

Perspective

From Hemispheric Asymmetry through Sensorimotor Experiences to Cognitive Outcomes in Children with Cerebral Palsy

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Abstract: Recent neuroimaging studies allowed us to explore abnormal brain structures and interhemispheric connectivity in children with cerebral palsy (CP). Behavioral researchers have long reported that children with CP exhibit suboptimal performance in different cognitive domains (e.g., receptive and expressive language skills, reading, mental imagery, spatial processing, subitizing, math, and executive functions). However, there has been very limited cross-domain research involving these two areas of scientific inquiry. To stimulate such research, this perspective paper proposes some possible neurological mechanisms involved in the cognitive delays and impairments in children with CP. Additionally, the paper examines the ways motor and sensorimotor experience during the development of these neural substrates could enable more optimal development for children with CP. Understanding these developmental mechanisms could guide more effective interventions to promote the development of both sensorimotor and cognitive skills in children with CP.

Keywords: development; hemispheric asymmetry; corpus callosum; sensorimotor experiences; cognition; cerebral palsy; interventions



Citation: Babik, I. From Hemispheric Asymmetry through Sensorimotor Experiences to Cognitive Outcomes in Children with Cerebral Palsy. *Symmetry* **2022**, *14*, 345. <https://doi.org/10.3390/sym14020345>

Academic Editors: Adriana Sampaio, Hsien-Yuan Lane and Ludmiła Zająć-Lamparska

Received: 14 September 2021

Accepted: 24 January 2022

Published: 9 February 2022

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1. Introduction

Hemispheric asymmetry reflects a fundamental principle of neuronal organization and plays a critical role in children's motor, sensorimotor, and cognitive development [1–3]. Early brain injury usually leads to atypical structural and functional brain asymmetries and interhemispheric connectivity, which may negatively affect children's motor control and use of upper extremities, resulting in suboptimal manual sensorimotor experiences [4–9]. Cerebral palsy (CP) defines a group of non-progressive neurodevelopmental disorders attributed to prenatal or perinatal brain injuries that negatively affect children's postural control and movement [10–12]. Because cognitive development is embodied in motor and sensorimotor experiences [13–18], children with CP may exhibit delays and impairments not only in motor and sensorimotor skills, but also in cognitive abilities [2,5,19–27].

The purpose of this perspective paper is to outline the neural mechanisms involved in the ways atypical hemispheric asymmetry, as a result of early brain insult, might affect the development of motor, sensorimotor, and cognitive skills. Understanding the role of these neural mechanisms in atypical developmental pathways should provide important insights into the nature of cognitive impairments in children with CP and enable the design and implementation of effective interventions (targeting early sensorimotor skills) that will promote children's cognitive development. This paper discusses the concept of typical hemispheric asymmetry, patterns of abnormal brain structure, and interhemispheric connectivity in children with CP, sensorimotor and cognitive impairments related to CP, the role of embodiment in the development of sensorimotor and cognitive skills, and possible interventions to improve developmental outcomes in children with CP.

2. Hemispheric Asymmetry and Information Processing

Functional hemispheric asymmetries reflect the fact that, although structurally quite similar, the two hemispheres have distinct representation in processing different types of information. The specialization of the two hemispheres increases the information processing efficiency by allowing parallel processing, decreasing duplication, and eliminating potential interhemispheric conflict [28–32]. In auditory information processing, the left hemisphere is responsible for distinguishing phonological differences of language-related sounds and producing those phonological distinctions during speech, whereas the right hemisphere specializes in processing melodies, rhythms, environmental noises, and the emotional prosody of speech [33–35]. In visual information processing, the left hemisphere is dominant for facial recognition and the generation of voluntary facial movements, whereas the right hemisphere is better at differentiating faces from non-faces [34]. Recent research also proposed that the left hemisphere is specialized for activation–inhibition coordination, thus justifying its dominance in both manual and verbal skills [36].

Importantly, previous research suggested that hemispheric specialization does not depend on the modality of processed information (e.g., haptic, auditory, or visual) but rather on the relative characteristics of the stimuli. One such account of the processing specialization that gained empirical support from previous research and is most applicable to the discussion of hemispheric lateralization in CP is the *frequency-dependent hemispheric processing hypothesis* [37,38]. According to this hypothesis, there are two neuronal systems associated with processing any complex, hierarchically organized stimuli: (1) extracting higher-frequency transitions in spatial and temporal patterns of *local stimuli*, thus specializing in phonological distinctions, facial recognition, and decoding letters/words, and (2) processing lower-frequency transitions, or *global stimuli*, which typically have a contextual character (e.g., rhythm, emotional tone, complex scenes, and relative position in space). Previous research reported that the left hemisphere is specialized in the *analytic processing* of high-frequency, local transitions, whereas the right hemisphere specializes in the *holistic processing* of low-frequency, global stimuli [36,39–44]. Note that the distinction between the two hemispheres in the “preferred” frequency of processed information is quite relative: each hemisphere is capable of processing the “non-preferred” range of frequencies but would not be as effective as the other one [37,45].

Given that hemispheric specialization increases the efficiency of information processing [28–32,46], stronger hemispheric asymmetry should be associated with better motor, sensorimotor, language, and cognitive performance. This hypothesis has been tested by relating children’s handedness to their developmental outcomes. Handedness may serve as a convenient marker of the hemispheric specialization of function [47–54], with strong hand-use preference representing stronger underlying hemispheric lateralization. Thus, strong and consistent hand-use preference has been predicted to be associated with better developmental outcomes. Indeed, previous research found the benefits of early-developing, strong, and consistent handedness for object management skills associated with symbolic development [55,56], block stacking skills associated with the comprehension of spatial words and language acquisition [57,58], and language skills [59–61]. To further emphasize the role of hemispheric specialization in optimal development, atypical hemispheric specialization has been widely associated with neurobehavioral dysfunctions and intellectual disabilities, such as developmental stuttering, dyslexia, autism, Down syndrome, schizophrenia, and psychosis [62–72].

3. Hemispheric Asymmetry in Children with CP

Cerebral palsy is usually attributed to prenatal or perinatal brain insult [10–12]. The most common brain insults associated with CP are white matter lesions in periventricular areas, basal ganglia and thalamus lesions, gray matter lesions in cortical and subcortical regions, cerebral malformations, enlarged ventricles, focal infarcts, and diffused grey matter lesions [73–77]. Sensory tracts may be less affected by periventricular white matter lesions that typically occur after the refinement of thalamocortical tracts, whereas lesions to

basal ganglia, thalamus, and cortical gray matter, occurring after thalamocortical projections reach cortex, may lead to severe disruptions in somatosensory function [73,76,78–82]. As a result, children with CP often exhibit abnormal patterns of tactile and visual information processing [83–91]. For example, in visual processing, children with CP often exhibit reduced contrast sensitivity and visual acuity, difficulty with fixation, abnormal saccadic movements, strabismus (an abnormal alignment of the eyes resulting in uncoordinated eye movements, double vision, difficulties in depth perception, etc.) and refractive errors [84,92–95]; in tactile processing, CP diagnosis is often associated with tactile registration and perception deficits [96,97]. Importantly, due to abnormal sensorimotor processing and interaction between sensory modalities, early spontaneous movements that allow for the refinement of sensorimotor connections in typically developing infants might not have this effect in children with brain lesions [98,99].

The motor system seems to be relatively more robust to early brain insults than the sensorimotor one; perhaps, its later developmental timeline permits considerable reorganization in the corticospinal tract, which is responsible for voluntary motor function. For example, in typically developing infants, during the first 6 (and up to 18) months after birth, competition between the hemispheres for information processing results in the gradual reorganization of neural pathways, with the reduction in the number of ipsilateral connections and strengthening of the contralateral ones. The latter exhibit lower thresholds, shorter latencies, and larger amplitudes compared to ipsilateral connections in response to transcranial magnetic stimulation [4,100]. Early brain damage in children with unilateral CP may disrupt contralateral corticospinal connections, resulting in atypical patterns of corticospinal tract connectivity [4,100–103]. Indeed, for about 30% of children with hemiplegic CP, control of the affected hand resides in the ipsilateral hemisphere [79,104–107]. Moreover, the movement of the affected hand typically corresponds to an increased activation in bilateral primary sensorimotor cortices [9,108].

On a behavioral level, this abnormal brain asymmetry leads to reduced control of the contralesional limb, spasticity, and mirror movements [104,106,109–111]. (Mirror movements are simultaneous, involuntary, and non-goal-directed movements of a limb that accompany goal-directed activity in the contralateral limb, typically prevalent in infants' motor repertoire during the 4.5–7.5-month age period [112,113]). Because ipsilateral connections are less effective than contralateral ones, the ipsilateral control of the affected hand in children with hemiplegic CP is typically associated with poor motor control and impaired performance [102]. The compromised transmission of sensory feedback from the affected hand to the motor cortex through inefficient ipsilateral connections, coupled with the manifestation of mirror movements and visual hemianopias (brain function conditions in which a person is only able to see one side of the visual field) likely forms the foundation for suboptimal motor control and bimanual coordination in children with unilateral CP [79,102,114]. Additionally, the interaction between the contralateral somatosensory pathways and ipsilateral corticospinal motor pathways may result in interhemispheric dissociation between sensorimotor inputs and outputs [2].

Unilateral brain injury leads to motor impairments in the contralateral side of the body, resulting in hemiplegic CP. The severity of motor impairment is highly associated with the extent of brain damage in the contralateral hemisphere [115–117]. Although both upper and lower extremities may be affected in hemiplegic CP, the current paper focuses on the function of the upper extremities. Children with hemiplegic CP tend to “disregard” the affected limb; the resulting lack of motor practice (i.e., “developmental disuse”) reduces the likelihood of spontaneous reaching and grasping movements in the affected limb, thus impairing “practice” with its motor control and performance [118,119]. The tendency to only use one hand further impedes bimanual coordination, sophisticated object exploration, and self-care abilities, thus negatively affecting a child's independence and quality of life [118,120–122].

4. Interhemispheric Connectivity in Children with CP

The corpus callosum (CC) is the major commissural tract connecting and coordinating the two cerebral hemispheres to allow the integration of sensorimotor information and the optimization of information processing [123,124]. According to some accounts, the CC enables hemispheric specialization by inhibiting one hemisphere during the activation of the contralateral hemisphere in cases when simultaneous activity would compromise information processing [125,126]. More recent research, however, suggests that efficient lateralized processing is achieved by weaker callosal connections between functionally lateralized homologous cortical areas and stronger callosal connections between the non-lateralized areas [127,128].

In typically developing children, the formation of the CC starts around the 12th week of gestation, with all fibers being in place by the 20th week of gestation. However, the process of myelination, which starts around the 4th prenatal month, continues well into adulthood [53,129–131]. Importantly, in the first years of life, the underdeveloped CC may not allow appropriate information sharing between the two hemispheres, thus restricting asymmetric sensorimotor processing to a specific hemisphere and facilitating the development of hemispheric specialization of function [132–135].

Previous research showed that children with CP have a smaller CC and reduced white matter integrity in the CC compared to their typically developing peers, with the extent of structural changes in the CC being directly related to the size of the lesion [5,9,136,137]. These structural differences in the CC may negatively affect motor and sensorimotor function in children with CP [5]. For example, the reduced white matter integrity in the CC is associated not only with motor impairment in the affected hand but also with motor deficits in the non-affected hand and poor bimanual skills [9,138–141]. Furthermore, a lack of transcallosal inhibition allows for the bilateral activation of primary sensorimotor cortices, which results in mirror movements [2].

Importantly, the CC is responsible for the integration of the motor and somatosensory information, as well as bilateral coordination in motor and visuomotor tasks, especially those requiring simultaneous/parallel processing and the timely adjustment of movements performed by two hands [123,140,142–144]. Note that the acquisition of new motor skills typically requires one to learn finely timed, ordered sequences of actions and the bimanual coordination of parallel movements, both requiring effective interhemispheric transfer via the CC [141,142,144–148]. Thus, an underdeveloped CC in children with CP might interfere with their execution of finely timed sequences of actions, bimanual performance, and motor learning in general [139,141,149–152].

5. Sensorimotor and Motor Outcomes in Children with CP

“Developmental disuse” of the affected limb in children with hemiplegic CP may manifest as: (1) motor neglect [119,153,154], (2) visuoperceptual and spatial neglect [155–157], or (3) deficits in body representation [153,158,159]. Each type is discussed below.

5.1. Motor Neglect in Manual Skills

In typical development, starting from weeks 7–8 prenatally, human fetuses exhibit spontaneous movements (also called general movements) of the extremities, which are highly predictive of future neurodevelopmental outcomes [160–165]. An abundance of variable and complex spontaneous movements allows appropriate motor and sensorimotor feedback that facilitates the refinement of motor and sensorimotor pathways, thus improving motor control and coordination [166–169].

Newborn infants typically demonstrate spontaneous, swiping arm movements [170,171]. With time, these diffuse movements become more coordinated and goal-directed, resulting in infants’ reaching for and grasping of objects at the age of 3–4 months [112,172–177]. By this age, infants are capable of both unimanual and symmetrical bimanual reaches [178]. Increasing specialization in brain activity and improved interhemispheric connectivity result in the gradual transformation of earlier synchronized and symmetrical bimanual

movements into de-coupled, asymmetrical role-differentiated bimanual manipulations by the age of 7–13 months [112,138,179–185]. (In role-differentiated bimanual manipulation, the two hands perform complementary actions while manipulating an object: one hand plays a passive, supportive role while the other one actively manipulates movable parts of a toy [186]). Furthermore, diverse motor and sensorimotor experiences continue to increase the specificity of the developing motor system: pruning of ipsilateral corticospinal pathways and increasing callosal functioning both lead to a decrease in mirror movements during the 9–12-month age period [100,112,187,188].

Infants with CP exhibit a lack of spontaneous movements or abnormal spontaneous movements (e.g., cramped-synchronized movements – sudden, synchronous movements of the trunk and limbs; [162,166,189–191], which result in missed opportunities to establish an adequate “forward” internal model, thus negatively affecting the child’s ability to predict the sensorimotor consequences of their own movements and execute anticipatory motor planning [192–194]. Moreover, children with CP demonstrate not only atypical spontaneous activity and decreased active range of motion but also impaired selective motor control that is manifested in muscle group synergies and mirror movements [195–197]. Muscle synergies interfere with the execution of voluntary, goal-directed movements; for example, a simple act of bringing a cup to the mouth would require simultaneous wrist extension and elbow flexion; atypical flexor synergy, in this case, would prevent wrist extension and, thus, impede the functional movement [195]. It is important also to recognize the crucially collaborative role of pyramidal (corticospinal) and extrapyramidal tracts in the development of motor control; for example, reticulospinal and vestibulospinal tracts were found to be associated with the coordination of finger movements that typically rely upon corticospinal tracts [198].

Furthermore, mirror movements of fingers, hands, and arms in children with CP may impede effective independent control of the hands [196]. Whereas mirror movements disappear with increasing age in typically developing children, those with CP show no such trend: strong mirror movements (15 times stronger than those observed in typically developing controls) were recorded in children with CP at the ages of 6–18 years [196]. Some research suggested that mirror movements are more prevalent in the affected hand [199,200], whereas more recent research found stronger mirror movements in the unaffected hand as a result of the voluntary activity of the affected hand [196,201]. On a behavioral level, damage to one or both hemispheres in children with CP disrupts movement in the contralateral side of the body; the resulting “developmental disuse” of an affected limb negatively affects bimanual coordination during tasks that require the participation of both hands [120]. Mirror movements further disrupt bimanual coordination and performance in children with CP, given that bimanual activities typically require independent control of the two hands, achieved by the inhibition of involuntary movements [196,202,203]. Thus, children with CP often exhibit significant delays and impairments in motor control, the execution of goal-directed movements, and bimanual coordination, which may impede their motor and sensorimotor awareness and anticipatory motor planning.

5.2. Visuoperceptual and Spatial Neglect

Importantly, “developmental disuse” of the affected limb in children with hemiplegic CP may stem not only from motor dysfunction but also visuoperceptual deficits [153,155–157,204]. Indeed, previous research showed that early brain injuries produce specific spatial cognitive deficits [205–209]. Unilateral brain damage in children with hemiplegic CP may disrupt the processing of visual information, resulting in unilateral spatial neglect manifested as an inability to attend, process, and report on sensory events occurring in one side of extrapersonal space [155–157,210,211]. For example, children with hemiplegic CP tend to draw asymmetrical pictures of the human body, often distorting the side of the picture corresponding to their own affected limb [153,212]. Although spatial neglect in children with hemiplegic CP is often identified with paper-and-pencil tests, the latter might be less effective than functional assessments [211]. In general, the scarcity of quality research on

spatial neglect in pediatric populations has resulted in the lack of valid assessment and treatment methods [211].

Note that there are two generally hypothesized functionally distinct visual pathways in the cerebral cortex: (1) the ventral (occipito-temporal) pathway, responsible for the discrimination of shapes, objects, words, and faces, and (2) the dorsal (occipito-parietal) pathway, mapping complex visual scenes and executing visually guided movements, such as reaching and grasping [213–215]. Previous research showed a strong association between periventricular leukomalacia (PVL—a form of brain injury affecting white matter near the ventricles; PVL is closely associated with premature birth) and cerebral visual impairment, which could manifest as deficits in both ventral and dorsal pathways [83–86,88,90]. In addition, disruptions in structural and functional hemispheric connectivity as a result of periventricular leukomalacia reportedly affect visual pathways involved in the processing of body motion [216]. As a result, children with CP may exhibit deficits in visual attention, the recognition of object and faces, handling of complex scenes, and navigation. Neuroimaging research supported behavioral observations: visuoperceptual deficits have been associated with white matter reduction and ventricular enlargement in the occipital and parietal regions of the brain, as well as structural abnormalities of the corpus callosum's splenium [217–220].

In agreement with the *frequency-dependent hemispheric processing hypothesis* (Sergeant [37–39]), suggesting the right-hemisphere dominance in global processing and the left-hemisphere specialization in local processing, children with right-hemisphere lesions reportedly showed difficulties in spatial integration, whereas children with left-hemisphere lesions struggled with processing pattern detail in both two-dimensional and three-dimensional arrangements [205,207]. For example, in their drawings of people and houses, children with right-hemisphere damage would depict appropriate parts but fail to arrange them into spatially coherent, meaningful forms [209]. Spatial cognitive deficits were found to be more persistent in children with right-hemisphere lesions [205]; these findings correspond well with previous research showing limitations in brain plasticity for non-verbal functioning as a result of early right-hemisphere insult [157,207,209,221,222].

Importantly, deficits in both manual and visuospatial skills in children with CP often result in their impaired visuomanual coordination. For example, children with CP, especially those with right-hemisphere lesions, exhibited difficulty with drawing, copying designs/complex figures, and handwriting skills [207,209,223,224]. Note that in typically developing children, the visuomotor coordination skill of design copying, measured at the age of 3–4 years, was found to be predictive of reading, math, and science performance from kindergarten through to the age of 13–14 years [225,226].

I propose that the relation between early visuomanual skills and future linguistic and mathematical performance may be mediated by the influence of visuomanual skills on a child's symbolic development. Given that pictures and designs are symbols representing reality, the ability to perceive, analyze, and coordinate the movements required to reproduce a picture should promote a child's symbolic development [227–229]. This symbolic development, in turn, is relevant for the development of linguistic and mathematical processing [230–237].

5.3. Body Representation and Mental Imagery

Mental representation of one's own body involves the processing and monitoring of afferent visual, somatosensory, and motor inputs, as well as interoceptive and proprioceptive feedback as a result of motor execution [238–240]. *Triadic taxonomy* is the most common way to describe different aspects of body representation. The triad is: (1) the Body Schema, relying on sensory–motor information to define the body's position in space, (2) the Body Structural Representation, consisting of a mental topographic map of the body, and (3) the Body Semantics (also called Body Image), reflecting the linguistic and conceptual representation of the body used in communication and self-identity [241–243].

Previous research identified cortical areas responsible for the processing of these three body representation types: the Body Schema was reportedly associated with the posterior parietal cortex, the Body Structural Representation was linked to the ventral lateral occipitotemporal transition, whereas the Body Semantics was related to the insula [244]. Although the hemispheric laterality of body representations and body motion is still unclear [244], previous research suggested that adolescents and adults with left-hemisphere damage (right hemiparetic CP) showed significant deficits in their processing of the Body Schema and Body Structural Representation [159,245–248].

During typical development, the Body Semantics (measured with the Object–Body Part Association Task [249]) seems to reach a more complete pattern of performance first—by the age of 4–5 years, followed by the Body Structural Representation (measured with the Frontal Body Evocation Task of the Body Representation test [250]), which seems to reach an adult-like pattern of performance by the age of 9–10 years. The Body Schema (measured with the Hand Laterality Task [251]) seems to take the longest to reflect adult-like performance [250,252–256]. The concept of the Body Semantics has been found to be positively related to that of the Body Structural Representation [253,257]. The Body Schema is usually evaluated using so-called “*motor imagery*” tasks that require mental simulation of physical movement to make laterality judgments based on pictures of body parts (e.g., hands and feet) presented in different orientations. Typically developing individuals tend to show a linear increase in reaction time in response to increasing rotation angle [158,159,242,249,258].

Among children with CP, 63.64% of 5–12-year-olds showed poor performance in body representation processing in at least one of the three types: 56.3% in the Body Structural Representation, and 21.2% in both the Body Schema and the Body Semantics [158]. The performance of children with CP on the three body representation types seems to follow the same developmental sequence observed in typically developing children: among 5–7-year-old children, there was no difference found in mental imagery performance between those with CP and their typically developing peers, whereas 8–12-year-old children with CP showed deficits in the Body Schema and the Body Structural Representation, but not in the Body Semantics [158]. Additionally, adolescents with hemiplegic CP were slower in their hand laterality judgments compared to a neurologically healthy control group, especially while judging pictures representing the affected hand, suggesting that deficits in motor control negatively affect motor imagery [259].

Moving beyond the triadic taxonomy, processing *self-body representation* has been shown to be as affected in children with CP as processing generic body representations discussed above. Using self-portraits to study self-body representation, significantly more asymmetry between the length of the affected vs. non-affected upper limbs was found in the drawings of 5–10-year-old children with CP compared to typically developing controls [212]. Interestingly, children with CP exaggerated the asymmetry of their own body not only in comparison to their typically developing peers, but also in comparison to other children with hemiparesis; these asymmetries in body representations of children with CP may reflect their perception of their own functional deficits experienced in the hemiparetic limb [212,260].

Impairments in the production of body motion in individuals with CP are closely associated with deficits in *body motion perception* [216,261,262]. The latter is typically studied using series of static point-light body motion displays in which bright white dots on a black background represent the main joints and the head of a “walking” or “gesture-producing” human body [262,263]. Previous research associated the processing of body motion with portions of the parietal and frontal cortices, the right posterior superior temporal sulcus, the right parieto-temporal junction and fusiform gyrus, as well as the amygdala [264–276]. The involvement of the amygdala should not be surprising, because the correct interpretation of others’ body movements, or body language, provides valuable social cues to other people’s emotions, dispositions, and intentions [277–279], which would guide approach vs. avoidance reactions.

Typically developing children gradually improve their perception of body motion in point-light displays until ceiling levels are reached at the age of 5 years [263]. By contrast, children and adolescents with CP show significant difficulties in the processing of body motion and gestures [262,263,280,281]. For example, individuals with hemiplegia show deficits in both the recognition of gestures that appeared to be performed by their affected arm [262] and the imitation of meaningful gestures pointing to different parts of the body [245,282]. Note that gestures advance children's symbolic development: children's pointing to an object often triggers their caregivers' naming the object, thus forming the connection between the label (symbol) and the object it stands for in the child's mind [283–285]. Gestures also mediate the positive relation between motor and language development [231,284,286–290]. Thus, difficulties with gesture processing in children with CP might have negative consequences for their language and cognitive development.

Importantly, deficits in body representations in children with CP might stem from difficulties in other domains, such as linguistic, semantic, visual, attentional, or *mental imagery* [158]. In this case, similar deficits would be observed in both body-related and non-body-related stimuli. Indeed, in the control, non-body stimuli condition, 41.9% of children with CP showed difficulties in visuospatial tasks and 48.5% struggled with mental rotation [158]. Mental rotation, representing mental imagery, is a spatial skill that requires the mental transformation of a stimulus (e.g., object) to accurately predict the stimulus' appearance from a different angle or to judge whether two stimuli viewed from different perspectives are the same [291,292]. Research in typically developing children showed that active object exploration and self-locomotor experience (e.g., crawling) advance mental rotation skills [293–295], suggesting that visuomanual coordination, multimodal exploration (e.g., visual, auditory, oral, or tactile), and proprioceptive experiences during object exploration might inform children's high-level cognitive abilities [296]. Furthermore, mental rotation abilities are positively related to reading English, which requires discrimination between mirror-image letters such as “b” and “d”, or “p” and “q” [297,298]. Mental rotation was also positively related to children's performance in math [299–303] and geometry [304].

Mental rotation is a very useful skill that we use in everyday life to *navigate* our environment: we might make left–right–left turns on our way to a grocery store, but then we have to make right–left–right turns to come back home; we also need mental rotation skills to read maps and decide which way to turn according to the map. Not surprisingly, CP individuals with periventricular leukomalacia, as well as those with hippocampal volume reduction, often exhibit difficulties navigating their environment and finding their way [305–309]. Visual navigation has been associated with the right prefrontal lobe and hippocampus [310–312]. Note that the volumetric extent of the right frontal lesions in individuals with periventricular leukomalacia was negatively related to visual navigation ability, as tested by the paper-and-pencil labyrinth test of the Wechsler Intelligence Scale for Children III [313]. It has been proposed that periventricular lesions, especially those to more anterior areas, may disrupt connectivity between the hippocampus and frontal cortices, thus negatively affecting visual navigation [216]. Importantly, pictures, schemes, and maps depicting a scaled version of our environment are symbols representing that environment; thus, an ability to interpret a map represents a child's symbolic development [227–229], a sophisticated cognitive skill later used for language development in that words are symbolic representations of objects and ideas [230,232,234–237].

Furthermore, body awareness (i.e., perception of own body) and motor imagery performance are fundamental for *anticipatory motor planning* [159,314] and motor control [239], which, in turn, affect the execution of daily-life activities (e.g., personal hygiene, dressing, eating, using tools, and ambulating) and one's overall quality of life [118,122]. Motor planning is typically tested using end-state comfort tasks in which a subject is required to sacrifice the postural comfort of the initial grasp in order to place an object (e.g., a cup) into a particular orientation with the comfortable final-state grasp [315,316]. In this case, the end-state comfort is more important than the initial-grasp comfort, because the latter would result in the participant's inability to complete the task due to biomechanically

impossible end-postures [159]. Individuals with hemiplegic CP, especially those with congenital damage to the left hemisphere, showed inadequate anticipatory planning in end-state comfort tasks [159,246,314,317–321].

These findings are in line with the previously reported involvement of the left hemisphere in action planning [322,323]. The reduced capacity for motor imagery may prevent individuals with CP from performing the required mental simulation of the perceptual–motor consequences of the initial grasp in order to achieve a biomechanically comfortable end-posture [159,324–326]. Motor planning also is critically important in sequential tasks that involve role-differentiated bimanual manipulation (e.g., acquiring an object with the non-preferred hand to actively manipulate movable parts of the object with the preferred hand [179]) or means-end problem solving and tool-use, both requiring one to act on the “means” object to affect the “end” object [327–333]. In summary, motor imagery is embodied in motor control and the execution of actions: the performance of movements results in motor and sensorimotor afferents that stimulate the development of neural motor programs, which consist of body representations to guide new movements [259,334–336].

6. Cognitive Outcomes in Children with CP

The heterogeneous nature of CP makes any generalizations in the realm of cognitive function difficult. On the other hand, matching abnormal structures and neuronal activation in specific brain areas to cognitive outcomes provides important insights into brain substrates of cognitive functioning. Importantly, clinical data on children with CP provides non-refutable evidence that cognitive development is embodied in early motor and sensorimotor experiences (discussed in more detail in Section 7 below).

6.1. Linguistic Skills

In children with CP, the results of dichotic listening tests suggested that language lateralization transferred to the right hemisphere after left hemisphere damage [21,337]. Importantly, damage to either hemisphere reportedly alters the typical lateralization of language [21,337]. Additionally, **irrespective of the lesion side**, the size, location, and timing of the lesion would determine, to a large extent, the pattern of brain reorganization [21,337]. For example, cortical–subcortical lesions were associated with the interhemispheric reorganization of language, whereas lesions to periventricular white matter resulted in intrahemispheric reorganization [337]; lesions at term age were more likely to result in interhemispheric reorganization than those occurring preterm [337]; and the size of the lesion was also directly related to the extent of atypical language lateralization [21]. Importantly, atypical language lateralization after left-hemisphere lesions was associated with deficits in expressive vocabulary and receptive–expressive grammar [338–341]; a short-term (15 months post-baseline) follow-up showed more deficits in expressive language skills in children with left-hemisphere damage compared to those with right-hemisphere damage [21]. Thus, early neural plasticity (the ability of spared cortical areas to assume functions typically assigned to the damaged areas [341]), reflected in the reorganization of the hemispheric lateralization of language after damage to the left hemisphere, may come at a cost of slow language acquisition [21,338,341].

Interestingly, previous research with typically developing adults showed significantly better verbal comprehension in cases when language and spatial processing were dissociated between the two hemispheres as compared to cases when the two types of information were processed in the same hemisphere [46]. This cognitive advantage of hemispheric specialization was explained with the “*hemispheric crowding*” hypothesis [105,106,342–345], which suggests that the overload of one hemisphere with processing of multiple types of information (e.g., linguistic and spatial) would result in cognitive deficits due to computational capacity limits of that hemisphere. In this case, individuals with early left-hemisphere damage and interhemispheric language reorganization, having both linguistic and spatial processing “crowded” in the right hemisphere, would be expected to show cognitive deficits.

Although atypical hemispheric lateralization seems to affect children's performance across multiple linguistic subdomains [346], some skills may be affected more than others. For example, 7-to-14-year-old children with left-hemisphere damage (right hemiplegia) have been shown to have more difficulties with syntactical awareness and sentence repetition than with receptive vocabulary [347]. To explain these findings, it was proposed that neural reorganization as a result of early brain lesions may produce competition of different functions for synaptic sites; as a result of such competition, early-developing functions (e.g., receptive vocabulary) might "crowd-out" later-developing, more sophisticated functions, such as syntactical awareness [342,347].

Furthermore, children with CP often exhibit slower reading despite adequate letter recognition [22,348–350]. Most reading difficulties in children with CP could be attributed to their deficits in phonological processing and/or visuospatial perception [22,351]. The latter deserves special attention in the context of the current paper. Note that fast reading is achieved through the holistic, global processing of meaningful high-frequency words, whereas analytic processing is typically used by beginners or individuals with reading deficits [352–355]. Whereas for typically developing individuals global processing seems to precede local processing [43], deficits in global processing in individuals with CP make them deviate from this typical pattern of information processing [19,356]. Thus, reading difficulties in children with CP may stem from the lack of global advantage, but future research should test this hypothesis.

6.2. Subitizing, Counting and Arithmetic Skills

The development of more sophisticated math skills, such as counting and arithmetic, may depend on earlier-developing subitizing skills [23,25,26,356]. Subitizing is an ability to rapidly and accurately estimate the number of presented items without counting them [357]. Subitizing involves the seemingly automatic recognition of visual patterns (e.g., a triangle made of three dots, a rectangle made of four dots) involving up to 4–6 elements [358–361]. Children with CP exhibited a much lower subitizing limit and a sharp decline in accuracy with an increase in the number of elements in presented patterns than typically developing controls [19]. In contrast to typically developing children, those with CP also showed equal difficulty with classic subitizing (providing a number estimation) and pattern recognition (naming the presented pattern), suggesting that their subitizing difficulties are not number dependent, but rather stem from impaired visuospatial short-term memory, a deficit in visuospatial pattern recognition, and/or an inability to perceive spatial patterns as a Gestalt [19]. A Gestalt represents a holistic form of pattern perception (similar to global processing, discussed above) that allows the integration of local elements into global entities [362,363], such as seeing a big letter H despite the fact that it is constructed from small letters S [43].

On a behavioral level, subitizing is remarkably similar to Gestalt perception in that they both require the processing of information in the top-down manner, quickly incorporating low-level elements into high-level configurations and attending to the latter first [364]. On a neural level, subitizing and global processing seem to share the same substrates: subitizing reportedly relies on posterior temporo- and occipito-parietal areas [356,365–368], whereas Gestalt perception involves posterior temporo-parietal brain regions [369–375].

Importantly, previous research suggested that children with CP are delayed not only in subitizing [19,356], but also counting [27,356] and arithmetic skills [24]. It is likely that subitizing is a prerequisite for later-developing, more sophisticated math skills. Although previous research showed a positive relation of subitizing to counting and arithmetic skills [23,25,26,356], it is hard to establish causality here, in that all of these skills may rely on the same set of sensorimotor and cognitive skills. Indeed, both subitizing and counting skills depend on adequate visuomanual coordination [356,376]. For example, finger agnosia (difficulties with finger recognition and discrimination) was found to be highly predictive of both subitizing limit [356] and numerical abilities (abilities to group, compare, and count small numbers of objects) in children with CP [377], whereas dyspraxia

(a neurological disorder that negatively affects motor coordination) in children with CP resulted in difficulties with coordination of pointing and counting, which impeded quantity evaluation [378].

Additionally, visuomanual coordination may assist young children in counting, because they typically use fingers for pointing at objects before they learn to rely on visual pointing; manual pointing allows one to keep track of already counted elements and likely facilitates the acquisition of mental number representations and counting principles [379–384]. Given that both goal-directed manual actions and number processing activate the same brain regions (e.g., intraparietal sulcus [385]), there may be a close relation between these domains [27,386]. Importantly, visuomanual coordination may enable the perception of global structures within local elements in spatial arrangements, which should further facilitate subitizing [356].

Finally, language plays an important role in solving arithmetic problems that have a verbal component [387]. Neuroimaging research showed that linguistic areas (e.g., left angular gyrus) are activated by math word problems [388]. Even after controlling for general intelligence and working memory, numerical abilities were associated with children's grammar skills, word decoding, and phonological awareness [27,389]. Thus, difficulties in language skills in children with CP may contribute to their suboptimal math performance.

In terms of hemispheric specialization, a strong association has been reported between subitizing and right hemisphere processing. For example, the use of a tachistoscopic technique in typically developing adults showed right-hemisphere (left visual field) advantage in subitizing [390–393]. Similarly, in children with CP, right-hemisphere lesions were related to difficulties with subitizing, especially on canonical (i.e., dice patterns) rather than random patterns [19,356]. Thus, previous research in both typically and atypically developing children and adults suggests that damage to the right hemisphere may negatively affect subitizing through disruptions in Gestalt processing. There is more ambiguity in the research on neural substrates of counting. Whereas research on typically developing adults suggested left-hemisphere (right visual field) advantage in counting tasks [392], in children with hemiplegic CP, poor arithmetic skills were associated with right-hemisphere lesions (left-hand impairment), suggesting the involvement of the right hemisphere in the processing of complex mental calculations [27,348,394–396]. It could be the case that lateralization for the complex skill of counting shifts with age, with early counting skills (dependent on visuomotor processing) residing in the right hemisphere, but with later-developing, more sophisticated counting skills (dependent on analytical processing) being processed in the left hemisphere. Alternative explanations are also possible: (1) children with hemiplegic CP might show atypical lateralization of this process; or (2) in children with CP, this skill may critically depend on bilateral recruitment.

6.3. Executive Function Skills

Executive functions are high-level neurocognitive skills that include goal-directed behavior: attention, impulse control, flexible thinking, problem-solving, and planning to achieve short- and long-term goals [20,397]. Information processing related to executive functions is predominantly coordinated by the prefrontal cortex [398–400], with deficits in executive functions (e.g., inhibition and shifting skills) being associated with atypical lateralization in the frontoparietal network [401,402]. Because executive functions depend on the integrity of white matter (especially in the periventricular and anterior areas) that permit extensive connectivity between different brain regions, brain lesions in children with CP place them at risk for impairments in executive functions [20,403]. Additionally, white matter disruptions may be associated with the reduced speed of information processing, which further negatively affects children's performance of executive functions [20,404,405]. Indeed, children with unilateral or bilateral CP were found to be significantly impaired in working memory, sustained and divided attention, response inhibition, and shifting skills [20,405–409].

Deficits in impulsive inhibition in children with CP [20,405,408] may signal a potential for behavioral problems and impairments in social skills in this population [410,411], whereas impaired working memory, attention, and shifting skills may result in learning difficulties and cognitive delays. For example, previous research showed that subitizing, counting, and arithmetic skills depend on executive function skills, such as focused attention, shifting, working memory, and updating (the latter facilitates the performance of mental operations through replacing no longer relevant facts in the working memory with incoming relevant information) [24,396,397,408,412–419]. Thus, executive function deficits in children with CP might negatively affect the development of their subitizing, counting, and numerical abilities, which, in turn, are precursors for later-developing math skills [420–423]. Additionally, deficits in sustained and divided attention in children with CP are potentially detrimental for academic success [20,405,409].

Deficits in attention skills in 9–13-year-old children with CP have been attributed to children's distractibility [20]. Interestingly, previous research found a positive relation between the number of extraneous movements and attention skills in typical development. For example, it has been demonstrated that 4.5-to-7.5-month-old infants who showed better visual attention during object manipulation exhibited fewer extraneous movements [113]. This finding can be compared to the report that more easily distracted school-aged children manifested more extraneous movements [424]. Perhaps, in typically developing children, these two behaviors may have inverse trajectories: whereas mirror movements decrease by the end of the first year of life [100,112,187,188], visual attention abilities gradually increase during the first year [425,426]. Thus, it is likely that persistent mirror/extraneous movements in children with CP disrupt the development of attention skills. In this case, interventions targeting early sensorimotor experiences and bimanual coordination may not only improve contralateral hemispheric connectivity and interhemispheric transfer of information but also facilitate attention skills through a reduction in mirror movements.

7. The Role of Experience in the Development of Hemispheric Asymmetry

There are two important conceptual frameworks that may explain developmental pathways during infancy and childhood: the embodied cognition and the dynamic systems theories. The *embodied (or grounded) cognition theory* proposes that the development of cognition stems from early motor and sensorimotor activities and experiences [13–15,18,427,428]. This connection between early sensorimotor experiences and later cognitive outcomes can be explained on both the neuronal and behavioral levels. On a neuronal level, spontaneous, self-generated movements provide children with multisensory feedback, thus establishing and gradually refining topological representations of surrounding objects, as well as the boundaries and abilities of their own body in their brains, further shaping afferent and efferent motor and sensory pathways and establishing the foundation for advances in perception, motor control, and visuomanual coordination [98,99].

As pointed out above, brain lesions in children with CP lead to abnormal brain structures and interhemispheric connectivity. These structural and functional changes result in the persistence of involuntary muscle synergies and mirror movements that disrupt movement coordination during voluntary, goal-directed activities and have an especially debilitating effect on bimanual coordination [2,139,152,195–197].

Furthermore, the abnormal prevalence of ipsilateral corticospinal connections over contralateral ones in children with CP not only produces less effective information processing but also further disrupts the development of hemispheric specialization [102]. Because hemispheric specialization is a foundation behind more effective information processing and optimal developmental outcomes [28–32], children with CP often exhibit delays and impairments in motor performance and cognition [2,5,19–27,149].

On a behavioral level, delays and impairments in spontaneous movements, postural control, locomotion, and hand control may diminish motor and sensorimotor feedback received by a child and decrease a child's opportunities to gather information and learn, thus leading to delayed or impaired cognitive functioning. Specifically, spontaneous

movements facilitate the development of motor control, postural control, and visuomanual coordination [164,166,169,429,430]. Adequate head and trunk control, in turn, promote independent sitting, thus freeing the child's hands for reaching and object exploration, which further improve motor control and visuomanual coordination [171,431–438].

Gradual de-coupling of the two hands enables the sophisticated, role-differentiated bimanual manipulation of objects, which allows a child to learn object properties and affordances, means-end relations between objects, and motor planning skills, later used for the execution of complex, finely timed action sequences in means-end problem solving, artifact construction, and tool-use [175,184,186,439–442]. Importantly, multimodal, goal-directed object exploration reportedly advances children's language and cognitive development [231,295,442–454]. Additionally, the development of independent sitting, crawling, and walking permits a different perspective on the surrounding environment: these developments enable more opportunities to approach objects and people, explore objects, communicate with others, and exercise very important skills of planning and decision making on seemingly trivial “when and where to move” choices; these postural and locomotor opportunities facilitate children's language, cognitive, and social outcomes [16,455–457].

In children with CP, early deficits in postural control impede the development of non-object-oriented exploration and reaching (non-object-oriented behaviors are exploratory behaviors of one's own body and surrounding objects in the absence of portable objects and people (e.g., head control against gravity, midline position of the head and hands, open hand posture, looking at hands, mouthing hands, touching own body or surfaces, etc. [166]), which, in turn, may result in limited opportunities to manipulate objects and explore the world [433,438,456], establish hand-eye coordination [433,458–460], and practice visuospatial skills [441]. In children with CP, delayed visuospatial abilities might concatenate into learning difficulties, impaired non-verbal and verbal intelligence, and difficulties in the acquisition of mathematical and executive function skills [19,22,27,347,377,394,406,461]. Thus, the embodied cognition theory reveals a critical role of experience in the development of children with CP.

The *dynamic systems theory* (DST [16,452,462–464]) also describes the ways in which disruptions of developmental pathways can lead to suboptimal outcomes in children with CP. DST suggests that a dynamic interplay among the child's biological constraints, experiences, environmental affordances, and developmental timelines controls the trajectory of development. There are two key principles of DST that are relevant for this paper: the continuity and dynamic nature of development. The *continuity principle* implies that early skills concatenate into more sophisticated, later-developing ones, and early experiences, to a large extent, determine a child's future abilities and outcomes [16,174,429,463,465]. For example, during the first two years of life, the sensorimotor behaviors infants use to explore their bodies and surrounding surfaces in the absence of toys (e.g., holding hands in midline, looking at hands, touching body with hands) are strongly associated with behaviors manifested by infants during object exploration tested in a separate procedure (e.g., the bimanual holding of objects, looking at an object in the hand, touching body with an object in the hand [429]).

It is also important to emphasize the relation of postural control and locomotor experiences to upper-extremity performance. The emergence of sitting, crawling, and walking imposes new constraints on a child's body control and requires significant reorganization in body schemas, which may affect a child's hand use and performance. For example, the onset of crawling, characterized by alternating hand movements, has been associated with the prevalence of unimanual reaches, whereas the onset of independent walking, typically stimulating a symmetrical, “high-guard” hands' position to keep balance, corresponded with the surge in bimanual reaching [466,467]. Importantly, as infants practice crawling, initiating the first movement with the preferred hand, their hand-use may become more lateralized; at the same time, it is also possible that the shift toward more lateralized reaching would facilitate the transition from rocking to crawling [468].

This bidirectional relation between different motor and sensorimotor skills highlights the *dynamic principle* of development. There are many examples of the dynamic nature of development. For instance, not only do reaching and object exploration facilitate cognitive development through information gathering, learning, and problem solving, but also the advanced cognition may, in turn, guide more sophisticated object exploration. First, infants only mouth every toy, extracting shape, texture, and other properties; later, they shake every toy, revealing audible, mass, and other properties; then, they start adjusting their actions to the properties of the toys—shaking toys that make noise, pushing the buttons, spinning the wheels, etc. Furthermore, according to the dynamic principle, biology may influence experience, but the latter, in turn, would influence the biological substrate. For example, as children with CP get more opportunities to use the affected hand in unimanual and bimanual tasks, the received sensorimotor feedback may further reorganize their brain structures and also enhance interhemispheric connectivity [469–471].

Thus, for both embodied cognition and dynamic systems theories, biological, psychological, and sociocultural contexts determine the motor and sensorimotor capacities of a child, which, in turn, allow or prohibit particular types of experiences that would shape specific cognitive outcomes [17]. Importantly, motor and sensorimotor experiences affect not only more sophisticated cognitive functions, but also the individual's biology (e.g., neuronal structures and connectivity). Although early brain insults tend to set an individual on a specific developmental trajectory, both embodied cognition and dynamic systems theories propose that it is possible to change this trajectory by changing the motor and sensorimotor experiences available to the individual.

8. Possible Interventions for Children with CP

Knowledge of the developmental trends and functional deficits in children with CP permits the design and implementation of effective, evidence-based interventions to improve children's development. As noted above, CP is considered a group of “non-progressive” disorders [11,12]; this means that the brain damage associated with CP is permanent and static [472]. However, that label should not prevent the investigation of potential developmental changes on neural, physiological, physical, or behavioral levels [473]. Modern accounts of brain plasticity allow for considerable progress in individuals' development even under conditions of brain damage [474–477].

However, there are a few complications in the rehabilitation of patients with CP. The first problem stems from the heterogeneous nature of CP: “one-size-fits-all” approaches are not effective due to significant differences in the timing of brain insult, location and extent of the damage, factors associated with the brain injury, as well as symptomatology and functionality in patients with CP [475,478–480]. Second, some interventions may have suboptimal effects in individuals with CP having comorbid disorders, such as deficits in sensation and perception, learning difficulties, cognitive impairments, communication disorders, behavioral issues, or epilepsy [481–483]. Third, in contrast to older patients with acquired brain lesions, children with CP born with brain lesions that negatively affect their motor and sensorimotor functions, do not have neural “memories” of typical movement or body control [194,473]. Thus, instead of focusing on the “recovery” of lost functions, intervention providers should create training paradigms that promote sensorimotor and motor development on the canvas of compromised brain structures and connectivity [472,484]. Due to existing brain lesions, it is often not feasible to re-establish the typical lateralization of functions in patients with CP. However, interventions may not only strengthen unilateral circuits residing in the atypical hemisphere, but also, and more importantly, facilitate the formation and activation of more efficient contralateral corticospinal connections [108,485,486].

Finally, given our current understanding of development [487], the timing of intervention also plays a critical role in its effectiveness, with early interventions (e.g., small steps, baby-bimanual, baby-constraint-induced movement therapy (baby CIMT), and the Goals, Activity and Motor Enrichment intervention (GAME) having better potential for improve-

ments in individuals with CP [488–494]. However, only about 60% of infants are typically referred for intervention before the age of 12 months [495,496] because the CP diagnosis, in most cases, gets confirmed only by the late age period of 13–19 months [497,498].

The results of published clinical trials suggest there are benefits to training-based interventions for individuals with CP. The following interventions have been shown to be effective: environmental enrichment, home programs, fitness training, constraint-induced movement therapy, bimanual intensive therapy, action observation training, goal-directed training, task-specific training, and mobility training using treadmills and partial body-weight support systems, among others [499–516]. Effective interventions focus on participants' motivation, attention, and sense of agency; the production of self-initiated movements; meaningful, context-focused, real-life activities; task-specific and goal-directed activities; and high intensity of training with incremental increases in task difficulty [477,493,517–519]. The largest benefits may come from early interventions that promote variability in children's postures and movement patterns and provide opportunities to self-generate movements, including erroneous movements, to allow learning from experience [98,517,520,521]. Additionally, if a training task seems interesting and meaningful to children, they are more likely to engage in it, see the results of their own actions, and enjoy the practice; such a positive attitude would likely stimulate spontaneous, self-initiated practice, thus improving retention, adherence to the training protocols, and stimulating further advancements in movement and function [477,518].

Active participation in activities instills a sense of agency in children with CP—being in control of their movements and being able to predict the sensory consequences of their own actions [522,523]. The latter ability develops as a result of the everyday motor and sensorimotor experiences of the child, and reduced interactions with the environment creates delays in the development of the predictive “forward” model in children with CP [192,193]. Importantly, the establishment of an adequate predictive “forward” model may be the mechanism behind improvements in motor performance as a result of active exploration of the environment in early interventions for children with CP [192–194,524,525]. Moreover, while active exploration advances predictive abilities, the latter, in turn, may further facilitate a child's motor and cognitive development [194]. By contrast, passive activities seem to be less effective, or completely ineffective, in children with CP: passive movements orchestrated by a physical therapist do not activate the child's motor circuits, do not engage the child in problem solving, and do not stimulate the development of the predictive “forward” model [493,518,526].

The most common form of CP is unilateral CP, which impairs one limb and negatively affects a child's ability to perform tasks requiring bimanual coordination [120]. Typical upper-extremity rehabilitation therapies for unilateral CP include: (1) forced-use therapy (FUT [527,528]), (2) CIMIT [118,529–533], and (3) bimanual intensive training (BIM) or hand–arm bimanual intensive therapy (HABIT [534–536]). FUT works through casting/splinting of the child's better functioning limb to encourage movement of the more affected limb; the unstructured physical training of the affected hand is supposed to take place as a natural consequence of restricting the other hand. However, unable to use the functional hand, the frustrated child, being in full control of the therapy, often chooses to neglect diligent practice, thus defeating the purpose of the therapy [118,527,528]. Obviously, FUT is not a therapy that fosters the child's positive attitude, engagement, and compliance. CIMIT is a more comprehensive form of restraint-based intervention, involving a constraint of the better functioning limb (similar to FUT) with an added structure provided by the supervising physical therapist, encouraging the use of the child's affected hand/arm [118]. Although logistically and financially taxing, CIMIT has been shown to be effective in advancing fine motor skills of the affected hand in children with hemiplegic CP [118,529,536,537]. However, both FUT and CIMIT, with their focus on unilateral behaviors, fail to train bimanual coordination [527,535]. By contrast, BIM, using the structural approach of CIMIT, but without any physical constraints, facilitates exercise regimens that emphasize bimanually coordinated activities, affords greater physical freedom to the patient, and typically results

in higher levels of the patient's enthusiasm [535]. However, BIM falls short of CIMT in the improvement of fine manual movement and the simultaneous, dissociated activity of both limbs [538]; it also shares CIMT's practical and financial limitations.

Another feasible therapy option would be a garment such as the PlaySkin Duo™ designed at the University of Delaware (Dr. Michele Lobo, Move to Learn Innovation Lab, Department of Physical Therapy; <https://emmazuckerman.wixsite.com/design/playskin-duo>; accessed on 15 January 2022). The PlaySkin Duo™ is a soft garment that slightly constrains the use of the healthy, or better functioning, hand/arm by connecting it to the torso of the garment using an elastic band, which increases the difficulty of moving this arm, while still allowing the child to use it. Every time the child reaches for a toy with the better functioning hand, the slight tug on the arm softly constrains the movement, encouraging the child to use the affected hand. In a sense, the PlaySkin Duo™ works like BIM, but without a physical therapist sitting with the child and constantly reminding the child to use the affected hand. Importantly, the PlaySkin Duo™ keeps the hands of the child unobstructed, thus allowing not only bimanual coordination, but also fine motor practice with both hands. Further research is needed to evaluate the effectiveness of the PlaySkin Duo™ garment on motor function in children with CP.

Early interventions are more effective than those implemented later in a child's life [488–490]. Despite the fact that CP is typically only diagnosed during the second year of a child's life [497,498], it is still possible to advance the sensorimotor and motor development of infants at risk for CP (e.g., those born preterm and/or with a brain injury) by embedding them into an enriched environment. Enriched environments stimulate the nervous system by providing children with more opportunities for exploration, object manipulation, and learning [194]. Enriched environment interventions can be implemented even before a child's motor and sensorimotor deficits become apparent. Early interventions implementing positioning a child in different postures (e.g., supine, prone, side-lying, supported sitting and standing, with frequent transitions among postures) to allow exploration of body affordances and body–environment interactions, as well as toy-oriented activities to promote reaching, visuomotor coordination, and object exploration, have been shown to be effective in facilitating children's motivation to play, self-generated movements, postural control, reaching, bimanual object exploration, crawling, walking, and problem-solving skills [435,448,539–549]. Similarly, early interventions such as the GAME intervention [492,494], the Supporting Play Exploration and Early Development Intervention (SPEEDI [550]), and the Sitting Together and Reaching to Play intervention (START-Play [551,552]) have been shown to improve children's sensorimotor and motor skills.

Furthermore, early interventions involving wearable technologies, such as “sticky mittens” [442,553] or exoskeletons [327,531,554–556] might help children with CP who struggle with low muscle tone. The “sticky mittens” may allow a higher level of object engagement and more sophisticated object exploration in the absence of fine-motor movements in the affected hand; the experience of “grasping” a toy with the assistance of Velcro may reinforce the action and allow children to observe the consequences of their own actions [442]. In typically developing infants, brief “sticky mittens” training improved bimanual reaching, object exploration, visual attention, and spatial skills [442,557–560]. Note that instead of “sticky mittens” that cover the child's hand, physical therapists may use a Velcro band [448] that permits the fingers to engage with objects and create a more typical visual and haptic sensory feedback.

Furthermore, the Playskin Lift™ (Playskin; <https://sites.udel.edu/move2learn/how-today/>; accessed on 15 January 2022) exoskeletal garment might offer the anti-gravity support, extend the child's reaching space, facilitate visuomanual coupling and bimanual reaching, as well as improve the multimodality, variability, and intensity of exploratory play behaviors [327,556]. Whereas “sticky mittens” deliver a more distal support at the hand, the Playskin provides a more proximal assistance at the shoulder. However, both “sticky mittens” and Playskin devices might not facilitate independent, unassisted object

play in children with hemiplegia; without explicit, external encouragement, children with hemiplegia might continue to disregard the affected limb.

Considerable disruptions of sensorimotor pathways in individuals with CP justify training methods that involve the use of sensory information in the motor task context. Thus, musical instrument practice may be a good rehabilitation method to stimulate multi-modal audio-visuomotor coordination, bimanual coordination, and the implementation of timely action sequences [473,561]. Indeed, both short- and long-term musical training reportedly corresponded with significant structural changes in the brain, resulting in a larger volume and thickness of motor and auditory cortices, a larger corpus callosum and cerebellum, increased white matter integration in pyramidal tracts, and larger gray matter density in precentral gyrus, involved in functional hand and finger movements [562–569]. Despite the obvious benefits of music training, this rehabilitation method has rarely been used in patients with CP, although the few studies on the effects of piano training in individuals with CP reported positive neural outcomes (better connectivity between primary motor cortex and the cerebellum [570]) and behavioral outcomes (keystroke timing variability and playing speed [570,571]). Although it was concluded that musical instrument training may improve not only motor coordination, but also sensorimotor interactions [473,561,572], more research is needed in this area.

Although current rehabilitation methods in individuals with CP are typically focused on motor execution, it is possible to facilitate motor performance through advances in motor planning by targeting children's motor imagery skills [573–576]. As noted above, motor imagery skills are involved in anticipatory motor planning and motor control [159,239,314]. A lack of motor experience in children with CP negatively affects their motor imagery [159,246,259,577]. Because both motor performance and motor imagery seem to share the same neural substrates (e.g., supplementary motor areas, premotor cortex, primary motor cortex (M1), and parietal lobe [578]), it may be possible to increase activation and connectivity in those areas by targeting both skills in parallel [576,577,579,580]. Previous research showed improvements in motor performance of the affected upper limb after motor imagery training in stroke patients [581,582] and those with CP [583]; however, more research is needed to provide evidence for the use of motor imagery in individuals with CP [576].

There is a lack of randomized clinical trials that show the efficacy of parental interventions to advance early motor and sensorimotor skills in children with CP [584]. More often, parental education is offered in conjunction with an ongoing physical therapy [492,585–587]. Importantly, in research with typically developing infants and those born preterm, parent-provided interventions encouraging infants' independent head control, frequent transitions among different postures, general arm movements, reaching to midline, and reaching with both hands led to significant improvements in children's postural control, reaching, and object exploration [435,442,448,542–546,588]. Future research should further investigate the utility of parent education in the rehabilitation of motor and sensorimotor skills in children with CP.

9. Conclusions

Modern neurodevelopmental research demonstrates that brain restructuring, as a result of brain damage, leads to atypical hemispheric specialization, as manifested in the predominance of ipsilateral corticospinal connections, reduced transcallosal transfer of information, diminished hemispheric specialization, and the allocation of multiple functions to the same hemisphere (e.g., language lateralized to the right hemisphere, along with visuospatial skills). These patterns of atypical hemispheric lateralization reduce the effectiveness of information processing and produce suboptimal cognitive outcomes in children with CP. These findings emphasize the need for early interventions that promote callosal functioning to establish optimal hemispheric asymmetry.

These intervention programs should be based on evidence-based research emphasizing the role of self-generated experiences in early development, as proposed by the

embodied cognition theory. Moreover, according to the dynamic systems theory, all the functions of a child are bidirectionally interrelated and codeveloping. For example, brain lesions may limit motor and sensorimotor exploration, but enhanced early motor and sensorimotor experiences, in turn, are capable of restructuring the brain and improving hemispheric connectivity. Additionally, early sensorimotor experiences promote motor control and coordination, thus permitting complex object manipulation, which provides unique learning opportunities and advances a child's cognitive development. Importantly, the resulting cognitive advances inform a child's object exploration, thus permitting more sophisticated object manipulations and stimulating learning in a circular feedback manner.

Basic research examining the system of core deficits associated with CP, along with understanding the developmental pathways from early motor and sensorimotor skills to cognitive outcomes, must influence the design and implementation of interventions, shifting their focus toward targeting early sensorimotor skills. Because early, self-generated, spontaneous movements establish the foundation for motor and postural control, locomotion, reaching, and object exploration (which collectively facilitate cognitive development), early interventions should focus on promoting and facilitating abundant and variable spontaneous movements in children with CP. Because the typical timeline of CP diagnosis (by the age of 13–19 months) may prevent early intervention, there also should be a focus on early diagnosis to ensure earlier interventions capable of promoting optimal development. Importantly, the analysis of early spontaneous movements can open a door to early diagnosis in children with CP [160,162,164,166].

Finally, despite the heterogeneous nature of CP, it is still possible to link specific brain lesions and structural abnormalities to corresponding cognitive outcomes with the implementation of multisite studies testing large numbers of subjects (e.g., thousands) with standardized assessment methods. In the same way, despite significant differences in the location, extent, and timing of brain damage in children with CP, it is still possible to determine factors capable of advancing their development through testing the effectiveness of different interventions using large, multisite studies. In this case, individual differences in responsiveness to intervention could be identified and appropriate adjustments could be made. Thus, the future of intervention research for CP seems to involve more multisite, large-scale studies.

Funding: There was no external funding for this review.

Institutional Review Board Statement: The current review covered studies that had IRB approval.

Informed Consent Statement: The current review covered studies that followed IRB guidelines while acquiring informed consent from the participants.

Data Availability Statement: The current review only addressed published data.

Acknowledgments: The author would like to thank her lifelong mentor, George F. Michel, for his continuous support and guidance.

Conflicts of Interest: The author has no conflict of interest to report.

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