependent plasticity (Morgan et al., 2013).

Early childhood education: Early childhood education has been shown to raise the intelligence of typically developing children in both the short and long terms (Reynolds et al., 2011; Walker et al., 2011; Protzko et al., 2013). In preterm infants and infants with social disadvantage, early childhood education improves cognitive outcomes (Adams and Tapia, 2013). A specific named early childhood education approach is Head Start, an American early-years educational childcare program designed to prepare children from disadvantaged backgrounds to enter mainstream schooling (Anderson et al., 2003). Early childhood education should be considered for every child with a disability and social disadvantage.

GAME: For a definition refer to Section "Rehabilitation interventions that fully harness neuroplasticity" and for a summary of the evidence refer to Table 23.1. GAME is a three-part intervention that includes enrichment of the child's home environment to promote intense motor and cognitive learning.

Home visiting: Home visiting is when health and educational professionals visit parents and infants in the child's own home, to equip parents with the skills and confidence they need to help and interact with their child and to enrich the child's environment through toy and book selection (Peacock et al., 2013; Reid et al., 2015; Spittle et al., 2015). A specific named home visiting approach is the Infant Health and Development Program

(IHDP), which in addition to parent education provides early-years educational childcare.

Learninggames: For a definition refer to Section "Rehabilitation interventions that fully harness neuroplasticity" and for a summary of the evidence refer to Table 23.1. The Learninggames curriculum provides parents with enjoyable games to play with their infant at home as an enrichment strategy to promote motor and cognitive development (Sparling and Lewis, 1979).

Nutritional supplements: Nutritional supplements high in long-chain polyunsaturated fatty acids added to either breast milk or food have been linked to improved childhood intelligence. Supplementation is theorized to provide critical resources for synaptogenesis and brain development (Protzko et al., 2013).

Pain management: Newborns experience pain and thus benefit from pain management, to prevent long-term maladaptive plasticity from unmanaged pain (Anand and The International Evidence-Based Group for Neonatal Pain, 2001). Assessment of pain in preverbal infants is complex and there are multiple sources of pain, including: procedures, gastroesophageal reflux, and muscle spasms. Nevertheless, international guidelines recommend avoidance of painful procedures and stimuli wherever possible plus early provision of pharmacologic and nonpharmacologic management strategies (e.g., sucrose, swaddling, facilitated tucking, pacifiers, skin-to-skin care, environmental interventions to reduce stress) (Anand and The International Evidence-Based Group for Neonatal Pain, 2001). Pain control optimizes the infant's environmental and behavioral state for learning and reduces the harmful effects on brain development and pain reactivity (Grunau, 2013).

Reading: Reading to children, especially in an interactive way, improves children's language development, literacy, and intelligence (Dunst et al., 2012). Reading is a form of cognitive and social enrichment.

Clinical implications

1. In the NICU environment, role-model a quiet and gentle approach to clinical care. Be a leader and supporter of enriched NICU care to promote brain development and prevent secondary brain damage (including kangaroo care, swaddling, tucking, massage, music, positioning and nonnutritive sucking).
2. Avoid inducing procedural pain whenever possible.
3. Ensure that children's books are available in the NICU environment. Discuss with parents the importance of reading to their child. Some parents may believe that their children are "not ready" for reading and it will be important to emphasize how reading exposes children to a rich vocabulary and symbolic concepts that promote brain development.
4. Postdischarge, confirm that the infant has access to adequate caloric intake to promote and sustain learning, either by oral or enteral feeding. Consider nutritional supplementation and/or referral to Gastroenterology and Dietetics, especially if the infant is suspected of having gastroesophageal reflux.
5. Infants identified at risk of autism, cerebral palsy, deprivation, or global delay should be referred to an early intervention service prior to discharge, preferably one that offers a home visiting service.
6. Inform parents about the importance of providing a home environment with: (a) accessible, open-ended, and stimulating toys; (b) space to play indoors and outdoors; and (c) limits to noise and television so that children can concentrate (Stewart, 2017).
7. Encourage parents to set up play environments where the child is independent and the parent's role becomes to support, stimulate, and extend their child's play (Stewart, 2017).
8. In follow-up visits, discuss the value of early childhood education with parents.

PARENT–CHILD INTERACTION INTERVENTIONS

Parent–child relationships are critical for fostering brain development (Kolb et al., 2013). The human infant's dependence on their parent has been described as a long learning "apprenticeship" that fosters human connection and ultimately builds advantageous cognitive flexibility that allows children to adapt to their environment and life circumstances (Stewart, 2017). An infant's favorite and most motivating toy is their parent (Stewart, 2017). When a parent responds to their infant's play and exploration, an infant experiences contingency learning, fostering a sense of self competence and autonomy because they realize they can affect the world around them (Stewart, 2017). Parents know their child best and can therefore fine tune and scaffold their learning better than any toy. Clinicians should recognize that promoting parent–child attachment and responsive parenting is a potent driver of child development, intelligence, and social skills. Preclinical and human data support the importance of responsive parenting for advancing brain development (Wolff and Ijzendoorn, 1997; Kolb et al., 2013). Children with and without brain injuries have better developmental outcomes and better social skills when their parents sensitively read and respond to their cues, because this type of parenting accelerates contingency learning (Wolff and Ijzendoorn, 1997). We will now describe the interventions that foster parent–child attachment and relationships and shape positive responsive parenting.

NICU-based parent–child interaction interventions

Within the intensive care environment, it is especially important to actively foster positive parent–child interactions. Parents initially hand over control of care to the healthcare team to ensure their infant's survival, which can make parents feel helpless and underinvolved. It is important that control is handed back to parents using a family centered care approach. Otherwise parents can become passive observers of their infant's care, which can interfere with bonding and elevate parental stress. When parents are trained to provide most of the care to their infant in the NICU environment, using an approach known as family integrated care (FIC), infant's outcomes are better (O'Brien et al., 2013).

FIC: The parent is provided with daily education, from a set curriculum, about how to provide care for their infant in the NICU, with the aim of them providing more than 8 h of care per day. Parents are taught to feed, bathe, dress, and hold their infant as well as providing skin-to-skin care and documenting in the medical charts. Parents also attend rounds and receive one-to-one specialist education about caring for their infant as needed (O'Brien et al., 2013).

The other major parent–child interaction interventions used with the NICU environment are kangaroo care and NIDCAP, which have been described in Section "NICU-based environmental enrichment interventions." Both kangaroo care and NIDCAP interventions have evidence to show they positively foster relationships in the short term. Kangaroo care is known to also improve parental mental health. The evidence for these interventions is summarized in Table 23.3.

Community-based parent–child interaction interventions

After an infant leaves the NICU, there are a number of evidence-based interventions that foster positive parent–child interactions. All the approaches have a similar therapeutic intent; they aim to foster: responsive parenting, positive parenting and upskilling, and empowering the parent to develop solutions to daily challenges. Parenting advice helps parents feel more confident and capable. Community-based parent–child interaction interventions include:

Parent coaching: Coaching involves provision of emotional support and information, and facilitation of parent-devised goals, parent-devised solutions, parent-devised plans, and parent reflections about the effectiveness of their actions (Novak, 2014).

Parent education: Educational interventions increase parental knowledge, skill, and self-efficacy in caring for their child. Education may include information, demonstrations, and/or feedback on parental performance (Kaminski et al., 2008; Benzies et al., 2013; Sanders et al., 2014). Most people learn parenting skills from their own parents or television and rarely do these role models include examples of how to parent a child with a disability. Education and support are therefore especially important for parents of children with disabilities, because the parenting experience can be very isolating and stressful without a blueprint to follow. A specific named parental education approach is the Positive Parenting Program (Triple P) (Sanders et al., 2014), which aims to prevent and treat social, emotional, and behavioral problems by enhancing the parent's knowledge and skills. Triple P effectively improves parenting skills and positive child behavior, with a substantial evidence base at the individual and population level. Triple P is currently being validated in the newborn population as an early treatment for cerebral palsy and brain injury.

Parent sensitivity training: Sensitivity training teaches parents to recognize their infant's cues, interpret the cues, and appropriately respond in a timely manner, to develop mutuality, reciprocity, turn-taking, and shared affect (Wolff and Ijzendoorn, 1997; Benzies et al., 2013; Spittle et al., 2015; Mountain et al., 2017). A specific named sensitivity training approach is the Mellow Parenting program (MacBeth et al., 2015), which aims to improve parenting skills and child behavior through teaching parent sensitivity but also addressing parent mental health.

Collectively, these interventions improve parent–child attachment and relationships because of the more responsive parenting. The interventions also improve child behavior plus improve parent mental health and coping. The evidence for these interventions is summarized in Table 23.3.

Clinical implications

- Openly discuss, validate, and normalize the stress of parenting an infant in the NICU and/or with a high risk of lifelong disability.
- Offer a referral to family support services or parent education during a NICU stay and/or for after discharge.
- Emphasize the importance of building an effective parent–infant relationship for accelerating brain development and learning, explaining that bonding and responding are important ways parents can help their child.
- Explain that parents of children with disabilities describe parent-to-parent support as sustaining and helpful for building knowledge and coping skills over the long term. Parents report finding it useful to connect with other parents in similar circumstance who understand and can share and exchange ideas (Shilling et al., 2013).

Table 23.3

Parent–child interaction interventions evidence base

Intervention	Population	Evidence	Outcome	Evidence alert and GRADE
Family integrated care (FIC)	Parents of infants in the NICU	Level 3: Pilot study | Low quality (O'Brien et al., 2013). Note: Definitive RCT underway	SHORT-TERM: Improved infant weight gain Improved rate of breastfeeding at discharge Decreased parent stress	Yellow WEAK +Probably do it
Kangaroo mother care	Preterm infants in the NICU	Level 1: Systematic review | Moderate quality (Athanasopoulou and Fox, 2014; Brouwer and van den Hoogen, 2015)	SHORT-TERM: Improved parent–child interactions Improved parent mood/mental health, e.g., lowered depression or anxiety	Green Do it
NIDCAP	Infants in the NICU	Level 1: Systematic review with metaanalysis | Moderate–high quality (Blauw-Hospers and Hadders-Algra, 2005; Bonnier, 2008; Ohlsson and Jacobs, 2013)	SHORT-TERM: Improved parent–child interactions No change in medical status LONG-TERM: No reduction in the rate of survival without a disability	Green Do it [Short-term]
Parent coaching	Infants at risk of disability	Level 1: Systematic review | High quality (Novak, 2014)	SHORT-TERM: Improved social emotional skills Improved motor skills LONG-TERM: Improved academic performance	Green Do it
	Autism spectrum disorder	Level 1: Systematic review | Low quality (Novak, 2014)	SHORT-TERM: Improved self-esteem LONG-TERM: Improved academic performance	Yellow WEAK +Probably do it
	Behavior disorders	Level 1: Systematic review | Low quality (Novak, 2014)	SHORT-TERM: Improved behavior	Yellow WEAK +Probably do it
	Cerebral palsy	Level 1: Systematic review | Low quality (Novak, 2014)	SHORT-TERM: Improved motor skills	Yellow WEAK +Probably do it
	Developmental delay	Level 1: Systematic review | Low quality (Novak, 2014)	SHORT-TERM: Improved function Improved communication Improved parental competence	Yellow WEAK +Probably do it
	Specific learning difficulties	Level 1: Systematic review | Low quality (Novak, 2014)	SHORT-TERM: Reduced parental stress	Yellow WEAK +Probably do it
Parent education	Preterm infants	Level 1: Systematic review | Moderate–high quality (Benzies et al., 2013)	SHORT-TERM: Reduced parental anxiety Reduced parental depression Limited effect on stress and parent–child interactions	Green Do it
	Behavior disorders	Level 1: Systematic review | Moderate–high quality (Kaminski et al., 2008)	SHORT-TERM: Improved parent–child interactions Improved social emotional skills Improved parenting consistency	Green Do it
	Behavior disorders and/or developmental disability	Level 1: Systematic review with metaanalysis of Triple P | Moderate–high quality (Sanders et al., 2014)	SHORT-TERM and LONG-TERM: Improved behavior Improved social emotional skills Improved parent–child interactions Improved parenting practices Improved parent satisfaction Improved parental adjustment	Green Do it
Parent sensitivity training	Preterm infants	Level 1: Systematic review with metaanalysis | Moderate–high quality (Wolff and Ijzendoorn, 1997; Benzies et al., 2013; MacBeth et al., 2015; Spittle et al., 2015; Mountain et al., 2017)	SHORT-TERM: Reduced parental anxiety Reduced parental depression Improved parent–child attachment Reduced disorganized behavior Improved cognition	Green Do it

GREEN, "GO" because high-quality evidence indicates effectiveness; *RED*, "STOP" because high-quality evidence indicates harm or ineffectiveness; *YELLOW*, "MEASURE" because insufficient evidence exists to be certain about whether the child will benefit.

FUTURE DIRECTIONS

We have described the numerous rehabilitative interventions that exist to help infants to both develop functional skills and prevent further complications. There are many effective approaches providing small positive gains, but none of these interventions are curative or substantially lessen the severity of childhood disability. Researchers are investigating whether stem cells, novel pharmacologic agents, and neuromodulation may deliver larger treatment effect sizes. Leading neuroplasticity researchers hypothesize that modulating neuroplasticity early after the brain injury might improve clinical outcomes over-and-above current care (Ismail et al., 2017).

A metaanalysis has demonstrated that stem cell treatment for people with cerebral palsy produces small improvements in gross motor skills, over and above the gains experienced from rehabilitation alone (Novak et al., 2016a). A variety of stem cell types have been tested, with the largest body of evidence being for autologous umbilical cord blood (UCB), because of the known safety profile of these cells and the ease of collection and infusion (Novak et al., 2016a). The rate of serious adverse events reported across all the early pilot trials was low (3% stem cells; 2% controls), suggesting an acceptable benefit:risk ratio of stem cell interventions for children (Novak et al., 2016a). Further clinical trials are therefore recommended to determine if stem cell interventions might be an additive intervention that could be included within standard care. Clinical trials are currently underway examining: (a) the safety of donor derived allogenic UCB, with the aim of establishing a safe, repeatable, high-dose UCB treatment for both cerebral palsy and/or ASD (NCT02599207; ACTRN12616000403437); (b) safety and comparative effectiveness of banked cord blood vs bone marrow (NCT01988584); and (c) the efficacy of very early autologous UCB infused within hours of a hypoxic brain injury for children with encephalopathy (NCT02612155).

Repetitive transcranial magnetic stimulation (rTMS) is a noninvasive neuromodulation intervention, where a rapidly changing magnetic field induces an electrical current to the cortex that excites the motor cortex as a strategy for improving motor function. It is hypothesized that neuromodulation might alter the regulatory mechanisms of plasticity, thus yielding changes in behavioral outcomes (Ismail et al., 2017). Pilot clinical trials have indicated that children with hemiplegic cerebral palsy who received TMS with CIMT had superior assisting hand function over children who received sham TMS (Gillick et al., 2013; Kirton et al., 2016). More research is currently being conducted to confirm the safety and efficacy in infants with brain injury (NCT02743728), so that the intervention might be applied early after the brain injury.

EMMA'S STORY REVISITED

Emma's medical history and HIE, Sarnat Grade 2 means she is at risk for disability, but 90% of children with Sarnat 2 have a normal outcome. Sophie and Liam of course want to know what Emma's future will be. To accurately predict whether she will have cerebral palsy or a cognitive impairment or a normal outcome, you evaluate her neuroimaging. The neonatal MRI indicated bilateral diffusion restriction in the basal ganglia, and damage to the posterior limb of the internal capsule, meaning the motor tracts are involved and cerebral palsy is likely. You order a General Movements assessment and HINE from a physical therapist and occupational therapist to further inform your decision making. Emma has "absent fidgety" General Movements meaning the quality of her movements is low, indicating high risk for cerebral palsy. Emma's Hammersmith score is 53. A Hammersmith score below 57 at 3 months is highly predictive of cerebral palsy. Hammersmith score between 40 and 57 indicates cerebral palsy with independent ambulation long term. The MRI, general movements, and Hammersmith scores are congruent, indicating Emma's likely long-term outcome is ambulant cerebral palsy. You compassionately communicate Emma's diagnosis of cerebral palsy to Sophie and Liam over a series of planned conversations. You organize parent-to-parent peer support for Sophie and Liam and refer Emma to cerebral palsy-specific early intervention and plan to order hip X-rays near her first birthday to ensure joint integrity. Emma receives intensive training-based interventions to optimize her motor outcome. At Emma's 2-year follow-up, you note that your early diagnosis of cerebral palsy was correct. She has spastic quadriplegic cerebral palsy, with dyskinesia present. Her parents are delighted to tell you that she has just started to walk, just as the Hammersmith tool predicted. Emma is classified as Gross Motor Function Classification System level 2 (i.e., ambulates independently but requires a rail to ascend stairs). Sophie and Liam are pleased with her progress and are making plans for Emma to attend mainstream school.

CONCLUSION

In conclusion, it is now possible to accurately diagnose major childhood disabilities early. Early diagnosis enables diagnostic-specific early intervention that harnesses neuroplasticity and improves child outcomes. Multiple effective treatments exist, with the most effective treatments involving child self-generated movements, child-led problem solving, intense repetition of practice, practice of real-life tasks that are meaningful to the child, environmental enrichment, and enhanced parent–child interactions.

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