UNIVERSITAT DE BARCELONA

Towards the Optimisation of Interventions to Enhance Cognitive Functions and Quality of Life in Children with Cerebral Palsy

Montse Blasco Sierra

Towards the Optimisation of Interventions to Enhance Cognitive Functions and Quality of Life in Children with Cerebral Palsy

Exploring Potential Far Transfer Effects

Thesis presented by

Montse Blasco Sierra

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Supervised by

Dr. Roser Pueyo Benito

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Dr. Roser Pueyo, professor at the University of Barcelona,

CERTIFIES that I have guided and supervised the PhD thesis entitled *Towards the Optimisation of Interventions to Enhance Cognitive Functions and Quality of Life in Children with Cerebral Palsy. Exploring Potential Far Transfer Effects*, presented by Montse Blasco Sierra. I hereby assert that this thesis fulfils the requirements to present her defense to be awarded the title of doctor.

Signature,

Dr. Roser Pueyo Benito
University of Barcelona

Barcelona, 26 July 2023

Als meus pares i al meu germà,
per l’amor i la tendresa infinita.

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FOREWORD

This thesis is presented for the Degree of Doctor of the University of Barcelona (international doctor mention) and is the result of the work carried out at the Department of Clinical Psychology and Psychobiology of the University of Barcelona (Barcelona, Spain) and the work performed in a 3-month research visit at the Department of Development and Regeneration of the KU Leuven (Leuven, Belgium). This thesis follows the published papers format and includes three studies. Two of these studies have been published, and the third is currently under review by international scientific journals.

- **Study 1:**

Blasco, M., García-Galant, M., Berenguer-González, A., Caldú, X., Arqué, M., Laporta-Hoyos, O., Ballester-Plané, J., Miralbell, J., Jurado, M.A. & Pueyo, R. (2023). **Interventions with an Impact on Cognitive Functions in Cerebral Palsy: A Systematic Review.** *Neuropsychology Review, 33*(2), 551-577. IF (2022): 5.8, Q1 (Clinical Psychology/Neurosciences).

- **Study 2:**

Blasco, M., García-Galant, M., Laporta-Hoyos, O., Ballester-Plané, J., Jorba-Bertran, A., Caldú, X., Miralbell, J., Alonso, X., Meléndez-Plumed, M., Toro-Tamargo, E., Gimeno, F. & Pueyo, R. (2023). **Factors Related to Quality of Life in Children with Cerebral Palsy.** *Pediatric Neurology*, 141, 101-108. IF (2022): 3.8, Q1 (Paediatrics), Q2 (Clinical Neurology).

- **Study 3:**

Blasco, M., García-Galant, M., Ballester-Plané, J., Laporta-Hoyos, O., Caldú, X., Leiva, D., Boyd, R., Ortibus, E., & Pueyo, R. **Far Transfer Effects of a Home-Based Computerized Executive Function Intervention in Children with Cerebral Palsy: a Randomized Controlled Trial.** Working paper under review in *Developmental Medicine & Child Neurology*, IF (2022): 3.8, Q1 (Paediatrics), Q2 (Clinical Neurology).

ABBREVIATIONS

ADHD	Attention Deficit Hyperactivity Disorder
ANCOVA	Analyses of Covariance
ASD	Autism Spectrum Disorder
BFMF	Bimanual Fine Motor Function
BRIEF	Behavior Rating Inventory of Executive Function
CEBM	Centre for Evidence Based Medicine
CENTRAL	Central Register of Controlled Trials
CINAHL	Cumulative Index to Nursing and Allied Health Literature
CP	Cerebral palsy
CP QoL	Cerebral Palsy Quality of Life
CVI	Cerebral Visual Impairment
dMRI	Diffusion Magnetic Resonance Imaging
fMRI	Functional Magnetic Resonance Imaging
GMFCS	Gross Motor Function Classification System
ICF	International Classification of Functioning, Disability, and Health
ID	Intellectual Disability
IQ	Intelligence Quotient
LOE	Levels of Evidence
MACS	Manual Ability Classification System
MeSH	Medical Subject Heading
MRI	Magnetic Resonance Imaging
MRICS	Magnetic Resonance Imaging Classification System
PEM-CY	Participation and Environment Measure for Children and Youth
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
QoL	Quality of Life
RCT	Randomized Controlled Trial
SCPE	Surveillance of Cerebral Palsy in Europe
sMRI	Structural Magnetic Resonance Imaging
VPI	Visual Perceptual Impairment
WHO	World Health Organization

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RESUM

La paràlisi cerebral és un trastorn que afecta el moviment i la postura, i és la principal causa de discapacitat física en infants, amb una prevalença global d'1,6 per cada 1000 nascuts vius. A banda dels problemes motors, les persones amb paràlisi cerebral poden presentar dèficits cognitius que afecten diverses àrees de la vida diària, com és la qualitat de vida. En conseqüència, la comunitat científica té l'objectiu d'explorar com millorar les funcions cognitives en persones amb paràlisi cerebral i mantenir els efectes de la intervenció a llarg termini. A més a més per obtenir majors beneficies en les funcions cognitives, és important avaluar tant els efectes sobre les funcions abordades per la intervenció (coneguts com a near transfer) com en les funcions no tractades directament (far transfer).

Per tant, l'objectiu principal d'aquesta tesi va ser optimitzar els efectes de les intervencions cognitives en infants amb paràlisi cerebral. En tres estudis originals, amb tres dissenys diferents cadascun, vam abordar aquest objectiu: una revisió sistemàtica (Estudi 1), un estudi transversal (Estudi 2) i un assaig clínic aleatoritzat (Estudi 3). En l'Estudi 1 es van revisar els estudis publicats fins al moment centrats en estudiar l'impacte de les intervencions en les funcions cognitives de les persones amb paràlisi cerebral, per tal d'identificar les intervencions més efectives i qualsevol possible mancança actualment en aquest sentit. En l'Estudi 2 es va investigar la relació entre les funcions cognitives i la qualitat de vida en infants amb paràlisi cerebral mitjançant un enfocament biopsicosocial. L'objectiu de l'estudi va ser identificar quina intervenció cognitiva específicament tenia un major impacte en la qualitat de vida. Finalment, en l'Estudi 3 es va provar l'eficàcia d'una intervenció optimitzada de les funcions executives a domicili examinant els far effects en altres funcions cognitives (habilitats visuoperceptives i memòria) i la vida diària (qualitat de vida i participació).

Els principals resultats dels tres estudis van ser els següents: (1) La millor evidència científica disponible va mostrar que les intervencions físiques són el principal tipus d'intervenció centrada en investigar millores en les funcions cognitives en la població amb paràlisi cerebral, amb millores en el funcionament cognitiu general i en el

control inhibitori de les funcions executives. Les intervencions multimodals també millores altres funcions cognitives com les habilitats visoperceptives; (2) En l'actualitat hi ha pocs estudis que investiguin l'impacte de les intervencions en les funcions cognitives, especialment en el camp de les intervencions cognitives. No obstant això, les intervencions centrades en les funcions executives obtenen near effect en les pròpies funcions executives; (3) Una intervenció a domicili de les funcions executives d'una durada de tres mesos, amb una dosi total de 30 hores, és eficaç per obtenir far effects no només en les habilitats visoperceptives, sinó també en la memoria; (4) Les funcions executives juguen un paper important en la qualitat de vida dels infants amb paràlisi cerebral, juntament amb la funció motriu gruixuda, les habilitats visuoperceptives, els trets del trastorn de l'espectre autista i l'estrès parental; (5) Les intervencions centrades en les funcions executives no han aconseguit far transfer effects en la qualitat de vida i la participació dels nens amb paràlisi cerebral; (6) Mitjançant una intervenció en funcions executives tampoc s'obtenen far transfer effects a llarg termini en les funcions cognitives, així com en la qualitat de vida i participació.

ABSTRACT

Cerebral palsy is a chronic condition that affects movement and posture and is the leading cause of physical disability in children, with an overall prevalence of 1.6 per 1000 live births. In addition to motor impairments, people with cerebral palsy may also experience cognitive difficulties which impact on several areas of daily life, such as the quality of life. Consequently, researchers investigate ways to improve cognitive functions in individuals with cerebral palsy and its maintenance over time. Moreover, to obtain benefits in multiple cognitive functions, studies have focused on evaluating the effects on abilities addressed by the intervention (near transfer effects) and changes in non-target functions (far transfer effects).

The overall aim of this thesis was to optimise the effects of cognitive interventions in children with cerebral palsy. In three original studies, we focused on addressing this general objective by employing three approaches: a systematic review (Study 1), a cross-sectional study (Study 2), and a randomized controlled trial (Study 3). Study 1 reviewed the impact of interventions on cognitive functions in individuals with CP, with the objective of identifying the most effective interventions and gaps in the current interventions. Study 2 investigated the relationship between cognitive functions and quality of life in children with cerebral palsy using a biopsychosocial approach. This study aimed to identify the specific cognitive intervention that could have the most significant impact on enhancing their quality of life. Finally, Study 3 tested the efficacy of an optimised home-based executive function intervention by examining its potential for far transfer effects on other cognitive functions (visual perception and memory) and daily life (quality of life and participation).

The main findings of the three studies were as follows: (1) The best evidence available showed that physical intervention is the main type of intervention focused on investigating cognitive function improvements in the cerebral palsy population, with improvements in general intellectual functioning and inhibitory control domain of executive functions. Multi-modal interventions also improve other cognitive functions such as visual perception; (2) Few studies have investigated the impact of interventions on cognition in cerebral palsy, and this scarcity is even more evident in the field of cognitive interventions; however, interventions targeting executive

functions obtain near transfer effects on a major number of core executive functions; (3) Home-based computerized executive function intervention for three months and a total dose of 30 hours is effective in obtaining far transfer effects not only in visual perception but also in memory in children with CP; (4) Executive functions play an important role in the quality of life of children with cerebral palsy, along with gross motor functioning, visual perception, autism spectrum disorder traits, and parental stress; (5) Interventions targeting executive functions have failed to improve the quality of life and participation in children with CP; (6) Long-term far transfer effects on cognitive functions as well as quality of life and participation were not obtained by a home-based computerized executive function intervention.

INTRODUCTION

GENERAL ASPECTS OF CEREBRAL PALSY

1. Definition of cerebral palsy

An overview of the historical evolution of the definition of **cerebral palsy** (CP) provides compelling evidence for the intricate and multifaceted nature of this neurological disorder, which has been present throughout human history. The first recorded cases of CP date back to ancient times. In fact, the Greek physician Hippocrates (460 – 370 BC), considered the father of medicine, was the first known to discuss the association between prematurity, congenital infection, and prenatal stress in relation to brain damage, referring to what would be known in relation to CP centuries later. Despite this early interest, the scientific understanding of CP has remained limited for many centuries (Panteliadis et al., 2013).

The first formal description of CP as a disease occurred several centuries later and was attributed to the orthopaedic surgeon William John Little (1810 – 1894). Little published *Deformities of the Human Frame* in the Lancet between 1843 and 1844, describing the presence of motor symptomatology in children. Later, Little published the monograph *On the Nature and Treatment of the Deformities of the Human Frame*. This publication was the first book dedicated entirely to children's deformities (Little, 1843). In this monograph, a description of 24 patients with generalised spasticity was presented, and these cases were related to difficulties in delivery, several neonatal asphyxia with convulsions, and prematurity. Given the importance of the description and examples provided by William John Little, CP was known as "*Little's disease*" (Panteliadis et al., 2013; Raju, 2006).

Over the course of the following decades, multiple professionals documented instances of CP in children (Schifrin & Longo, 2000), but it was not until the end of the nineteenth century that William Osler introduced the term "*Cerebral Palsy*". William Osler (1849 – 1929) used this term in his work *The Cerebral Palsies of Children*. In these lectures, Osler also included 151 cases, classifying them by the distribution and location of motor disturbances and attempted to correlate them with neuropathological findings (Osler, 1889b, 1889a; Shevell, 2019).

A third personality that contributed significantly to the field of CP in the nineteenth century was the neurologist Sigmund Freud (1856 – 1939). Between 1891 and 1897, Freud published several volumes entitled *Cerebral Palsy* Freud described the relationship between the location of cerebral injury and the degree of contracture (Freud, 1968). He also classified CP based on the following causal factors: (1) congenital (antepartum); (2) acquired during birth (intrapartum); and (3) acquired postnatally (postpartum). The classification system proposed by Freud continues to be used today (Panteliadis et al., 2013; Raju, 2006).

The most notable contributions of personalities such as Little, Osler, and Freud exemplify the scientific community's considerable interest in studying CP during the nineteenth century. However, the lack of consensus in the description has resulted in a decrease in the study of this disease during the first middle of the twentieth century (Shevell, 2019). In the second half of the twentieth century, this interest recovered owing to the adoption of different techniques and methods to treat CP. The orthopaedic surgeon Winthrop Phelps (1894 – 1971) published *The Management of Cerebral Palsy*, which describes and divides CP into five major categories: spasticity, athetosis, rigidity, tremor, and incoordination (or ataxia). Winthrop Phelps, the founder and first president of the American Academy for Cerebral Palsy, was one of the first celebrities to be interested in the **rehabilitation** and **treatment** of CP (Panteliadis et al., 2013; Phelps, 1941).

New definitions of CP were developed to clarify its characteristics. One of the most notable definitions was proposed by paediatrician Martin Bax in 1964, after an international working group. Bax defined CP as "*a disorder of movement and posture due to a defect or lesion of the immature brain*" (Bax, 1964). Later, Mutch et al. (1992) suggested that CP is "*an umbrella term that covers a group of non-progressive but often changing motor impairment syndromes secondary to brain lesions or anomalies arising in the early stages of development*". This definition highlights the heterogeneity of CP, which can vary depending on the location and severity of the brain lesions.

In 2004, an International Workshop on Definition and Classification of Cerebral Palsy, led by Peter Rosenbaum, was held in the USA. Experts who attended this workshop agreed that people with CP, in addition to motor impairments, might experience other symptoms associated with performance and behaviour (Rosenbaum et al., 2007). From this international workshop, the Definition and Classification of CP document was published with a description of CP that included an explanation of each term used. The current definition of CP is as follows (Rosenbaum et al., 2007):

> *"Cerebral palsy is 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 foetal or infant brain. Motor disorders of cerebral palsy are often accompanied by disturbances of sensation, perception, cognition, communication, and behaviour, by epilepsy, and by secondary musculoskeletal problems."*

The current definition of CP, which is widely accepted by health experts worldwide (Bialik & Givon, 2009), reflects the complexity of this disorder and its associated symptoms. Reaching an agreement on this definition has markedly increased the interest in CP within the scientific community. According to Klawonn et al. (2020), the number of publications related to CP raised from approximately 2000, between 1990 and 1995, to over 7000 between 2015 and 2020. Specifically, the number of publications focusing on rehabilitation increased from 377 to 2740. In addition, Klawonn et al. (2020) highlighted the growing interest in Quality of Life (QoL) in patients with CP. Based on a neuropsychological approach, this thesis explores the rehabilitation of individuals with CP, focusing on their quality of life, which is of growing interest in the field of CP research.

2. Classification

The classification of CP is complex because of the heterogeneous nature of the disorder, which can present with varying clinical forms and severity (Sadowska et al., 2020). Although numerous classification proposals have been suggested (Balf & Ingram, 1955; Rosenbaum et al., 2007), the most widely used classification system for CP is that adopted by the Surveillance of Cerebral Palsy in Europe (SCPE). This classification system is primarily based on clinical findings and depends on the predominant type of tone or movement abnormalities. The three main types of CP are spastic, dyskinetic, and ataxic (Cans, 2000; Cans et al., 2007).

Spastic CP is defined by increased muscle tone and pathological reflexes such as increased reflexes (e.g., hyper-reflexia) or pyramidal signs (e.g., Bakinski response).

This type of CP can be classified as unilateral (hemiplegia) or bilateral (diplegia or tetraplegia). In hemiplegia spastic CP, the limbs on one side of the body are involved, whereas spastic diplegia or tetraplegia CP is diagnosed when both sides are involved.

Dyskinetic CP presents with abnormal patterns of posture and/or movement, characterized by involuntary, uncontrolled, repetitive, and sometimes stereotypical movements, along with fluctuating muscle tone. Depending on the type of movement, dyskinetic CP can be dystonic or chore-athetotic. Dystonic CP is marked by hypokinesia (reduced activity) and hypertonia, which causes involuntary movements, distorted voluntary movements, and abnormal postures due to sustained muscle contractions. Choreo-athetotic CP is characterized by hyperkinesia (increased activity) and hypotonia.

Ataxic CP is defined as the loss of orderly muscular coordination, and movements are performed with an abnormal force, rhythm, and accuracy. In cases where there is a mixed form of CP with a clinical combination of motor/movement abnormalities, the SCPE considers that it should be classified according to the predominant movement disorder. Non-classified CP should be exclusively reserved for cases in which it is not possible to diagnose any other type of CP.

The SCPE considers a group of key elements to determine the functioning of individuals with CP (Cans et al., 2007). Among these, the SCPE recommends the use of scales to determine the level of motor functioning. To assess functioning, the Gross Motor Function Classification System (GMFCS) (Palisano et al., 2008) is used to determine functional mobility or activity limitation. On the other hand, the Manual Ability Classification System (MACS) (Eliasson et al., 2006) and/or Bimanual Fine Motor Function (BFMF) (Elvrum et al., 2016) are used to assess the functional grading of the upper limbs.

3. Epidemiology

Cerebral palsy is considered the leading cause of childhood physical disability, with a worldwide prevalence of 2.11 per 1000 live births (Oskoui et al., 2013). However, the global prevalence is difficult to determine because of several factors, such as differences in resources between regions and the lack of registers in many countries, particularly those with low- and middle-income levels. Consequently, global estimates of CP prevalence mainly reflect data collected from high-income countries (Jahan et al., 2021).

Specifically, within these high-income countries, the prevalence of CP is 1.6 per 1000 live births (McIntyre et al., 2022). Collaboration between the SCPE and Australian Cerebral Palsy Register networks has facilitated comparative studies in high-income countries (Sellier et al., 2020). Several works have exclusively focused on the prevalence of CP in these regions (Sellier et al., 2016; Smithers-Sheedy et al., 2016), with a significant decrease of approximately 25% over the last decade (Paneth & Yeargin-Allsopp, 2022). This decline in CP cases could be attributed to advancements in peri and neonatal care, improvements in diagnostic tests to detect motor abnormalities in children, and a clearer identification of specific genetic or metabolic conditions that can be treated (Larsen et al., 2022; Paneth & Yeargin-Allsopp, 2022).

Unfortunately, this decrease has not been observed in low- and middle-income countries. Some studies have reported an increasing trend (Jahan et al., 2021). The overall estimated prevalence of CP in low- and middle-income countries is 3.1 per 1000 live births (McIntyre et al., 2022), which is almost double that in high-income countries. Studies in specific regions, such as Uganda and Bangladesh, have estimated a similar prevalence (Kakooza-Mwesige et al., 2017; Khandaker et al., 2019). The difficulties in collecting epidemiological data from these countries have led to the creation of the Global Low- and Middle-Income Country CP Register (GLM-CPR) to provide information on the prevalence in these countries and develop a common platform to monitor advances in the diagnosis and evaluation of CP (Jahan et al., 2021; McIntyre et al., 2022). The creation of new international registers and the unification of existing methods and resources will enable us to gain a more accurate understanding of disease prevalence worldwide and in specific areas in the coming years. This, in turn, will help to identify factors that can reduce the prevalence of CP and provide a better understanding of health politics and treatments for newborns.

If we focus on the different types of CP, spastic CP is considered the most predominant type, comprising more than 85% of the cases. Unilateral spasticity accounts for 40% of patients in the spastic group, whereas bilateral spasticity accounts for the remaining 60%. Dyskinetic CP is the second most common type, accounting for 6 to 13% of cases, and ataxic CP is the least common type, accounting for 3 and 5% of cases (Jonsson et al., 2019; Smithers-Sheedy et al., 2016).

4. Aetiology

The development of CP involves multiple factors, making its aetiology complex and heterogeneous (Himmelmann et al., 2011). The identification of specific risk factors and causal mechanisms in most cases remains elusive; however, many risk factors have been identified during the preconception, prenatal, perinatal, and postnatal periods (Korzeniewski et al., 2018). Understanding the complex aetiology of CP is crucial for the development of effective prevention and treatment strategies.

Preconception risk factors such as maternal age, maternal diagnoses (thyroid disease, seizures, Intellectual Disability (ID), substance abuse, or maternal undernutrition), low socioeconomic status, and the use of assisted reproductive technology have been identified as potential factors for CP (Goldsmith et al., 2023; McIntyre et al., 2013; Paul et al., 2022; Schneider et al., 2018). Additionally, various studies have shown that genes p, including family incidence and genetic mutation polymorphisms, play a role in CP (Fahey et al., 2017; Korzeniewski et al., 2018; MacLennan et al., 2015; Michael-Asalu et al., 2019). Sex differences in the presence of CP are also possible indicators of the role of genes. The incidence of CP in males is higher than in females at all levels of gross and manual ability, with an overall male/female ratio of 1.4:1 (Himmelmann & Uvebrant, 2014; Romeo et al., 2023).

Prenatal risk factors are estimated to be the main cause of CP development, with a prevalence of approximately 70 – 80% (Jacobsson & Hagberg, 2004; Sadowska et al., 2020). During the prenatal period, maternal infections, such as TORCH (toxoplasmosis, rubella, cytomegalovirus, and herpes simplex virus) and chorioamnionitis, have been implicated in the development of CP (Jacobsson & Hagberg, 2004; Paul et al., 2022). Cerebral malformations, such as microcephaly, have also been linked to CP (Garne et al., 2008; Goldsmith et al., 2019). Multiple births also increase the risk of CP, with a four-fold higher prevalence in twins than in singletons (Korzeniewski et al., 2018).

Perinatal risk factors account for approximately 20 – 30% of CP cases and include the type of delivery, preterm delivery, low birth weight, neonatal infections, kernicterus, and birth asphyxia (Goldsmith et al., 2023; Jacobsson & Hagberg, 2004; Paul et al., 2022). Among the perinatal factors mentioned above, it is necessary to make a special mention the role of asphyxia in the aetiology of CP. Research in this field is controversial, because some reports have shown that only a few cases of CP are associated with asphyxia, whereas others have suggested that almost half of these cases are caused by this risk factor (MacLennan et al., 2015; Odding et al., 2006). During the 1980s and the 1990s, birth asphyxia was considered the main cause of CP. However, nowadays, it has been suggested that birth asphyxia plays a relatively minor role, accounting for less than 10% of cases (Jacobsson & Hagberg, 2004; MacLennan et al., 2015). Certainly, the behaviour of new-borns is similar regardless of whether they experience asphyxia or other complications, such as infection, placental and umbilical vessel thrombosis. The differences between past and current findings could be due to advances in research to identify the specific aetiology for each case. (Ellenberg & Nelson, 2013; MacLennan et al., 2015).

Recent studies exclusively focusing on **postnatal** risk factors have revealed their reduced prevalence, with a prevalence of less than 10 – 18% (Abd Elmagid & Magdy, 2021; Paul et al., 2022). Postnatal factors that occur between 28 days and two years of age include viral and bacterial infections (e.g., meningitis and/or encephalitis), vascular episodes, traumatic brain injury, and seizures (Goldsmith et al., 2023).

5. Neuroimage findings

The diagnosis of CP requires a multidisciplinary approach, which includes clinical observations and neuroimaging techniques. The use of techniques such as magnetic resonance imaging (MRI) helps to reveal the underlying aetiology of CP and understand the relationship between brain injury and clinical manifestations (Jacobs et al., 2023). Among the available neuroimaging techniques, structural magnetic resonance imaging (sMRI) has primarily been used for clinical purposes. Indeed, the SCPE has developed an MRI Classification System (MRICS) to evaluate and harmonize neuroimaging findings in CP (Himmelmann et al., 2017).

MRICS comprises five categories of pathogenic patterns, as described in Table 1. Studies using MRICS have demonstrated that more than 80% of individuals with CP exhibit abnormal brain imaging (Himmelmann et al., 2021). A recent study (Horber et al., 2020) using a European CP database of 3818 individuals with CP showed that **white matter injury** was the most common finding (49%), followed by **grey matter injury** (21%) and **maldevelopments** (11%). The distribution of the MRI patterns differed depending on the type of CP, as shown in Figure 1. MRI patterns of children with spastic and dyskinetic CP are mainly lesional (white and grey matter injury), whereas ataxic CP is characterized by maldevelopments, miscellaneous, and normal findings. Specifically, white matter injury was most common in spastic CP, prevalent in 47% and 58% of unilateral and bilateral spastic CP cases, respectively. In contrast, grey matter injury was the most common cause of dyskinetic CP (38%). Finally, normal findings were the most frequent in ataxic CP (32.5%), followed by maldevelopments (25.3%).

Table 1. The MRI classification system, adapted from Himmelmann et al. (2017).

A. **Maldevelopments**
   A.1. Disorders of cortical formation (proliferation and/or migration and/or organization)
   A.2. Other maldevelopments
   (e.g., holoprosencephaly, Dandy-Walker malformation, corpus callosum agenesis, cerebellar hypoplasia)

B. **Predominant white matter injury**
   B.1. PVL (mild/severe)
   B.2. Sequelae of IVH or PVHI
   B.3. Combination of PVL and IVH sequelae

C. **Predominant grey matter injury**
   C.1. Basal ganglia/thalamus lesions (mild/moderate/severe)
   C.2. Cortico-subcortical lesions only (watershed lesions in parasagittal distribution/multicystic encephalomalacia) not covered under C3
   C.3. Arterial infarctions (middle cerebral artery/other)

D. **Miscellaneous** (e.g., middle cerebellar atrophy, cerebral atrophy, delayed myelination, ventriculomegaly not covered under B, haemorrhage not covered under B, brainstem lesions, calcifications)

E. **Normal**

Abbreviations. IVH, Intraventricular Hemorrhage; PVHI, Periventricular Hemorrhagic Infarction; PVL, Periventricular Leukomalacia.

Around 20% of neuroimaging cases are classified as having **normal** patterns (Himmelmann et al., 2021). Although MRICS studies have primarily focused on sMRI, this technique has limitations for detecting microstructural abnormalities. Consequently, the emergence of techniques such as diffusion MRI (dMRI) and functional MRI (fMRI) has facilitated the clinical study of such cases, while also advancing research on brain connectivity and network organization in CP (Jacobs et al., 2023; Scheck et al., 2012).

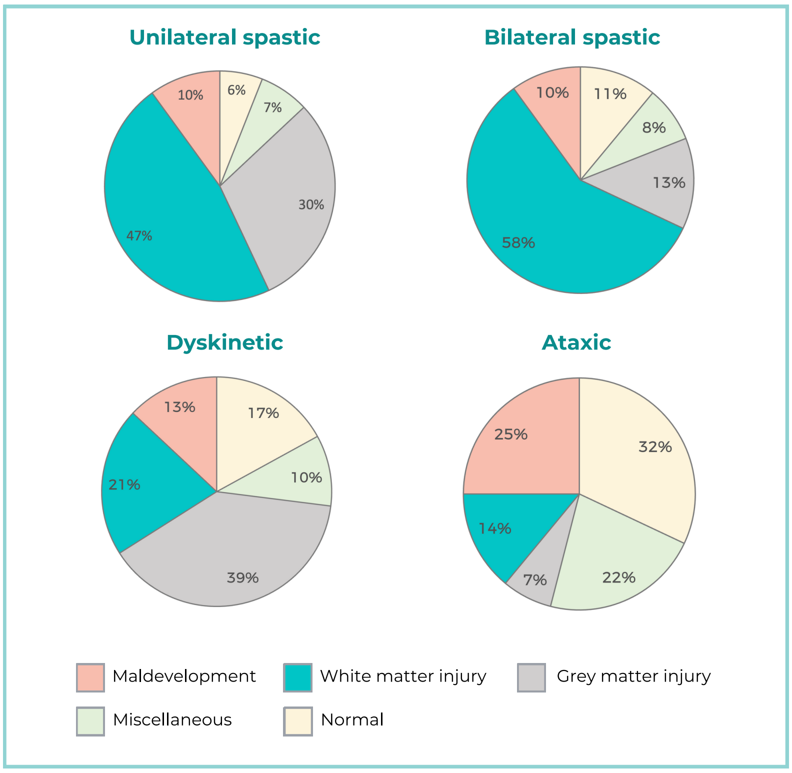


Figure 1. Distribution of MRI patterns in cerebral palsy types, adapted from Horber et al. (2020).
Abbreviations. CP, Cerebral palsy; MRI, Magnetic Resonance Imaging.

A systematic review about dMRI (Scheck et al., 2012) found that the corticospinal tracts, corticobulbar tract, and body of the corpus callosum were reduced in CP. Spastic CP is characterized by reduced connectivity in motor, sensorimotor, and premotor related areas as well as in calcarine areas. Additionally, increased connectivity has been observed in the default mode network in this type of CP (Jacobs et al., 2023). Dyskinetic CP has been associated with reduced interhemispheric connectivity, primarily in motor and premotor-related areas, along with the cerebellum, precentral supplementary motor area, anterior cingulate, and middle cingulate (Qin et al., 2019). To date, no dMRI and fMRI studies have specifically focused on ataxic CP, probably due to its low prevalence.

6. Non-neuropsychological associated impairments

Motor disturbances in CP, as indicated in the definition itself, are accompanied by sensation, communication, epilepsy, and musculoskeletal impairments, as well as a range of neuropsychological symptoms encompassing cognition, perception, and behavioural difficulties (Rosenbaum et al., 2007). It is important to note that the prevalence of associated comorbidities varies widely depending on the aetiology, and type of CP (Jonsson et al., 2019).

Communication and sensation disorders are the prevailing when considering non-neuropsychological symptoms (Figure 2). **Communication** symptoms vary; however, speech difficulties are the most prevalent, ranging from 61% – 82% (Mei et al., 2020; Virella et al., 2016). Speech disorders encompass a range of distinct impairments, including articulation and phonological disorders, dysarthria, and childhood apraxia of speech. Moreover, around 35 and 49% of CP cases present with unclear and non-understandable speech, respectively (Mei et al., 2016; Virella et al., 2016). **Sensation** disorders are frequently observed in individuals with CP, with visual difficulties being the most common. Visual disorders affect over half of individuals with CP, with refractive errors (52%), strabismus (48%), and nystagmus (11%) being the most commonly observed (Dufresne et al., 2014; Heydarian et al., 2022). Furthermore, a considerable 10% of individuals experience blindness (Novak et al., 2012). Hearing loss is another notable issue, with percentages ranging from 13 to 39%, and approximately 4% of people with CP are deaf (Delacy et al., 2016; Novak et al., 2012; Weir et al., 2018). **Epilepsy** is prevalent in 34 – 43% of people with CP (Pavone et al., 2020; Szpindel et al., 2022). Individuals with CP may present with various musculoskeletal problems, such as muscle or tendon contractures, bony torsion, osteoporosis, hip displacement, or spinal deformity (Colver et al., 2014; O'Connell et al., 2019; Rosenbaum et al., 2007).

In addition to the symptoms specified in the definition of CP, other associated symptoms, such as **pain**, are more prevalent. Approximately 30 – 70% of CP cases present with pain, and its frequency and intensity often increase with motor severity

(Alriksson-Schmidt & Hägglund, 2016; Van Der Slot et al., 2012). Among children who manifest pain, approximately 60% report that it disturbs daily activities (Eriksson et al., 2020). Moreover, gastrointestinal problems (e.g., vomiting, constipation, or bowel obstruction), urinary incontinence, pressure ulcers, and sleep disturbances are frequently observed as comorbidities (Krigger, 2006; Lélis et al., 2016; Vitrikas et al., 2020).

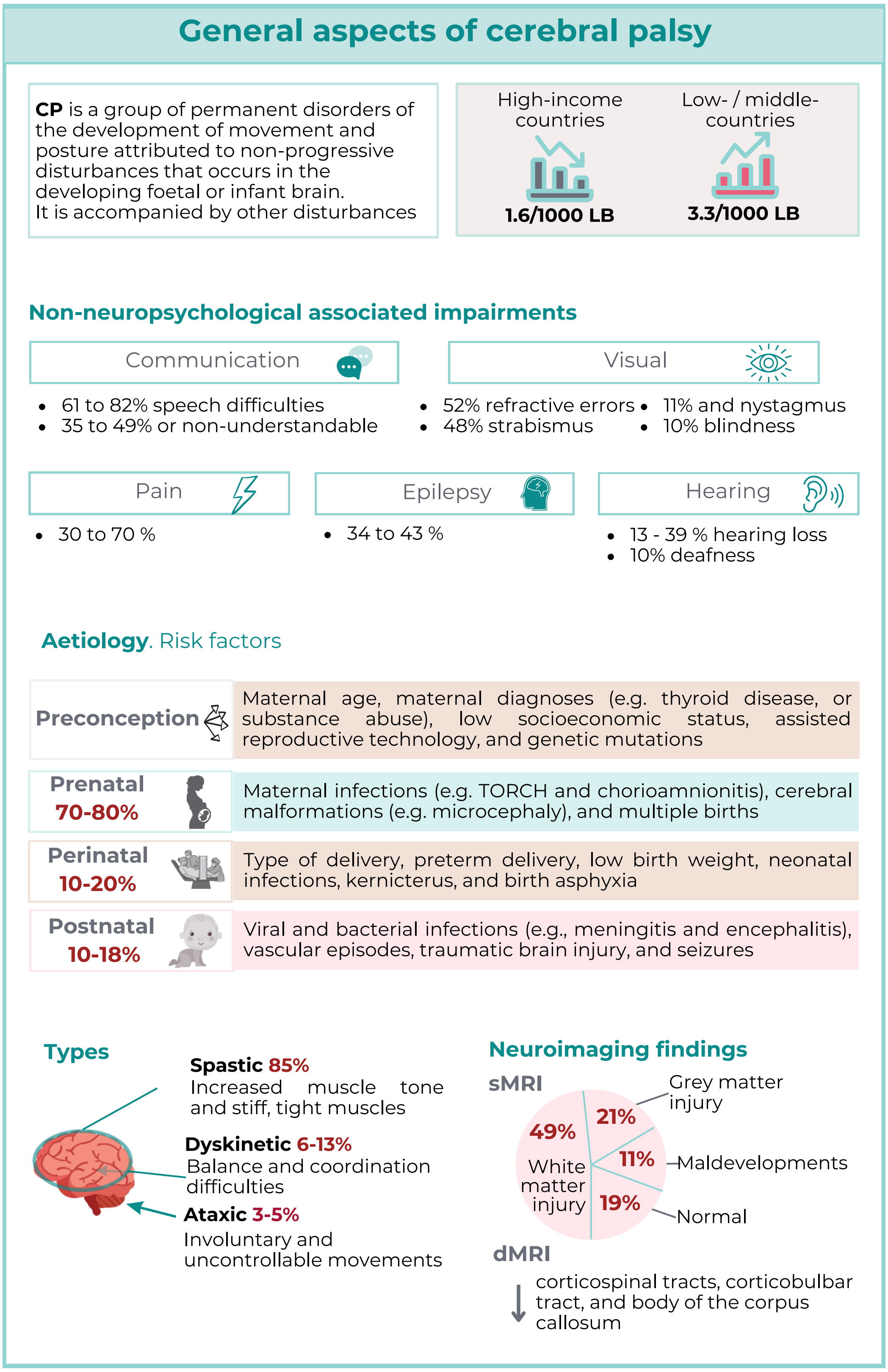


Figure 2. A summary of general aspects of cerebral palsy, created specifically for this thesis.

Abbreviations. CP, Cerebral Palsy; dMRI, Diffusion Magnetic Resonance Imaging; LB, Live Births; sMRI, Structural Magnetic Resonance Imaging.

NEUROPSYCHOLOGY OF CEREBRAL PALSY

1. Neuropsychological functioning and cerebral palsy

In addition to the abovementioned associated symptoms, the CP population also experiences neuropsychological impairments. Research has traditionally focused on motor symptoms, but there has been growing interest in understanding these neuropsychological symptoms to capture a wide range of cognitive profiles (Fluss & Lidzba, 2020; Straub & Obrzut, 2009). Therefore, a comprehensive neuropsychological assessment of individuals with CP helps determine **general intellectual functioning** and performance in **specific cognitive functions**, allowing interventions to be tailored for each case. In particular, the detection of cognitive impairments during childhood is essential for personalized interventions that benefit from brain plasticity (Graham et al., 2016; Schaffer & Geva, 2016). A description of these impairments and the interventions targeting them is presented in the next section (see Figure 3).

1.1. General intellectual functioning

Given its relevance in several areas of daily life in people with CP, general intellectual functioning has been widely investigated. The scientific literature has demonstrated its impact on health status (Beckung et al., 2008; Østensjø et al., 2003), social functioning, QoL, and participation in people with CP (Bottcher, 2010; Fauconnier et al., 2009; Voorman et al., 2010). In addition, general intellectual functioning can substantially contribute to the benefits of interventions for CP, such as selective dorsal rhizotomy (Kim et al., 2006) and botulinum toxin treatment (Fazzi et al., 2005). The International Classification of Functioning, Disability, and Health (ICF) states that general intellectual functioning is a core aspect of CP (Schiariti et al., 2015).

However, this assessment is not without difficulties. In some cases, the presence of fine motor and communicative impairments in CP makes it difficult to assess general intellectual functioning or obtain an intelligence quotient (IQ) through standardized neuropsychological assessment (Fluss & Lidzba, 2020). Consequently, general intellectual functioning is estimated by clinical judgement, degree of gross motor impairment, or interviews with parents in the most severe CP cases (Andersen et al., 2008; Hutton & Pharoah, 2002; Türkoğlu et al., 2017). Heterogeneity in assessment has shown discrepancies in the prevalence of general intellectual functioning in patients with CP (Coceski et al., 2022). Despite these difficulties in assessing IQ, a systematic review estimated that approximately 50% of the population with CP had an IQ below 70, which is considered an ID. Of the 50% of people with ID in CP, almost 28% have severe ID (IQ < 50) (Novak et al., 2012).

However, it should be noted that CP is a heterogeneous disorder (Stadskleiv, 2020), consequently, there is wide variability in general intellectual functioning, depending on the type of CP, motor severity, or other associated symptoms. Studies on spastic CP have shown that IQ in unilateral spastic CP is similar to that in the general population (Sigurdardottir et al., 2008), with approximately 81 – 89% of cases in this group within the normal range of IQ. General intellectual functioning decreases in the most severe motor cases of spastic CP, whereas around 30% of people with diplegic CP have ID, and the prevalence increases to approximately 80% in tetraplegic spastic CP (Stadskleiv, 2020). Few studies have reported general intellectual functioning in dyskinetic CP; however, differences in IQ have been reported depending on motor severity (Ballester-Plané et al., 2018). Children with mild to moderate motor severity (GMFCS I – III) and dyskinetic CP had similar performance to that of typically developing children, whereas performance was lower in severe cases (GMFCS IV – V).

However, neuroimaging studies investigating the relationship between different brain regions and cognition in CP are limited. These studies allow us to determine the relationship between brain injury and cognitive performance (Stadskleiv, 2020). However, the influence of other associated symptoms on cognitive severity, such as epilepsy, gestational age, and motor functioning, should be considered. Brain maldevelopment and cortical and subcortical lesions in the global thalamus and basal ganglia have been associated with severe ID in spastic CP (Riva et al., 2013; Scheck et al., 2012). Apart from studies focused on brain injury, dMRI techniques have allowed the identification of neural tracts involved in general intellectual functioning in dyskinetic CP, such as parieto-frontal and frontostriatal networks (Ballester-Plané et al., 2017).

1.1.1. Interventions to improve general intellectual functioning

Cognitive intervention refers to a treatment that involves repetitively performing demanding tasks over a period of time, to enhance cognitive functions (Strobach & Huestegge, 2017). To optimise cognitive interventions, improvements in a particular task are expected to produce benefits not only in the cognitive abilities directly related to the intervention, known as **near transfer effects**, but also in cognitive abilities different from those addressed by the program, as well as in daily life functioning, known as **far transfer effects** (Barnett & Ceci, 2002; Sala et al., 2019; Strobach & Huestegge, 2017).

In the case of general intellectual functioning, interventions usually involve the training of other cognitive functions, the most common of which are those focused on executive functions (Au et al., 2015; Buschkuehl & Jaeggi, 2010). The transfer effects of executive function interventions, specifically working memory training (domain explained in the next section), have been found on general intellectual functioning in typically developing children (Pugin et al., 2014; Studer-Luethi et al., 2016) and other disorders (Alloway et al., 2013). Pugin et al. (2014) found transfer effects on nonverbal intelligence in a group of typically developing children and adolescents (n = 55; 10 – 16 years old) after 3 weeks (30 min per day) of a computerized working memory intervention. Otherwise, Studer-Luethi et al. (2016) found improvements in verbal intelligence in a group of children (n =iii 99; mean age = 8.25 years, SD = 0.50) after the same type of intervention. These beneficial effects have also been observed in children with learning disabilities (n = 94; mean age = 11.2), where improvements in both verbal and nonverbal intelligence were observed after 8 weeks of intervention (4 times a week) (Alloway et al., 2013).

Studies on interventions to improve general intellectual functioning are scarce. However, research has also found that physical interventions, where physical activity is the main task, affect general intellectual functioning (Ardoy et al., 2014; Tomporowski et al., 2008). A study in adolescents (n = 67) demonstrated that a higher intensity of physical activity over 4 months (55 min per day, 4 times a week) improved general intellectual functioning (Ardoy et al., 2014).

Interventions to improve general intellectual functioning in cerebral palsy

Research on interventions to manage CP has largely focused on addressing motor symptoms, leaving limited attention to cognitive impairments (Novak et al., 2013). Considering the high prevalence of associated symptoms, including cognitive impairments, and the burden of children with CP and their families (Ballantyne et al., 2019), it is important to optimise interventions in this population. Therefore, from an integrated perspective, it remains uncertain whether cognitive interventions targeting executive functions, such as working memory, or physical interventions, have the potential to enhance general intellectual functioning in individuals with CP, as observed in other populations.

1.2. Specific cognitive functions

While general intellectual functioning is used as a general measure of cognition, specific cognitive functions allow for the identification of strengths and difficulties (Påhlman et al., 2019). Moreover, specific cognitive functions seem to make a major contribution to daily life and well-being compared to general intellectual functioning (Diamond, 2020; Williams et al., 2011). However, in the field of CP, greater efforts should be dedicated to understanding the performance of specific cognitive functions within the CP population. This understanding is essential for the development of interventions to improve these functions.

At the outset of this thesis, there was a lack of systematic reviews on available interventions to enhance specific cognitive functions. Nevertheless, it is crucial to determine the interventions that can effectively address the diverse and specific cognitive impairments observed. Moreover, although this thesis did not cover neuroimaging analysis, advances in neuropsychology of CP will enable neuroimaging studies related to cognition, and as such, these types of studies have been scarce until now (Di Lieto et al., 2017; Weierink et al., 2013).

Beyond expressive language impairments in speech and their impact on communication, as mentioned earlier, research has shown impairments in other specific cognitive functions. Among these difficulties, **executive functions** and **visual perception** have received the most attention and extensive studies, whereas studies focusing on **memory** impairments are scarce. Given the focus of this thesis on executive functions, visual perception, and memory skills, the research findings in these areas will be presented in detail in the following sections.

1.2.1. Executive functions

Executive functions are a set of interrelated mental skills that control, organise, and direct cognitive activity, emotional response, and behaviour towards achieving a goal (Gioia et al., 2001). These functions are crucial in several areas of daily life, including cognitive and psychological development, mental and physical health, and academic and professional achievement (Diamond, 2013).

Despite the importance of executive functions, this umbrella term has proven challenging, and different frameworks have been proposed to describe the executive function system and its major domains (Anderson et al., 2010; Diamond, 2013). This thesis focuses on Diamond's model (2013), one of the most used in research and clinical settings, which distinguishes between core and higher-order executive functions. Three **core** executive functions are distinguished: inhibitory control, working memory, and cognitive flexibility. From these core executive functions, **higher-order** executive functions are built, including planning, problem solving, and reasoning. A description of each domain is presented in Table 2. Executive functions can be divided into hot and cool types (Diamond, 2020; Zelazo & Carlson, 2012). Hot executive functions are related to emotionally charged situations, and cool executive functions are related to affectively neutral situations (e.g., academic achievement) (Brock et al., 2009; Kim et al., 2013). These findings support a relationship between executive functions and social cognition (Li et al., 2014). Impairments in executive functions have been associated with social problems (Bottcher, 2010).

Executive functions are the last cognitive functions to fully mature (Powell & Voeller, 2004), developing gradually from early infancy to adulthood. This could be explained by the fact that executive functions depend on brain regions that continue to develop during adolescence, such as the prefrontal, anterior cingulate, and parietal cortices (Weierink et al., 2013). Each domain has its own developmental period (Fluss & Lidzba, 2020; Powell & Voeller, 2004). For instance, working memory shows marked improvements around eleven years of age, whereas planning continues to improve throughout adolescence (Diamond, 2020).

Table 2. Description of executive function domains, adapted from Diamond et al. (2013) and Cristofori et al. (2019).

Core	Inhibitory control	Involves being able to control one's attention, behavior, thoughts and/or emotions to override a strong internal predisposition or external lure, and instead do what you intend to do.
	Working memory	Ability to hold information in mind and mentally working with it. Depending on the content, we can distinguish between verbal and non-verbal working memory.
	Cognitive flexibility	Capacity to being flexible enough to adjust to environmental changes. Cognitive flexibility is linked with inhibitory control and working memory and develops later.
Higher-order	Planning	Involves the formulation, evaluation and selection of actions required to achieve a goal.
	Problem solving	Ability to work through details of a problem to reach a solution.
	Reasoning	Core ability of generalization and abstraction processes that enable concept formation and creativity

Executive functions in cerebral palsy

Executive function impairments in CP have been observed in both core and higher-order executive function domains (Fluss & Lidzba, 2020). Research suggests that these difficulties appear in early childhood (Freire & Osório, 2020) and persist throughout adulthood (Laporta-Hoyos et al., 2019; Pueyo et al., 2009). Nevertheless, few studies have investigated all executive functions domains in CP (Bodimeade et al., 2013; Di Lieto et al., 2017; Freire & Osório, 2020; Laporta-Hoyos et al., 2019). Bodimeade et al. (2013) found impairments in core and higher-order executive functions in a group of 46 children with unilateral spastic CP, regardless of the laterality of the motor impairment. Di Lieto et al. (2017) reported similar difficulties in 19 children with spastic diplegia. Later, Freire and Osorio (2020) investigated core executive functions in a mixed group of 14 participants with unilateral and bilateral spastic CP. In this study, the authors found worse performance in cognitive flexibility and inhibitory control compared with the typically developing group, but there were no differences in the working memory domain. As can be seen, studies have mainly focused on spastic CP samples. To compare executive function performance between different types of CP, Laporta-Hoyos et al. (2019) compared three groups: spastic CP, dyskinetic CP, and typically developed individuals in a total sample of 124 participants aged 6 to 62 years. The results indicated that both the CP groups (spastic and dyskinetic) showed significantly worse performance than the typically developed group. Notably, the dyskinetic CP group showed significantly better cognitive flexibility scores than the spastic CP group did. In the other domains of executive function, the dyskinetic CP group seemed to perform better than the spastic CP group, although the difference was not statistically significant.

Impairments in executive functions in populations with CP have been related to difficulties in social cognition and emotional regulation (Belmonte-Darraz et al., 2021; Caillies et al., 2012; Li et al., 2014). In addition, executive functions have been related to QoL in adults with dyskinetic CP (Laporta-Hoyos et al., 2017). However, no previous studies have explored the role of executive functions in QoL in other types of CP or in children with CP.

1.2.1.1. Interventions to improve executive functions

Among the different types of cognitive interventions, **executive function training** is the most popular in children, because, as seen previously these functions continue to develop during this life stage, and the presence of executive dysfunction affects daily life during childhood and adolescence (Diamond, 2013).

Executive function interventions have shown promising beneficial effects in other paediatric populations, such as in children with Attention Deficit Hyperactivity Disorder (ADHD) (Klingberg et al., 2002; Thorell et al., 2009), language disorders (Acosta et al., 2019), and extremely low birth weight (Grunewaldt et al., 2013, 2016; Løhaugen et al., 2011). In the ADHD population, a study with children (n = 14; 4 – 5 years old) in three groups (inhibitory intervention, working memory, and active control group) demonstrated that after 5 weeks of computeried intervention (15 minutes per session, total dose = 6 hours), the working memory group had more beneficial effects than the inhibitory intervention and active control groups. Apart from improvements in working memory, far transfer effects have also been found in inhibitory control, problem solving, and processing speed (Thorell et al., 2009). Furthermore, a study of children and adolescents with ADHD (n = 49; 7 – 15 years old) reported improvements in visuospatial working memory and non-trained cognitive function, such as reasoning, after 13 hours (25 minutes each day for 30 sessions) of computerized working memory intervention (Klingberg et al., 2002). Research on children with language disorders (n = 32; 5 – 11 years old) found changes in working memory (verbal and visual) and far transfer effects on immediate memory (both verbal and visual) and processing speed after non-computerized working memory training (18h, 72 sessions of 15 min each) (Acosta et al., 2019). Moreover, studies have demonstrated that physical activities involving motor skills can potentially have executive function benefits, particularly in core executive functions (Erickson et al., 2019; Grassmann et al., 2017; Koščak Tivadar, 2017).

In addition to considering far transfer effects, it is crucial to monitor the maintenance of both near and far transfer effects over time. This is important for determining the effectiveness and optimisation of the interventions. Therefore, assessing of **follow-up effects** is essential for cognitive intervention. These effects have been investigated in other populations of children population (Grunewaldt et al., 2013, 2016; Løhaugen et al., 2011). Grunewaldt (2013, 2016) reported near transfer effects in working memory and far transfer effects on auditory attention and, visual and verbal memory after 5 weeks of intervention (30 – 40 minutes per day, 5 days per week) in a sample of children (n = 20; 5 – 6 years old), which were maintained for 7 months after the completion of the intervention. On the other hand, Løhaugen (2011) showed changes in working memory and verbal learning in a group of adolescents after 5 weeks of intervention (30 – 40 minutes per day, 5 days per week). The beneficial effects of this intervention persisted for 6 months after it ended.

In summary, the evidence suggests that executive function interventions can be used to improve cognition in children and adolescents. The most notable aspect of this intervention is that it improves not only trained cognitive functions but also untrained cognitive functions, especially memory skills. Moreover, few studies have investigated the follow-up effects, but the results seem to suggest that improvements could be maintained for months after the completion of the intervention.

Interventions to improve executive functions in cerebral palsy

Executive function intervention is of special relevance in the context of CP due to the high prevalence of executive function impairments, the impact on other cognitive functions and daily life, as well as their demonstrated effectiveness in improving near and far transfer effects in other paediatric populations. However, to the best of our knowledge, no executive functions interventions have been conducted in children with CP to determine near and far transfer effects as well as to maintain these improvements over time. The project in which this thesis is the first to publish a protocol (García-Galant et al., 2020) aimed at investigating the near and far transfer effects of these interventions in the CP population.

1.2.2. Visual perception

Visual perception is the ability to receive, recognise, interpret, and elaborate on visual information (Schneck, 2013). In visual perception, two types of pathways can be distinguished, ventral and dorsal. The ventral (occipito-temporal) stream, also known as the "what" pathway, is responsible for recognising faces, objects, and shapes using pattern, texture, and colour vision. The dorsal stream (occipito-parietal pathway), on the other hand, is described as the "where" pathway, which includes visuospatial processing, visuomotor coordination, and visual guidance of movement, and is often referred to as visuospatial abilities (Cloutman, 2013; Philip & Dutton, 2014). In the general population of children, visual perception is essential for everyday activities, with an impact on visual-motor integration and academic achievement in school, such as reading and mathematics skills (Philip & Dutton, 2014; Williams et al., 2011).

Cerebral Visual Impairment (CVI) is an umbrella term that includes all types of visual impairment due to brain damage or dysfunction. CVI is defined as a neurological disorder caused by a dysfunction that cannot be attributed to anterior visual pathway disorders or any potentially co-occurring ocular impairment (Sakki et al., 2018). Individuals with CVI can present with a wide range of visual disorders, ranging from reduced acuity/visual field and oculomotor incoordination to complex visuo-cognitive disorders, such as recognizing faces or objects and figure-ground perception. The presence of difficulties in this higher-order visual processing may result in **Visual Perceptual Impairments** (VPIs), which can manifest clinically as difficulties in recognising faces or objects, finding a toy in a cluttered toy box, or getting lost in known locations (Dutton, 2013; Fazzi et al., 2004, 2007; Philip & Dutton, 2014).

Visual perception in cerebral palsy

VPIs are one of the most common cognitive impairments observed in individuals with CP. Ego et al. (2015) conducted a systematic review to determine the prevalence of VPI in the CP population and possible patient characteristics. The authors found that the prevalence of VPI in CP was approximately 40 – 50% and that the subtype of CP, side of motor impairment, or presence of epilepsy did not influence the prevalence of VPIs (Ego et al., 2015). However, other authors have reported that differences in the degree of impairment vary depending on CP subtype (Philip & Dutton, 2014; Pueyo et al., 2009; Stiers et al., 2002). In a systematic review (Philip & Dutton, 2014) a higher prevalence of VPIs was reported in both bilateral and unilateral spastic subtypes (Ego et al., 2015; Stiers et al., 2002).

VPI in CP is associated with difficulties in academic achievement, such as the acquisition of literacy and arithmetic skills (Critten et al., 2018, 2019), as well as everyday motor skills including bimanual coordination and motor planning (James et al., 2015a). As will be discussed in more detail in this thesis, VPIs also impact QoL in CP (Mitry et al., 2016).

1.2.2.1. Interventions to improve visual perception

Although executive functions are more commonly used and have been found to have both near and far transfer effects, visual perceptual interventions have been reported to have a transfer effect on visual perception in the paediatric population (De Lisi & Wolford, 2002; Poon et al., 2010). For example, a study of children with learning difficulties (n = 26, 6 – 7 years old) found changes in visual perception after 8 weeks (45 min per day, 1 day per week, total dose = 6 hours) of a computerized visual perception intervention compared to the control group. Similarly, a study of typically developing children (n = 47; 8 – 9 years old) demonstrated the effectiveness of the Tetris game in mental rotation (De Lisi & Wolford, 2002). Furthermore, interventions that include both executive and visual perceptual tasks have shown improvements in the latter (Brock et al., 2018). Even far transfer effects have been found in visual perception in children with ID (n = 46, mean age = 10.9 ± 3.9 years) after a 16 week physical intervention (60 min per day, 3 days per week) (Chen et al., 2015).

Interventions to improve visual perception in cerebral palsy

To date, no randomized controlled trials (RCTs) have investigated the effects of cognitive interventions on this population. However, a pre-test post-test design examined the effects of a non-computerized visual perceptual program on these skills in a sample of children (n = 56, 4 – 6 years old) with spastic CP (Cho et al., 2015). The study found significant improvements in visual perception after 8 weeks of intervention (30 minutes per day, 3 times a week, total dose = 12 hours). As VPI is a common symptom in individuals with CP, it is particularly important to explore the impact of cognitive interventions on visual perception. Although no RCTs have been conducted in CP populations, the available evidence of CP and other clinical populations shows promise for improving these functions.

1.2.3. Memory skills

Memory is a fundamental function involving the ability to encode, store, and retrieve information. It is complex and encompasses several types of memory, which can be broadly divided into three main categories: immediate memory, learning, and long-term memory (Lezak et al., 2004).

Immediate memory is the first stage of memory, and a limited capacity store of information is transferred to a more permanent store. It typically lasts for approximately 30 seconds to several minutes. It is essential to clarify the differences between immediate memory and working memory (one of the core executive function domains). Immediate memory refers to the ability to hold information in mind, whereas working memory involves both holding and manipulating information (Alloway et al., 2004; Gathercole et al., 2004). Notably, executive functions and memory are two distinct yet closely interrelated cognitive functions. The transfer of information from working memory to long-term memory is a slow process that requires information maintenance over time (Baddeley, 1998; Baddeley et al., 2011).

Finally, **learning** refers to the ability to acquire information, whereas **long-term memory** stores this information for long periods, from minutes to years (Lezak et al., 2004). Memory skills play a crucial role in academic and knowledge acquisition (Smith, 2009).

As known the involvement of prefrontal in working memory, the medial temporal lobe regions, particularly, the hippocampus, perirhinal and parahippocampal structures, are involved in learning and the creation of new memories. Finally, hippocampus and neocortex are important in the retrieval of long-term memories (Amoah, 2022; Lee et al., 2014; Ofen, 2012; Tang et al., 2018).

Memory in cerebral palsy

Few studies have examined memory performance in people with CP (Fluss & Lidzba, 2020) and results across studies are inconsistent (Ballester-Plané et al., 2018; Beckung et al., 2008; Østensjø et al., 2003; Pueyo et al., 2009; Toomela, 2012). Regarding verbal memory, impairments in immediate memory and learning have been observed in patients with spastic CP (Østensjø et al., 2003; Toomela, 2012). Long-term verbal memory difficulties appear in both spastic and dyskinetic CP (Ballester-Plané et al., 2018; Pueyo et al., 2009). Studies on visual memory are scarce. However, in a study focusing on a dyskinetic population, visual memory difficulties were more prevalent than verbal memory (Ballester-Plané et al., 2018).

1.2.3.1. Interventions to improve memory

Although specific memory interventions have been widely investigated in adults, particularly in elderly individuals with memory impairments such as dementia (Zehnder et al., 2009), their use in children is not as common. In the paediatric population, a combination of memory, executive function, and visual perceptual tasks have been used to target cognition (Schaffer & Geva, 2016). Cognitive interventions have been shown to improve learning and memory in other paediatric populations, such as children with malaria (Bangirana et al., 2009, 2011), and acquired brain injury (Van't Hooft et al., 2005). Van't Hooft and Norberg (2010) reported improvements in immediate and long-term memories in children with acquired brain injury (n = 40; 9 – 16 years) after 17 weeks (30 min per day) of intervention, which included inhibitory control and memory tasks. Similarly, Bangirana et al. (2011) investigated the effects of an intervention that included memory, inhibitory control, and visuomotor tasks in a group of 71 children with severe malaria aged 5 to 12 years, and the intervention group improved learning after 12 weeks of intervention.

Interventions to improve memory in cerebral palsy

Memory difficulties in children with CP have not been properly investigated, and there is no evidence of effective treatment for these skills. Despite the limited research on CP, it is important to identify interventions that can improve these skills due to their importance in daily life, particularly in school and the acquisition of knowledge (Smith, 2009). Studies conducted in other populations have shown that interventions involving executive function tasks (Bangirana et al., 2011; Van't Hooft et al., 2005; Van't Hooft & Norberg, 2010) or solely executive function interventions (Acosta et al., 2019; Grunewaldt et al., 2013, 2016) can have beneficial effects on memory skills, likely because of the interrelationship between the memory and executive function systems. Therefore, based on the existing scientific literature, evidence led us to hypothesize that executive function intervention in children with CP could produce a far transfer effect on memory skills.

1.3. Other neuropsychological impairments

People with CP are at a higher risk of developing mental health symptoms that often appear during childhood and escalate in adulthood (Downs et al., 2018; Van Der Slot et al., 2012; Weber et al., 2016; Whitney et al., 2019). A meta-analysis (Downs et al., 2018) reported that approximately 28 – 35% of children and adolescents with CP reported **psychological symptoms**. Among the children manifesting mental health symptoms, approximately 30% showed anxiety symptoms and 8% presented with depressive symptoms.

The prevalence of comorbid disorders such as **Autism Spectrum Disorder** (ASD) and **ADHD** is significantly higher in children with CP than in typically developing children. In 2007, The National Institute for Health and Care Excellence Guideline for diagnosing, assessing, and managing CP highlighted the importance of investigating the prevalence of ASD and ADHD in individuals with CP (Shaunak & Kelly, 2018). This has increased the number of studies that have investigated the presence of these disorders. A recent study (Påhlman et al., 2021) reported that 45% of the children had ASD and/or ADHD, regardless of the severity of motor impairment. The study revealed that 15% of the children had ASD alone, approximately 14% had ADHD, and 16% were diagnosed with both neurodevelopmental disorders. Given the high prevalence of neuropsychological symptoms in individuals with cerebral palsy, it is crucial to consider these variables in both the evaluation and treatment of the condition, as well as their potential impact on an individual's well-being.

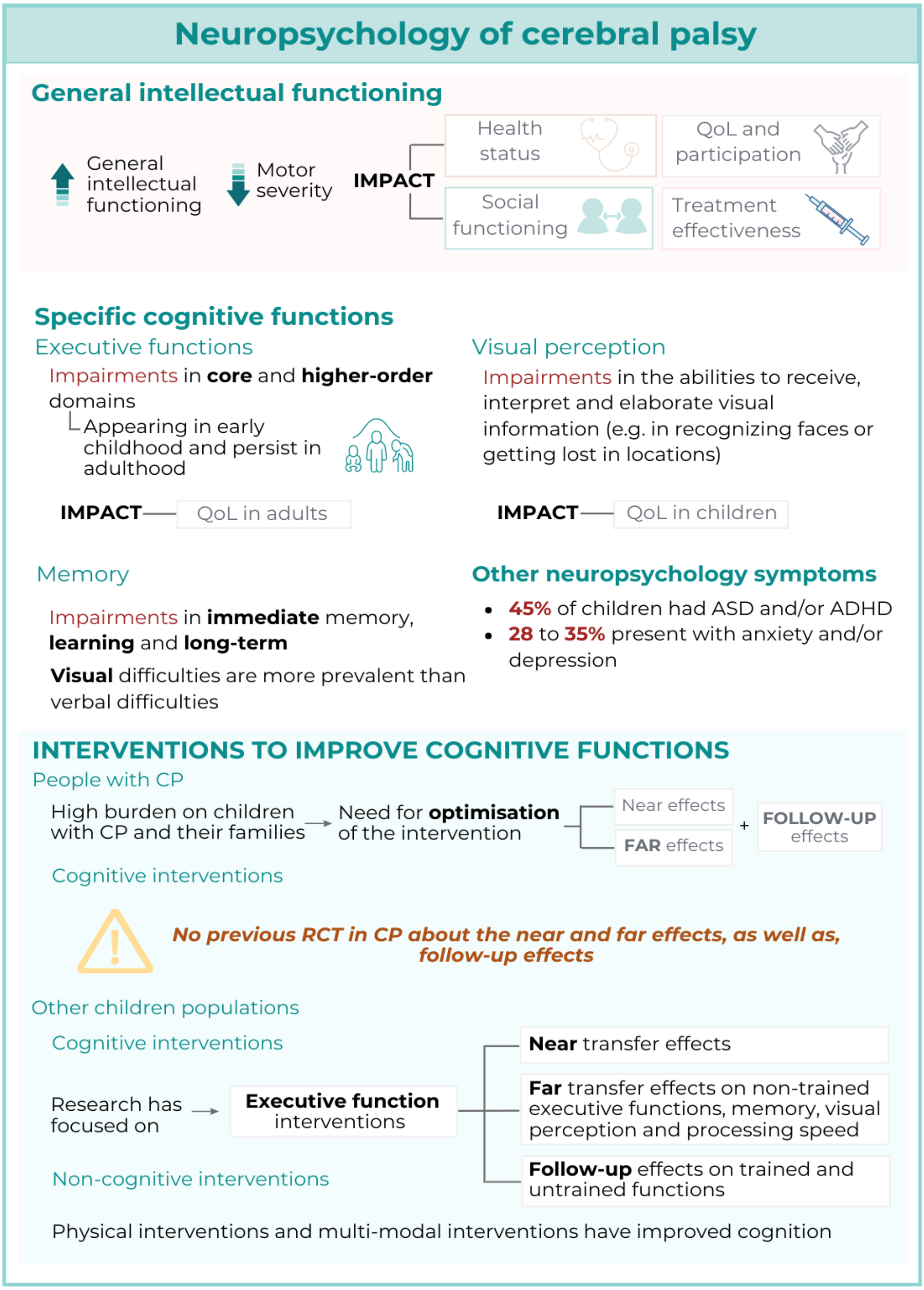


Figure 3. A summary of neuropsychology aspects of cerebral palsy, created specifically for this thesis.

Abbreviations. ADHD, Attention Deficit Hyperactivity Disorder; ASD, Autism Spectrum Disorder; CP, Cerebral Palsy; QoL, Quality of Life; RCT, Randomized Controlled Trial.

People with chronic diseases often face multiple challenges that can significantly affect their daily lives. The impact on daily activity in individuals with CP translates into a decrease in QoL and participation (Calley et al., 2012). Rehabilitation programs for CP have highlighted QoL and participation as essential outcomes in assessing therapeutic effectiveness (Noreau et al., 2004), with some interventions specifically aimed at improving these aspects (Colver, 2009). However, defining and understanding the complex concepts of QoL and participation remain challenging. The World Health Organization (WHO) has been actively working to improve the understanding of these aspects since recognizing their importance in chronic diseases (WHOQOL GROUP, 1995; WHO, 2001).

1. Participation in daily activities

Participation is an important outcome of the ICF from the WHO (WHO, 2001). It refers to involvement in life situations or daily activities (WHO, 2007). The **ICF** is a comprehensive and useful **biopsychosocial framework** that describes and understands function and health, and is applicable to clinical care (Noten et al., 2022; Schiariti et al., 2015). Functioning is described by the interrelationship between four components: (1) body function and structures; (2) activities and participation; (3) personal factors, and (4) environmental factors. In the context of CP, participation gained relevance after the introduction of the ICF model. There is general consensus that participation contributes to QoL (Law, 2002). For the CP population specifically, the Study of Participation of Children with Cerebral Palsy Living in Europe (SPARCLE), a multicentre European observation-based study, was designed to investigate the relationship between participation, QoL, and the environment (Colver, 2006).

2. Quality of life

Although QoL is not part of the ICF model, several authors consider that QoL should be evaluated by considering all components of the framework. McDougall et al. (2011) proposed a modified version of the ICF model to better understand QoL (Figure 4). The WHO defines QoL as an "*individual's perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards, and concerns*" (WHOQOL GROUP, 1995). This concept is all-encompassing and intricate, intertwining various aspects of an individual's life, such as physical well-being, psychological state, autonomy level, social relationships, personal convictions, and interactions with significant aspects of their surroundings (WHOQOL GROUP, 1995). Most instruments assessing QoL include sections related to emotional, social, material, physical well-being, self-esteem, and self-determination (Colver, 2009). Assessing QoL in people with CP is relevant as it provides a subjective indication of well-being across these domains (Gilson et al., 2014). Furthermore, QoL assessments can complement objective measures used to determine functioning (Majnemer & Mazer, 2004).

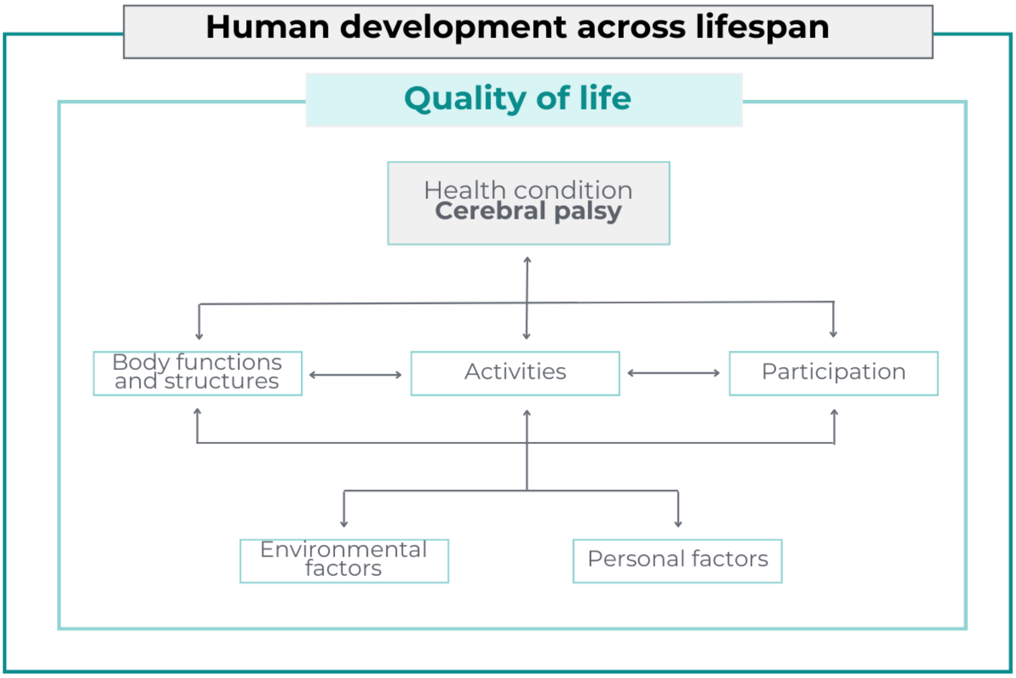


Figure 4. The World Health Organization's model of functioning and disability including quality of life, adapted from McDougall (2011).

2.1. Factors influencing quality of life in cerebral palsy

Multiple factors can influence the QoL of individuals with CP and affect their life satisfaction (Figure 4) (Colver, 2009; Gilson et al., 2014). Identifying factors related to QoL can help determine appropriate assessments and interventions to improve the daily lives of individuals with CP. The following section provides an overview of the outcomes associated with QoL which are categorized as clinical, demographic, neuropsychological, and psychosocial.

2.1.1. Clinical variables

Clinical factors, together with demographic variables, are the most explored outcomes for determining aspects that could influence QoL in patients with CP. The mainly clinical variables examined in CP have been motor functioning, type of CP, motor distribution, pain, epilepsy, and communicative impairments.

Multiple studies have found that greater impairments in **gross motor function** (Badia et al., 2016; Böling et al., 2016; Chen et al., 2014; Liu et al., 2009; Majnemer & Mazer, 2004; Mc Manus et al., 2008; Park, 2017; Rapp et al., 2017) and **fine motor skills** (Böling et al., 2016; Chen et al., 2014; Laporta-Hoyos et al., 2017; Park, 2017) are associated with lower QoL, particularly in the physical domains of QoL. Additionally, CP type and motor distribution have been identified as determinants of QoL (Böling et al., 2016; Jiang et al., 2016; Ozkan, 2018). Specifically, individuals with tetraplegia tend to have a lower QoL than those with hemiplegia and diplegia CP (Ozkan, 2018).

Other associated symptoms have also been identified, such as higher levels of **pain** (Elema et al., 2016; Findlay et al., 2016; Giray et al., 2018; Rapp et al., 2017) and the presence of **epilepsy** (Jiang et al., 2016). Pain and epilepsy are more common in individuals with higher motor severity, which is also related to lower QoL in CP. Finally, difficulties in everyday **communication** have been associated with a decreased QoL (Böling et al., 2016; Laporta-Hoyos et al., 2017; Omura et al., 2018; Rapp et al., 2017).

2.1.2. Demographic variables

Personal factors related to **age**, **sex**, and **socioeconomic status** have been shown to influence the QoL of individuals with CP. Studies have reported that higher age (Radsel et al., 2017), male sex (Badia et al., 2016; Türkoğlu et al., 2016), and higher-level socioeconomic status CP (Laporta-Hoyos et al., 2017) are predictors of worse QoL.

2.1.3. Psychosocial variables

Among the psychosocial factors studied in relation to CP, **parental stress**, **type of schooling**, and **participation** have emerged as being particularly important. Parents of children with CP often experience stress and burden because of the challenges associated with this condition (Guyard et al., 2010). Research focusing on QoL has indicated that parental stress plays a significant role and is predictive of lower QoL (Rapp et al., 2017). Studies have presented inconclusive findings regarding type of schooling. While some studies have reported higher levels of QoL when children attend special schools (Badia et al., 2016), others have found the opposite effect (Beckung et al., 2008; Majnemer et al., 2007). Finally, as mentioned previously, participation is associated with QoL (Burak & Kavlak, 2019; Omura et al., 2018).

2.1.4. Neuropsychological variables

The relationship between neuropsychological variables and QoL is the least explored in CP, and available studies have focused mainly on IQ (Badia et al., 2016; Böling et al., 2016; Jiang et al., 2016; Rapp et al., 2017). **General intellectual functioning** is associated with several QoL domains in children with CP (Arnaud et al., 2008; Badia et al., 2016; Böling et al., 2016; Jiang et al., 2016; Rapp et al., 2017). Rapp et al. (2017) showed that IQ was a predictor of several domains of QoL in a sample of children (n = 551, age range 8 – 12 years) with CP, with a greater effect in cases of severe intellectual impairment (IQ < 50). Additionally, this influence has been demonstrated in the physical health domain of QoL among young adults with CP (Jiang et al., 2016).

Regarding specific cognitive functions, only two studies have investigated the influence of **executive functions** (Laporta-Hoyos et al., 2017) and **visual perception** on QoL (Mitry et al., 2016). On the one hand, Laporta-Hoyos et al. (2017) reported that executive functions predicted overall QoL and several domains of QoL. The most remarkable result of this study is that, among executive functions, cognitive flexibility predicted the total QoL score and four domains in a sample of adolescents and adults with dyskinetic CP (n = 50, age range 12 – 62 years). No previous studies have been conducted on the other types of CP. Moreover, no studies have investigated its role in children with CP, but previous studies have demonstrated its relationship with other paediatric populations (De Vries & Geurts, 2015; Love et al., 2016; Sanz et al., 2018; Schraegle & Titus, 2016; Sherman et al., 2006). In contrast, Mitry et al. (2016) investigated the effects of visual perception in children with CP (n = 180, age range 6 – 11 years). The results of this study suggested that the presence of VPIs is associated with decreased overall QoL and emotional/social subscale scores.

Nevertheless, no previous research has investigated the influence of executive functions, visual perception and memory, on QoL to determine which of them has a higher role in QoL in the CP population. Additionally, no research has investigated the association between memory and QoL in individuals with CP, although verbal memory has been linked to QoL in other paediatric populations, such as children with epilepsy (Hrabok et al., 2013).

Behavioural and **emotional** problems affect the QoL of children (Chen et al., 2014; Majnemer et al., 2007; Park, 2017) and adolescents with CP (Colver et al., 2015; Rapp et al., 2017). However, no previous study has explored the relationship between ASD traits and QoL in the CP population. Owing to the high prevalence of ASD symptomatology in this disorder, its impact on QoL in individuals with CP should be investigated further.

2.2. Interventions to improve quality of life

With the scarcity of studies examining the effects of cognitive interventions on untrained cognitive functions, there are even fewer studies investigating far transfer effects in daily life that incorporate QoL as an outcome measure. Moreover, the findings of these studies are inconsistent, as some indicate post-intervention improvements in QoL (Çalik et al., 2012), whereas others do not report such enhancements (De Vries et al., 2015; Dovis et al., 2015).

Interventions to improve quality of life in cerebral palsy

No previous studies have explored the impact of cognitive interventions on QoL in individuals with CP (Figure 5). However, QoL is considered an outcome of physical interventions to determine improvements in well-being. A systematic review (Tsoi et al., 2012) revealed that physical interventions improve QoL in CP, albeit with limited effectiveness. Although the association between executive functions and QoL in children with CP remains unexplored, findings from studies conducted in adult population (Laporta-Hoyos et al., 2017) suggest that interventions targeting executive functions may offer a promising alternative to physical interventions to achieve a more significant impact on QoL. Consequently, further investigations are required to confirm this hypothesis.

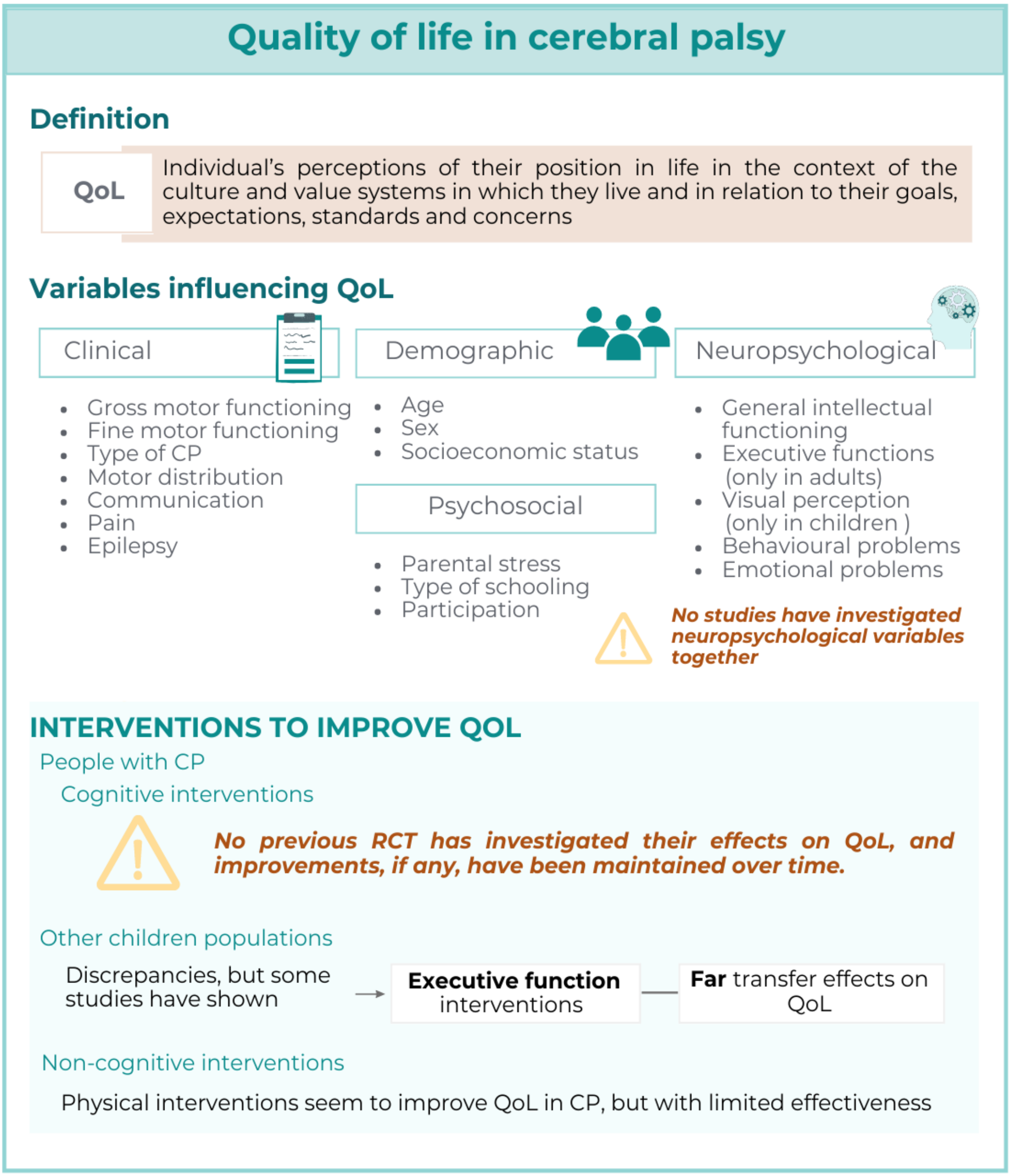


Figure 5. A summary of quality of life aspects in cerebral palsy, created specifically for this thesis.
Abbreviations. CP, Cerebral Palsy; QoL, Quality of Life.

AIMS AND HYPOTHESES

Cerebral palsy is a multifaceted disorder that presents challenges for both children and their families. The considerable burden on individuals with CP can significantly impact on their daily lives. Beyond the motor impairment, the introduction of this thesis provides an overview of the cognitive function impairments experienced by people with CP throughout their lives. Existing evidence highlights difficulties in specific cognitive functions, such as executive functioning and visual perception. Additionally, memory impairments are also present, but they have been less studied. However, studies on the effectiveness of interventions to improve cognitive functions in individuals with CP are scarce and require further investigation. Additionally, although the impact of cognitive functions on QoL in CP has been acknowledged, there is a paucity of literature that thoroughly investigates this association. Consequently, studies that consider all cognitive functions along with other variables to elucidate the factors influencing QoL in CP are lacking. Furthermore, while executive function interventions in other children's populations have shown a far transfer effect on other cognitive functions, no previous research has demonstrated the far transfer effects of this type of intervention on memory and visual perception, and even on QoL in children with CP. The follow-up effects of these interventions remain unknown. This thesis employed different scientific study approaches, including a systematic review, a cross-sectional study and an RCT, with the main aim of optimising the effects of cognitive interventions in children with CP. Each study included in this thesis considered the following specific aims and hypotheses:

STUDY 1

1. To systematically outline the most effective interventions for improving cognitive functions in individuals with CP based on the best available evidence.

   Hypothesis: given that interventions in CP are mainly focused on motor aspects (Novak et al., 2013), we assume that the predominant type of intervention investigating its effect on cognitive functions would be physical interventions. It is expected that physical interventions will have beneficial effects on general intellectual functioning, executive functions, and visual perception, based on previous evidence regarding the effectiveness of these interventions in other populations (Ardoy et al., 2014; Chen et al., 2015; Erickson et al., 2019; Koščak Tivadar, 2017; Tomporowski et al., 2008).

2. To identify gaps in the existing literature regarding interventions with an impact on cognitive functions in people with CP.

   Hypothesis: research on cognitive interventions in individuals with CP is currently limited (Cho et al., 2015; Novak et al., 2013), with no RCT focusing on the effects of cognitive interventions, specifically in this population. Nevertheless, considering the available research in other populations (Acosta et al., 2019; Grunewaldt et al., 2013, 2016; Klingberg et al., 2002; Løhaugen et al., 2011; Thorell et al., 2009), whether cognitive interventions are used in CP, even in the absence of RCTs, we hypothesize that they will be mainly executive function interventions.

STUDY 2

2. To investigate the relationship between QoL and neuropsychological variables in children with CP, using a biopsychosocial approach, including other clinical, demographic, and psychosocial variables.

Hypothesis: executive function would be related to overall and several specific domains of QoL in children with CP, taking into account its impact on daily life during childhood (Diamond, 2013) and the relationship found in adults with CP (Laporta-Hoyos et al., 2017) and other children's populations (Sherman et al., 2006). Our second hypothesis is that visual perception would be associated with overall QoL and specific domains, as found in previous studies in this population (Mitry et al., 2016), and its relationship with academic achievement and everyday motor skills of children with CP (Critten et al., 2018, 2019; James et al., 2015a). Our third hypothesis is that memory would be linked to QoL, as demonstrated in other paediatric populations, highlighting its role in academic settings (Smith, 2009) and its impact on QoL (Hrabok et al., 2013). Finally, we expect to find a relationship between general intellectual functioning and QoL, based on previous results in individuals with CP (Arnaud et al., 2008; Badia et al., 2016; Böling et al., 2016; Jiang et al., 2016; Rapp et al., 2017).

STUDY 3

1. To test whether a home-based computerized executive function intervention produces far transfer effects on other cognitive functions (memory and visual perception).

   Hypothesis: based on previous literature involving interventions targeting executive function tasks in various paediatric populations (Acosta et al., 2019; Bangirana et al., 2011; Grunewaldt et al., 2013, 2016; Løhaugen et al., 2011; Van't Hooft & Norberg, 2010) together with the interrelationship between executive functions and memory skills (Baddeley et al., 2011), we expect to find a far transfer effect of a home-based computerized executive function intervention on learning and memory in children with CP. Furthermore, based on earlier studies conducted on children in which cognitive interventions included executive function tasks (Brock et al., 2018), we also expected to observe enhanced performance in visual perception among the intervention group.

2. To test whether a home-based computerized executive function intervention produces far transfer effects on daily life (QoL and participation), while considering potential variables that could influence the effectiveness of the intervention.

   Hypothesis: considering that executive function interventions have improved QoL (Çalik et al., 2012), together with the fact that executive functions have been associated with QoL in the CP population (Laporta-Hoyos et al., 2017) and other paediatric populations (Sherman et al., 2006), it is expected to observe beneficial effects on QoL and participation after executive function intervention.

3. To determine whether the effects found immediately after the end of the intervention, if any, are maintained for more than half a year.

   Hypothesis: given that the maintenance of far transfer effects on untrained cognitive functions has been found in other child populations (Grunewaldt et al., 2013, 2016), we anticipate observing the preservation of these far transfer effects on cognitive functions during the follow-up assessment.

METHODS

The present thesis comprises three studies, each with a different approach design, to address the general aim of **optimising the effect of cognitive interventions in children with CP**. First, a **systematic review** was conducted to identify previous research on interventions that affect cognitive function in individuals with CP (Study 1). Second, a cross-sectional study was conducted to determine the factors influencing QoL (Study 2). Finally, an **RCT** was implemented to investigate the far transfer effects of a home-based cognitive intervention (Study 3). The following section provides a brief description of the methods used in each study. Due to differences in sample characteristics and study design, the description of each study is explained separately. More detailed information about the methods can be found in the respective methodology descriptions of each study in the Results section of this thesis. The three studies are included in the research project "*Executive training in cerebral palsy: participation, quality of life and brain connectivity*" (ETCONNECT, PSI 2016-75979-R). The research project ETCONNECT was approved by the University of Barcelona's Institutional Ethics Committee, Institutional Review Board (IRB 00003099, assurance number: FWA00004225; http://www.ub.edu/recerca/comissiobioetica.htm).

1. Study 1

1.1. Design

A **systematic review** was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for reporting systematic reviews (Moher et al., 2015). The PRISMA statement is an international guideline that helps authors properly report the results of systematic reviews. It consists of a 27-item checklist and a flow diagram that outlines the essential information to be included in this type of study and guarantees the quality of the reported results. The systematic review protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO; registration number: CRD42020152616) in September 2019.

1.2. Information sources and search strategy

A **literature search** was carried out using the PubMed, PsycINFO, CENTRAL, CINAHL, and ERIC databases through the EBSCO host. The selected databases covered all the relevant literature in the fields of health sciences, psychology, and education. Studies published between January 2010 and December 2021 were included. The first electronic search was performed in October 2019, followed by a second search in December 2021 to update the results. The Participants (P), Interventions (I), Comparisons (C) and Outcomes(O), PICO, approach was used to facilitate the identification and selection of key information needed to formulate and conduct the search. Accordingly, the systematic review focused on (P) participants with a diagnosis of CP; (I) non-pharmacological, non-invasive interventions that did not require highly specialized resources; (C) comparators where the presence of a control group or non-control group; and (O) included outcomes were cognitive outcomes.

To ensure effective electronic search results, the search terms were carefully reviewed considering Medical Subject Heading (MeSH) terms and following the expertise and knowledge of our team. The search terms were: “cerebral palsy” AND (intervention OR rehabilitation OR neurorehabilitation OR training OR therap* OR treatment OR stimulation OR program OR computerized) AND (cogniti* OR executive func* OR language OR memory OR visual percep* OR attention OR neuropsych*). The search items were limited to the title, abstract, and keywords.

1.3. Selection strategy

After eliminating duplicate articles, the titles and abstracts were independently screened by two reviewers. The inclusion criteria are listed in Table 3. Disagreements were resolved through discussion, and when no consensus was reached, a third author resolved any differences. Studies whose titles and abstracts made it difficult to consider inclusion were read in the full text to make a final decision.

Table 3. Inclusion criteria of Study 1.

1) Original articles published in English or Spanish.
2) CP population: participants diagnosed with CP, or when the studies included participants with other conditions, those in which > 75% of participants had CP or the results were presented separately for CP.
3) Therapies that include a cognitive assessment if they were non-invasive, non-pharmacological, and did not require highly specialized resources such as transcranial magnetic stimulation procedures.

Abbreviations. CP, Cerebral Palsy.

1.4. Data collection and quality assessment

Data extraction was performed by two reviewers. The extracted information included: (1) author and year of publication; (2) sample characteristics, such as number of participants, age, type of CP, and motor ability; (3) description of the study design, including type of study, group characteristics, and number of measures; (4) details of the intervention, such as type, frequency, and total dose; and (5) outcome measures, including both cognitive and non-cognitive assessments.

As mentioned above, research on interventions that impact cognitive function is scarce. For this reason, different types of design studies were included to consider all practices that may occur in CP. To classify the quality of these studies, a **quality assessment** was conducted using the Oxford Centre for Evidence-Based Medicine (CEBM) 2011 (OCEBM Levels of Evidence Working Group, 2011). The CEBM Levels of Evidence (LOE) for treatment benefits include five levels: (1) systematic reviews of RCTs or n-of trials; (2) RCTs or observational studies with dramatic effects; (3) non-randomized controlled cohort/follow-up studies; (4) case series, case-control studies, or historically controlled studies; and (5) mechanism-based reasoning.

The **risk of bias** of the **RCTs** (LOE level 2) was evaluated using the Cochrane Collaboration risk of bias tool (Higgins & Green, 2011). This tool covers six domains of bias: sequence generation, allocation concealment, blinding (participants, personnel, and outcome assessors), incomplete outcome data, selective outcome reporting, and other biases. A description of each domain is presented in Table 4. Every risk of bias was classified as low (+), high (-), or unclear risk of bias (?) when there was a lack of information.

Table 4. Cochrane Collaboration's tool for assessing risk of bias, adapted from Higgins et al. (2011).

Bias domain	Source of bias	Description	Examples
Selection	Random sequence generation	Describe the method used to generate the allocation sequence in detail to allow an assessment of whether it should produce comparable results.	*Low risk of bias:* using a computer random number generator. *High risk of bias*: allocation by the judgment of clinician or birthdate.
	Allocation concealment	Describe the method used to conceal the allocation sequence in detail to determine whether intervention allocations could have been foreseen before or during enrolment.	*Low risk of bias:* using sequentially numbered, opaque, and sealed envelopes. *High risk of bias:* translucent envelopes.
Performance	Blinding of participants and personnel	Describe all measures used to blind participants and researchers from knowledge of which intervention a participant received.	*Low risk of bias:* participants and personnel blinding are maintained. *High risk of bias:* incomplete or broken blinding.
Detection	Blinding of outcome assessment	Describe all measures used to blind outcome assessment from knowledge of which intervention a participant received.	*Low risk of bias:* blinding and unlikely that the blinding could have been broken. *High risk of bias:* no blinding and measurement likely to be influenced
Attrition	Incomplete outcome data	Describe the completeness of outcome data for each main outcome, including attrition and exclusions from the analysis. Indicate whether attrition and exclusions were reported, the number of participants in each intervention group (compared with the total number of randomized participants), reasons for attrition or exclusions where reported, and any reinclusions in analyses for the review.	*Low risk of bias:* reasons for missing data not related to outcome. *High risk of bias:* dropouts are very large.
Reporting	Selective reporting outcome	Indicate how selective outcome reporting was examined and what was found.	*Low risk of bias*: all prespecified outcomes are reported. *High risk of bias:* protocol not available and/or outcomes reported incompletely.

2. Studies 2 and 3

2.1. Design

2.1.1. The cross-sectional design

This cross-sectional study (Study 2) investigated the relationship between QoL and cognitive functions in children with CP. Of the 60 participants who participated in the ETCONNECT project, 58 completed the Cerebral Palsy Quality of Life (CP QoL) – Child questionnaire. The neuropsychological assessment and CP QoL questionnaire completed at baseline (T0) were included in Study 2.

2.1.2. The randomized controlled design

Neuropsychological assessment was carried out before the intervention (T0, baseline), immediately after the intervention (T1, post-intervention), and after 9 months the intervention finished (T2, follow-up). The QoL and participation measures were also assessed at T0, T1, and T2.

Randomization

Participants were matched in pairs according to sex, age (8-10.5/10.6-12 years), level of functional grading of the upper limb (MACS levels I-II/III) (Eliasson et al., 2006), and intelligence quotient (<80/≥80) (Raven et al., 2011). The participants were randomly assigned to the intervention or waitlist control groups. The researcher who conducted the neuropsychological assessment was blinded to the group status of the participants (intervention group or waitlist control group) until the data collection was completed.

Intervention group

The intervention consisted of a **computerized home-based executive function program** NeuronUP (www.neuronup.com). The total dose was 30 hours (15 min/session, 10 sessions per week for 12 weeks). The intervention included core executive function, higher-order executive function, and social cognition tasks. The intervention was specifically designed for the ETCONNECT project, incorporating tasks from the program itself as well as additional tasks proposed by the research team. Our team thoroughly selected the tasks of the computerized program. Two psychologists independently analysed the tasks and classified them according to the main domain of executive function they targeted.

After task classification, sessions (n = 120) were created by combining different tasks according to the proportion of domains worked in each session (see Figure 6). The level of difficulty for each task was automatically adjusted, depending on the child's level of performance. Figure 7 shows an example of tasks included in the intervention. A personalized schedule decorated with the children's preferences was delivered, including program instructions, important appointments for neuropsychological assessment, and a specific area designed for recording the activities conducted by the children during the 12 weeks. Adherence was monitored by a health professional by using website reports after each intervention session. The health professional who monitored adherence to the intervention contacted the participant's family weekly to provide feedback on recorded information.

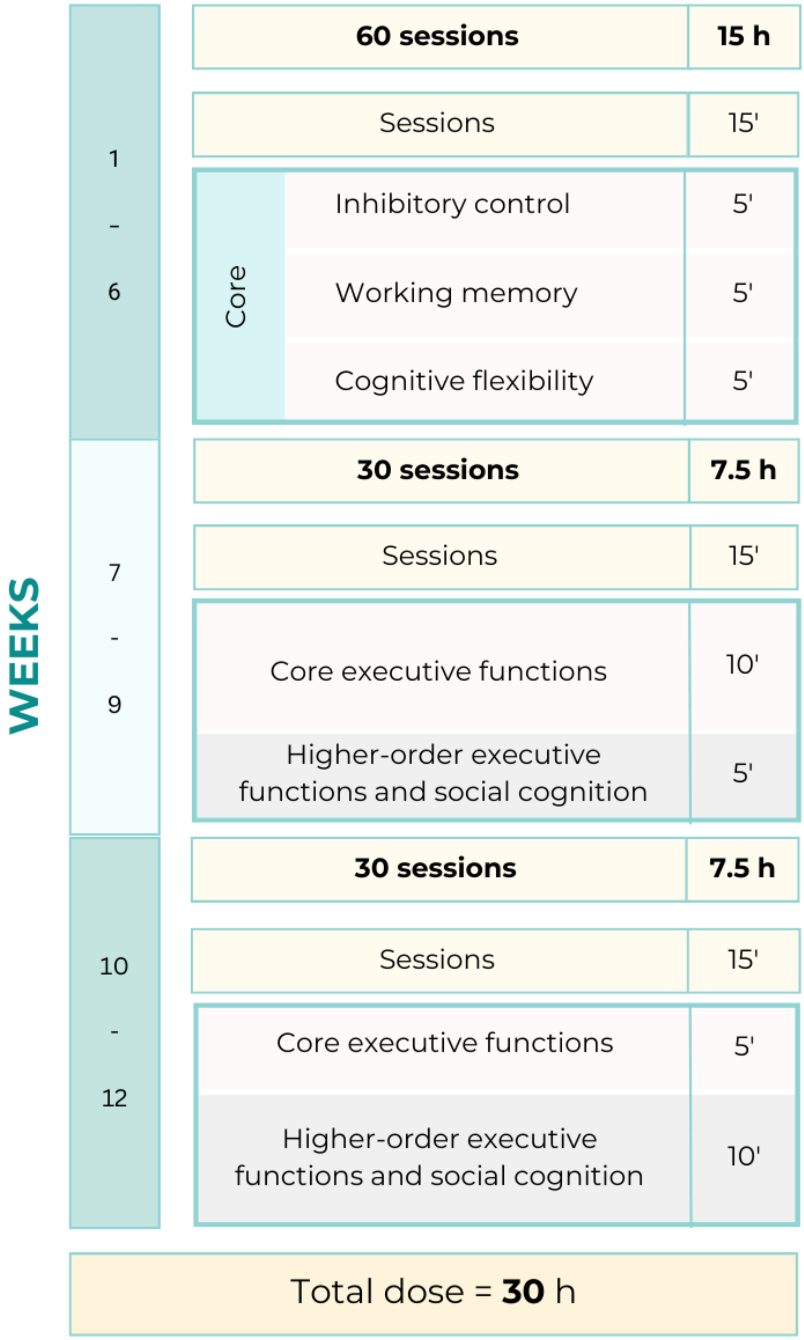


Figure 6. Structure of intervention in RCT, created specifically for this thesis. Abbreviations. RCT, Randomized Controlled Trial.

Figure 7. Example of NeuronUP tasks included in the intervention conducted in Study 3.

Waitlist control group

The participants randomized to the waitlist control group maintained their **usual care**. Children in the waitlist control group also received a personalized schedule with important information and a specific area to register the activities conducted by the children during the 12-week period, to ensure that no changes in routine occurred. Health professionals contacted the participants' families weekly to maintain adherence. Once the children in the waitlist control group completed the three neuropsychological assessments (T0, T1, and T2), the intervention was offered.

2.2. Participants

Studies 2 and 3 shared a common recruitment process (Figure 8). Participants were recruited from the Sant Joan de Déu-Barcelona Children's Hospital (Department of

Neurology and Rehabilitation and Physical Medicine), Vall d'Hebron University Hospital (Department of Rehabilitation and Physical Medicine), and ASPACE Catalunya Foundation (Department of Health Services and Rehabilitation) in Barcelona. Health professionals from these institutions (such as paediatric neurologists and occupational therapists) informed parents of potential participants about the possibility of participating in the research project. The protocol was registered at ClinicalTrials.gov (NCT04025749) and published (García-Galant et al., 2020). In addition to these institutions, the sample was recruited from our project website (https://etconnectub.wixsite.com/etconnect) and from a previous study by the research group (Ballester-Plané et al., 2016).

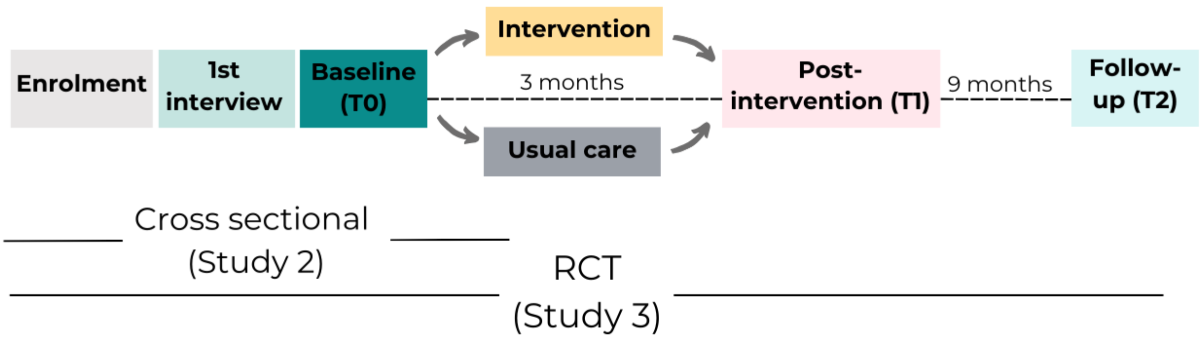


Figure 8. Design of the studies 2 and 3, created specifically for this thesis.
Abbreviations. RCT, Randomized Controlled Trial.

Parents who were interested in participating received a phone call from a team member to provide details about the study, including its purpose, procedures, and duration. Once willingness to participate was confirmed, team members arranged their first appointment. The study procedure consisted of a minimum of four appointments, including the appointment mentioned, over a period of one year.

At the first visit, once team members ensured that the participants met the inclusion criteria (Table 5), all participants' caregivers signed a written informed consent form in accordance with the Helsinki Declaration. Subsequently, parents were interviewed to obtain demographic and clinical data. Children were assessed to confirm the inclusion criteria for basic grammar comprehension. General intellectual functioning was also assessed at the same visit, which was used as a matching criterion in Study 3.

Once the participants were randomly allocated to the intervention or waitlist control group, three neuropsychological assessments were performed to determine cognitive functioning before the intervention (T0), after the intervention (T1), and 9 months after the intervention finished (T2). Enrolment started in November 2017, and the anticipated data collection was expected to be completed in April 2020. Data collection was extended to January 2022 because of the severe lockdown in Spain during the Covid-2019 pandemic.

Table 5. Inclusion and exclusion criteria of Studies 2 and 3.

Inclusion criteria	Exclusion criteria
▪ Clinical diagnosis of CP. ▪ Age from 8 – 12 years old. ▪ MACS I – III (Eliasson et al., 2006) ▪ Competency to understand simple instructions as assessed by the STSG (Toronto, 1973). ▪ Availability to participate in the study for one year. ▪ Accessibility to internet at home.	▪ Severe hearing and/or visual difficulties that preclude neuropsychological assessment and cognitive intervention.

Abbreviations. CP, Cerebral Palsy; MACS, Manual Ability Classification System; STSG, Screening Test of Spanish Grammar.

2.3. Assessment

2.3.1. Demographic and clinical data

The children's medical records were reviewed to obtain demographic and clinical data. The demographic data included age, sex, and socioeconomic variables. Clinical variables included (1) functional ability, such as motor and communication measures (Table 6), (2) motor CP type and distribution of motor impairment; (3) gestational age; and (4) presence of additional symptoms (e.g., epilepsy and pain). Additionally, interviews with the parents were conducted to complete the information.

Table 6. Classification systems used to measure functional status.

Functional ability		Classification system
Motor function	Gross motor	GMFCS (Palisano et al., 2008)
	Manual ability	MACS (Eliasson et al., 2006)
		BFMF (Elvrum et al., 2016)
Communication	Everyday communication	CFCS (Hidecker et al., 2011)
	Speech production	VSS (Pennington et al., 2013)

Abbreviations. BFMF, Bimanual Fine Motor Function; CFCS, Communication Function Classification System; GMFCS, Gross Motor Function Classification System; MACS, Manual Ability Classification System; VSS, Viking Speech Scale.

2.3.2. Neuropsychological assessment

A **comprehensive neuropsychological test** battery was used to evaluate the cognitive functions of the participants in Studies 2 and 3. The tests were carefully selected to minimize the influence of motor skills and execution time, ensuring that the majority of the participants could respond autonomously. The test selection was based on previous research findings on people with CP (Di Lieto et al., 2017; Piovesana et al., 2015; Pirila et al., 2004), including the research experience of our team in previous projects (Ballester-Plané et al., 2016; Laporta-Hoyos et al., 2017; Pueyo et al., 2008, 2009). Neuropsychological assessments included measures of general intellectual functioning, executive functions, visual perception, and memory. Table 7 shows the performance-based tests used in each study.

The duration of the neuropsychological assessment depended on the case, varying between two and five hours. In cases where fatigue was present or the evaluation exceeded 2 hours, the assessment was conducted in two or three separate appointments to avoid fatigue that could influence the results. It should be noted that the original tests were used, and no adaptations in the administration or scoring of the tests were used. Finally, the raw scores were converted into standardized scores to homogenise the scores across different tests by correcting for age and providing clinical significance to the interpretation. IQ scores were used for general intellectual functioning, and Z-scores for specific cognitive functions. A parent-proxy-reported version of the Behavior Rating Inventory of Executive Function–Second Edition (BRIEF-2) was used to assess the behavioural manifestation of executive functioning in everyday life (Gioia et al., 2000). No participant scored below 70 in general intellectual functioning. The number of participants in the sample with impairments in each cognitive function is presented in Table 8. For extended details on cognitive impairments within each group at the three time points (T0, T1, and T2) refer to Annex 1.

Table 7. Neuropsychological performance-based tests.

Cognitive function		Test	Study 2	Study 3
General intellectual functioning		RCPM (Raven et al., 2011)	✓	✓
Executive functions	Inhibitory control	Digit Total Score – WISC-V (Wechsler et al., 2015)	✓	
		Auditory Attention – NEPSY-II (Korkman et al., 2014)	✓	
	Working memory	Digit Span Backward – WISC-V (Wechsler et al., 2015)	✓	
	Cognitive flexibility	Response Set – NEPSY-II (Korkman et al., 2014)	✓	
	Planning	Tower – D-KEFS (Delis et al., 2001)	✓	
Social cognition		Theory of Mind – NEPSY-II (Korkman et al., 2014)	✓	
Memory	Immediate, verbal	Digit Span Forward – WISC-V (Wechsler et al., 2015)		✓
	Immediate, visual	Spatial Span Forward – WNV (Wechsler & Naglieri, 2006)		✓
	Learning and long-term, verbal	Word Selective Reminding – TOMAL (Reynolds, 1998)	✓	✓
	Learning and long-term, visual	Memory for Designs – NEPSY-II (Korkman et al., 2014)	✓	✓
Visual perception	Object recognition	Facial Recognition Test (Benton et al., 1994)	✓	✓
	Visual spatial perception	Arrows – NEPSY-II (Korkman et al., 2014)	✓	✓

Abbreviations. D-KEFS, Delis-Kaplan Executive Function System; NEPSY-II, A Developmental NEuroPSYchological Assessment-Second Edition; RCPM, Raven's Coloured Progressive Matrices; TOMAL, Test of Memory and Learning; WISC-V, Wechsler Intelligence Scale for Children-Fifth Edition; WNV, Wechsler Non-Verbal Scale of Ability.

Table 8. **Participants with impaired cognition at baseline** (n = 60).

Neuropsychological outcome	Measure	n	%
Executive functions			
Inhibitory control	Digit Total Score – WISC-V	21 [a]	35
	Auditory Attention – NEPSY-II	17 [a]	28
Working memory	Digit Span Backward – WISC-V	13 [a]	22
Cognitive flexibility	Response Set – NEPSY-II	23 [a]	38
Planning	Tower – D-KEFS	14 [a]	23
Executive functions in daily life	Behavioral Regulation Index – BRIEF-2	19 [b]	32
	Emotional Regulation Index – BRIEF-2	24 [b]	41
	Cognitive Regulation Index – BRIEF-2	24 [b]	42
	Global Index of Executive Function – BRIEF-2	24 [b]	42
Social cognition	Theory of Mind	21 [a]	35
Memory			
Immediate, verbal	Digit Span Forward – WISC-V	9 [a]	15
Immediate, visual	Spatial Span Forward – WNV	18 [a]	30
Learning, verbal	Word Selective Reminding – TOMAL	22 [a]	37
Learning, visual	Memory for Designs – NEPSY-II	29 [a]	48
Long-term, verbal	Word Selective Reminding Delayed – TOMAL	9 [a]	15
Long-term, visual	Memory for Designs Delayed – NEPSY-II	28 [a]	47
Visual perception			
Object recognition	Facial Recognition Test	6 [a]	10
Visual spatial perception	Arrows – NEPSY-II	24 [a]	40
Psychological adjustment	Total difficulties SDQ	10 [c]	18
ASD traits	ASSQ	9 [d]	16

Notes. [a] Impairment was determined by considering a Z-score < -1.5; [b] Impairment was determined by considering a T-score > 65; [c] Presence of behavioral problems was considered by direct scores ≥ 17; [d] Presence of ASD was considered by direct scores > 19.

Abbreviations. ASSQ, Autism Spectrum Screening Questionnaire; BRIEF-2, Behavior Rating Inventory of Executive Function-Second Edition; D-KEFS, Delis-Kaplan Executive Function System; NEPSY-Second Edition, A Developmental NEuroPSYchological Assessment-II; RCPM, Raven's Coloured Progressive Matrices; SDQ, Strengths and Difficulties Questionnaire; TOMAL, Test of Memory and Learning; WISC-V, Wechsler Intelligence Scale for Children-Fifth Edition; WNV, Wechsler Non-Verbal Scale of Ability.

2.3.3. Quality of life and participation

QoL and **participation** were assessed to evaluate the daily activities. The CP QoL-Child questionnaire was used to assess QoL. The CP QoL-Child questionnaire contains seven domains: Social Well-being and Acceptance, Participation and Physical Health, Feelings about Functioning, Emotional Well-being and Self-Esteem, Pain and Impact of Disability, Access to Services, and Family (Waters et al., 2007). The Participation and Environment Measure for Children and Youth (PEM-CY) questionnaire was used to assess participation in home, school, and community activities (Coster et al., 2011). The proxy-reported versions of both questionnaires were completed by participants' parents. A summary of proxy-reported questionnaires included in each study is presented in Table 9.

Table 9. Proxy-reported questionnaires.

Outcome	Questionnaire	Study 2	Study 3
Executive functions in daily life	BRIEF-2 (Gioia et al., 2000)	✓	
Quality of life	CP QoL-Child (Waters et al., 2007)	✓	✓
Participation	PEM-CY (Coster et al., 2011)	✓	✓

Abbreviations. BRIEF-2, Behavior Rating Inventory of Executive Function-Second Edition; CP QoL, Cerebral Palsy Quality of Life Questionnaire; PEM-CY, Participation and Environment Measure for Children and Youth.

3. Statistical analyses

3.1. Study 1

In addition to following the standard PRISMA guidelines, **effect sizes** were calculated when the data allowed it, to facilitate comparison between studies. Moreover, the effect sizes reported by the authors were coded. To compare the results across different studies (RCT and non-RCTs), individual effect sizes (standardized mean differences) were calculated and transformed into a common metric (Morris & DeShon, 2002)

3.1.1. Effect size for controlled trials

In controlled trials (levels 2 and 3 of LOE), the effect size was calculated as a pre-post mean change in the treatment group minus the pre-post mean change in the control group divided by the pooled pre-intervention standard deviation with a bias adjustment (d_{ppc2}). The d_{ppc2} formula is as follows (Morris, 2008):

$$d_{ppc2} = Cp\left[\frac{(M_{post,T} - M_{pre,T}) - (M_{post,C} - M_{pre,C})}{SD_{pre}}\right]$$

The $\mathrm{M}_{\mathrm{pre,T}}$ and $\mathrm{M}_{\mathrm{post,T}}$ indicate the pre- and post-test mean for the intervention group, respectively. Likewise, the $\mathrm{M}_{\mathrm{pre,C}}$ and $\mathrm{M}_{\mathrm{post,C}}$ indicates the pre- and post-test mean for the control group.

Where $$\mathrm{C_p} = 1 - \frac{3}{4\,(\mathrm{n_t}+\mathrm{n_c}-2)-1}$$

The n_T consist in the number of participants in intervention group and the n_C in the control group.

The pooled standard deviation (SD_{pre}) is defined as:

$$SD_{pre} = \sqrt{\frac{(n_T - 1)\, SD^2_{pre,\,T} + (n_c - 1)\, SD^2_{pre,\,C}}{n_T + n_c - 2}}$$

The standard deviations for the intervention and control groups are $SD_{pre,\,T}$ and $SD_{pre,\,C}$, respectively.

3.1.2. Effect size for non-controlled trials

In uncontrolled trials (level 4 of LOE), the effect size (d) was calculated as pre-post changes in the mean divided by the standard deviation of the pre-intervention with a bias adjustment. The d formula was (Morris & DeShon, 2002):

$$d = C\left[\frac{\left(M_{post} - M_{pre}\right)}{SD_{pre}}\right]$$

The M_{pre} and M_{post} are the pre and post-test means for the groups, respectively. The SD_{pre} indicates the standard deviation in the pre-test measure. C is calculated using next formula:

$$C = 1 - \frac{3}{4\,(n-1)\,1}$$

Effect sizes were interpreted according to Cohen's criteria: small (0.2), medium (0.5), and large (0.8).

3.2. Studies 2 and 3

Statistical analyses were performed using IBM SPSS Statistics version 25 (Studies 2 and 3) and R 4.2.2 (Study 3). The assumption conditions for each analysis were examined. Descriptive statistics were used to report participants' demographic and clinical characteristics.

3.2.1. Study 2

Pearson, Spearman, and Kendall **bivariate correlations** were performed to analyse the relationship between QoL domains/total scores and other variables (demographic, clinical, neuropsychological, and psychosocial). Linear regression models (stepwise method) were used to identify the best explanatory models for the total score and domains of the questionnaire. Variables that correlated significantly after the Holm-Bonferroni correction were introduced into the linear regression model.

3.2.2. Study 3

To address the aims of Study 3, **analyses of covariance** (ANCOVAs) per-protocol were performed to compare the differences between the intervention and waitlist control groups. The pre-intervention score for each outcome was introduced as a covariate in the models. Furthermore, the effects of other variables (pain, ASD traits, psychological adjustment, family QoL, and parental stress), described in Table 10, were considered as potential covariates. Pearson, Spearman, and Kendall bivariate correlations were performed using the Bonferroni correction (p=0.01). After the Bonferroni correction, significant variables were introduced as covariates in the ANCOVAs model. Intention-to-treat analyses were performed to compare the results, including all participants, with the baseline measure of each outcome.

Table 10. Covariates included in Study 3.

Covariates	Measure
Physical pain	Bodily Pain and Discomfort – CHQ (Landgraf, 2020)
ASD traits	ASSQ (Ehlers et al., 1999)
Psychological adjustment	Total Difficulties Score – SDQ (Goodman, 1997)
Family QoL	FQoL (Hoffman et al., 2006)
Parental stress	PSS (Berry & Jones, 1995)

Abbreviations. ASSQ, Autism Spectrum Screening Questionnaire; CHQ, Child Health Questionnaire; FQoL, Beach Center Family Quality of Life Scale; PSS, Parental Stress Scale; SDQ, Strengths and Difficulties Questionnaire.

RESULTS

In this section, we present the three original studies compiling the present thesis.

STUDY 1

Interventions with an Impact on Cognitive Functions in Cerebral Palsy: a Systematic Review

Neuropsychology Review (2023)

Blasco, M., García-Galant, M., Berenguer-González, A., Caldú, X., Arqué, M., Laporta-Hoyos, O., Ballester-Plané, J., Miralbell, J., Jurado, M.A. & Pueyo, R.

Abstract

This systematic review aimed at investigating those interventions that impact on cognitive functioning in children and adults with cerebral palsy (CP). A systematic database search was conducted and twenty-eight studies suitable for inclusion were identified, of which only nine were randomized controlled trials (RCTs). Among all the studies included, ten were multi-modal (cognitive and physical tasks), eleven physical, five cognitive, and two alternative and augmentative communication interventions. The evidence suggests that multi-modal and physical interventions improve general cognitive functioning. Multi-modal and cognitive interventions have an impact on visual perception. Both interventions, together with physical interventions have an effect on a specific executive function domain (inhibitory control), and only cognitive interventions improved other executive function domains such as working memory. However, no RCT assessed the effects of all executive function domains. Few studies have looked at interventions to improve memory and language, and there is a scarcity of long-term research. Future RCTs must be of higher quality and better account for age and sex differences, as well as the clinical heterogeneity of CP. To date, there is evidence that multi-modal, cognitive or physical interventions have an impact on general cognitive functioning, visual perception and executive functions in children with CP, which may support their cognitive development.

The protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO): CRD42020152616.

1. Introduction

Cerebral palsy (CP) is the most common cause of childhood physical disability, with an overall median prevalence estimated at 2.11 per 1000 live births (Oskoui et al., 2013; SCPE, 2000). Attributed to non-progressive disturbances that occurred in the developing fetal or infant brain (Rosenbaum et al., 2007), CP is a life-long condition associated with permanent disorders of movement and/or posture development that causes activity limitations. The motor impairments in CP are often accompanied by disturbances of sensation, cognition, perception, communication, and behavior. To date, research into CP has focused on aspects related to motor function, such as its assessment and treatment, but there is a growing body of literature that recognizes the importance of associated cognitive impairments in daily life (Gosling, 2017; Rosenbaum et al., 2007; Straub & Obrzut, 2009).

Intellectual impairment can lower physical and mental health (Beckung et al., 2008; Parkes et al., 2008) and affect both quality of life and participation in the diverse life situations of children with CP (Arnaud et al., 2008; Dickinson et al., 2007; Fauconnier et al., 2009). There is a broad variability in intellectual impairment, with some people having normal intelligence quotient (IQ) and others having low IQ. Indeed, 30 – 50% of people with CP have low intelligence (IQ < 70) (Delacy et al., 2016; Fluss & Lidzba, 2020; Novak et al., 2012; Stadskleiv, 2020), while 28% show severe intellectual impairment (IQ < 50) (Novak et al., 2012). Cognitive domains commonly affected in CP are visual perception, executive functions, memory and language (Bottcher, 2010; Fluss & Lidzba, 2020; Stadskleiv, 2020).

Visual perception is the cognitive domain mostly affected in CP. It refers to the capacity to analyze and process visual information, including facial and object recognition, visual spatial discrimination, and appraisal of spatial relations. A systematic review (Ego et al., 2015) found that 40 – 50% of children with CP may experience impairments in visual perception. These appear very early in life and persist throughout adolescence (Paul et al., 2014), regardless of the type of CP, laterality of motor impairment, IQ, neuro-ophthalmological outcomes or presence of seizures (Ego et al., 2015; Murias et al., 2014; Paul et al., 2014; Stiers & Vandenbussche, 2004). Impairments in this function are important to quality of life (Mitry et al., 2016).

Difficulties in multiple domains of executive function, such as working memory, inhibitory control, and planning, have also been reported in CP (Bodimeade et al., 2013; Bottcher et al., 2009; Di Lieto et al., 2017; Freire & Osório, 2020; Gagliardi et al., 2011; Pirila et al., 2011). It is known that more than half of the children with CP have deficits in their attention and executive functions (Di Lieto et al., 2017; Pirila et al., 2011), with the executive impairments present in pre-school age children (Freire & Osório, 2020) and persisting in adolescence and adulthood (Pueyo et al., 2009). Executive functions have also been suggested to determine quality of life in CP (Laporta-Hoyos et al., 2017).

Although learning and memory problems have been identified in children and adolescents with CP, few studies have focused on them, and when they have, results have been inconclusive (Ballester-Plané et al., 2018; Fluss & Lidzba, 2020; Østensjø et al., 2003; Pueyo et al., 2009; Toomela, 2012). The few available findings suggest that nearly half of the children show learning problems and that these impairments persist in adulthood (Østensjø et al., 2003; Toomela, 2012). Østensjø et al. (2003) reported that learning problems were strongly related to self-care, mobility, and social functioning.

Studies of language indicate that 61% of children with CP present language impairments and that 15% use augmentative and alternative communication (AAC) (Mei et al., 2016; Virella et al., 2016). Language skills are important for acquiring skills in reading, spelling and writing, and they are related to participation and social functioning in children (Schenker et al., 2005; Voorman et al., 2010).

Together, research suggests that children with CP present with cognitive impairments that adversely affect quality of life, participation in different situations, and social functioning. Furthermore, cognition not only plays a role in daily life but also seems to mediate the effectiveness of specific motor treatments for CP (Fazzi et al., 2005; Kim et al., 2006). In one review, it was found that attention was critical to the success of motor rehabilitation (Reid et al., 2015a).

Moreover, CP is a long-life disorder for which life expectancy depends on the severity of associated impairments, with some people having a normal expectancy (Amankwah et al., 2020; Himmelmann & Sundh, 2015). The World Health Organization considers that cognitive training reduces the risk of cognitive decline and/or dementia (World Health Organization, 2019). Thus, it is necessary to identify efficient interventions to treat neuropsychological deficits in adults with CP, which may help to prevent cognitive decline.

Given the importance of cognitive impairment in CP, interest has grown to discover interventions to improve these functions (Mak et al., 2018; Piovesana et al., 2017). However, there has been no specific systematic review outlining the findings of cognitive interventions in children and adults with CP. Existing systematic reviews about interventions in CP have mainly centered on the effectiveness of physical training in motor abilities in children (Anttila et al., 2008; Dewar et al., 2015; Dodd et al., 2002; Morgan et al., 2016a; Myrhaug et al., 2015; Verschuren et al., 2008). Others, by contrast, have focused on specific therapies for motor abilities, including constraint-induced movement therapy (Dong et al., 2013; Hoare et al., 2007), hydrotherapy (Roostaei et al., 2017), hippotherapy (Whalen & Case-Smith, 2012), surgery (McGinley et al., 2012), and virtual reality (Ravi et al., 2017). Only one systematic review (Novak et al., 2013), which was recently updated (Novak et al., 2020), has considered all interventions for children with CP. Novak et al. (2013, 2020) through a helicopter view method have allowed the possibility to have a general description of all existing interventions but have not provided specific details of different cognitive domains. Moreover, there have been no previous reviews of interventions to improve cognition in adults with CP.

The aim of the present systematic review was to outline the evidence for interventions with an impact on cognitive functioning in children and adults with CP and to identify the potential gaps in the literature. This knowledge is key to understanding the current state of the field and to driving future research.

2. Methods

This systematic review was registered in PROSPERO: International Prospective Register of Systematic Reviews (CRD42020152616), and it was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guideline (Moher et al., 2015). Study selection, data extraction and quality assessment were conducted by two independent reviewers, with any disagreements solved by consensus or by an external reviewer when no agreement was reached. Agreement between reviewers was assessed with Cohen's Kappa Coefficient (k) (Cohen, 1960).

2.1. Search strategy

A systematic electronic search was conducted using EBSCO host to search PubMed, PsycINFO, Central Register of Controlled Trials (CENTRAL), CINAHL, and ERIC databases. The following search terms were used: "cerebral palsy" AND (intervention OR rehabilitation OR neurorehabilitation OR training OR therap* OR treatment OR stimulation OR program OR computerized) AND (cogniti* OR executive func* OR language OR memory OR visual percep* OR attention OR neuropsych*). Search terms were selected using Medical Subject Heading (MeSH) terms and contributing authors' knowledge of the field. The electronic search was performed in October 2019 and updated in December 2021, including papers published between January 2010 and December 2021.

2.2. Selection process

All articles retrieved by the systematic search were initially screened for eligibility by title and abstract review. The eligibility criteria were as follows: (1) original articles published in English or Spanish; (2) participants were diagnosed with CP, or when the studies included participants with other conditions, those in which >75% of participants had CP or the results were presented separately for CP; and (3) therapies that include a cognitive assessment if they were non-invasive, non-pharmacological, and did not require highly specialized resources such as transcranial magnetic stimulation procedures.

2.3. Data extraction

Data were extracted regarding (1) author and year of publication; (2) sample (number of participants, age, type of CP, and motor ability); (3) study (type, group characteristics and number of measures); (4) intervention (type, frequency, and total dose); (5) cognitive outcomes; and (6) non-cognitive outcomes.

2.4. Quality assessment

A qualitative evaluation of the studies was performed according to the Oxford Centre for Evidence Based Medicine (CEBM) 2011 (OCEBM Levels of Evidence Working Group, 2011). Level of evidence was graded from 1 (high) to 5 (low): level 1, systematic review of randomized controlled trials (RCTs) or n-of-trials; level 2, RCTs or observational study with a dramatic effect; level 3, non-randomized controlled cohort/follow-up study; level 4, case series, case-control study or a historically controlled study; and level 5, mechanism-based reasoning. Risk of bias in RCTs was assessed with the Cochrane Collaboration's risk of bias tool by considering sequence generation, allocation concealment, blinding (participants, personnel and outcome assessors), incomplete outcome data, and selective outcome reporting (Higgins & Green, 2011).

2.5. Effect size

In order to compare results across different studies, individual effect sizes (standardized QoL difference) were calculated and transformed into a common metric in significant results (Morris & DeShon, 2002), when data allowed it. In controlled trials (levels 2 and 3 of LOE), effect size (d_{ppc2}) was calculated through the pre-post QoL change in the intervention group minus the pre-post QoL change in the control group divided by the pooled pre-intervention standard deviation with a bias (Morris, 2008). In uncontrolled trials (level 4 of LOE), effect size (d) was calculated based on the pre-post changes in QoL divided by the pre-intervention standard deviation with a bias adjustment (Morris, 2002). Cohen's interpretative criteria was applied considering small (.2), medium (.5) and large (.8) effects (Cohen, 1992).

3. Results

The results of the search strategy are shown in Figure 1. The searches returned 2428 articles: 973 from PubMed, 405 from PsycINFO, 551 from CENTRAL, 466 from CINAHL, and 33 from ERIC. Removing duplicates resulted in 1611 articles, and screening titles and abstracts resulted in 93 full-text articles for review. Finally, 30 articles were considered eligible for inclusion and were analyzed in the qualitative analysis (87% written in or after 2015). When data from a study was reported in more than one publication, it was considered a single study (James et al., 2015b; Mak et al., 2018, 2020; Piovesana et al., 2017). The findings of the twenty-eight included studies are summarized in Tables 1 and 2. Table 1 includes studies with a higher quality and Table 2 includes studies with a lower quality. Overall, the agreement between reviewers was good, with a k between 0.74 and 0.79.

3.1. Sample characteristics

The characteristics of the 670 participants included in the twenty-eight reviewed studies are presented in Table 3. Age ranged from 15 weeks to 29 years. Among those studies that reported sex, 312 (49%) participants were female. Of the twenty-eight studies, twenty-five included only children and the remaining three included young adults (Peny-Dahlstrand et al., 2018; Sajan et al., 2017; Teixeira-Machado et al., 2017). Concerning studies where type of CP was reported, 98% of the participants were diagnosed with spastic CP. The Gross Motor Function Classification System (GMFCS) level of participants was included in seventeen studies, amounting to 410 participants. Most had mild motor impairment, with a GMFCS of I (n = 162) or II (n = 136), indicating that they could walk independently or with assistive devices.

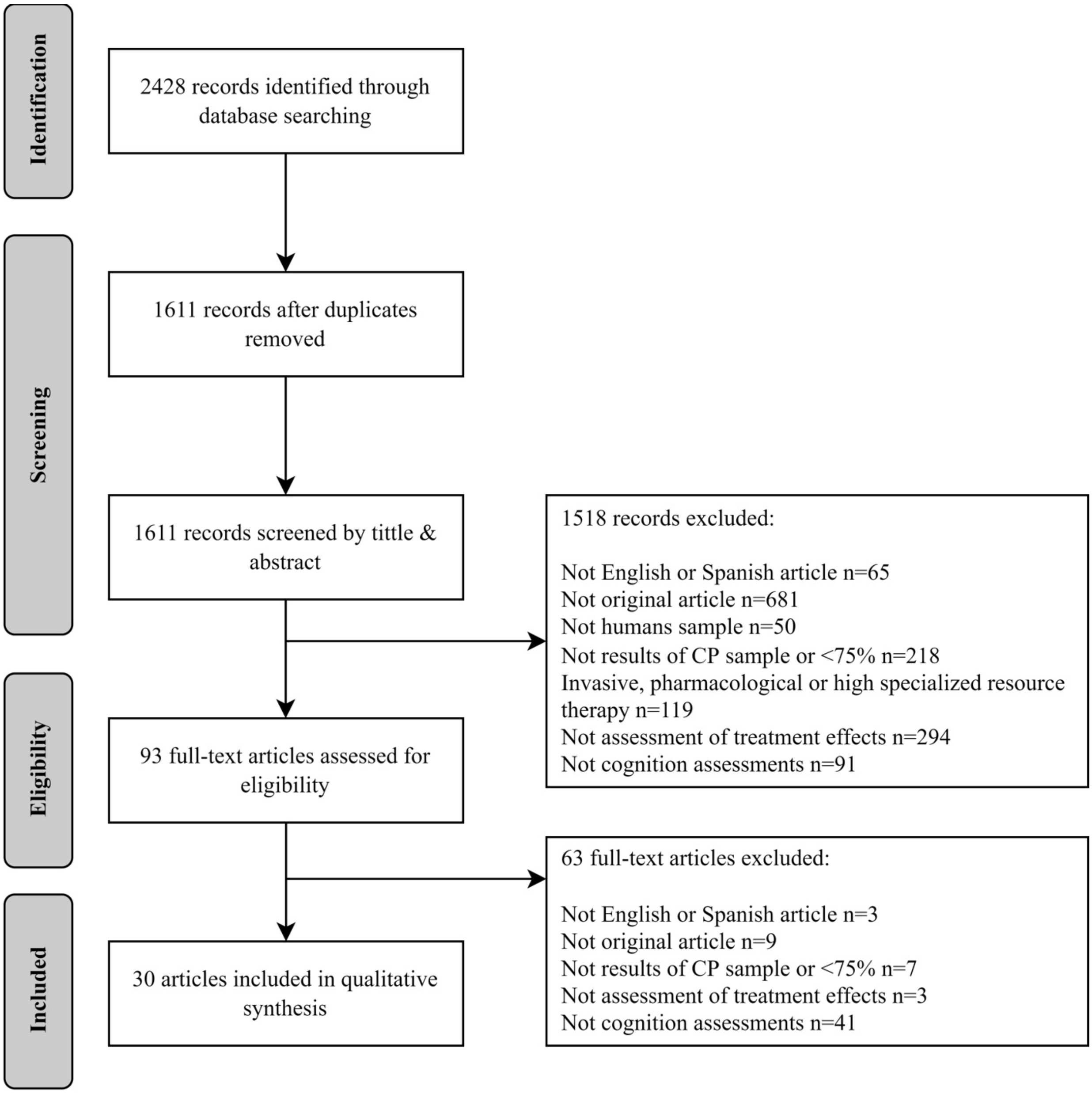


Figure 1. PRISMA Flow Diagram of Included Articles.

Abbreviations. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-analysis.

3.2. Dose

Both the duration and intensity of the interventions varied across the studies. Intervention duration in studies with more than one session ranged from 6 to 216 hours. There were also large differences among studies in the number of weeks each intervention lasted, including less than 7 weeks (Christensen et al., 2017; Di Lieto et al., 2021; Heathcock et al., 2015; Lakes et al., 2019; Martiny & Aggerholm, 2016;

Ramkumar & Gupta, 2016; Sajan et al., 2017), 8–12 weeks (Alwhaibi et al., 2020; Aran et al., 2020; Cherriere et al., 2020; Cho et al., 2015; Desai et al., 2014; Hsieh et al., 2017; Lins et al., 2019; Mak et al., 2018; Muriel et al., 2014; Shin & Song, 2016; Soto & Clarke, 2018; Teixeira-Machado et al., 2017; Yildirim et al., 2021), and more than 12 weeks (Ahn et al., 2021; Bilde et al., 2011; Morgan et al., 2016b; Pereira et al., 2019; Piovesana et al., 2017; Sørensen et al., 2016). One study performed training in a single 45 minute session (Abuin-Porras et al., 2019). Finally, one study did not report the number of weeks of intervention (Peny-Dahlstrand et al., 2018).

3.3. Risk of bias

The methodological quality (level of evidence) of the twenty-eight included studies was assessed, indicating level 2, 3, and 4 evidence in nine (32%), one (4%), and eighteen (64%) studies, respectively. A summary of the risk of bias in studies classified as level 2 (RCT) is shown in Figures 2 and 3. Studies were classified from low to high risk of bias (Figure 2). The study by Piovesana et al. (2017) was considered to have the lowest risk of bias (83% low risk of bias), followed by Aran et al. (2020), Mak et al. (2018), Morgan et al. (2016) and Sajan et al. (2017) (67% low risk of bias). Among the nine level 2 studies, the risk of bias due to lack of blinding of participants and personnel was high in four and unclear in the other four; three studies had a high risk of bias for blinding of outcomes, while this was unclear in five studies; high risk of attrition bias was detected in only one of the nine studies. A lack of information hindered analysis of every bias overall, resulting in complete analysis being possible for only one of the six biases (reporting bias).

3.4. Characteristics of the interventions

Intervention type was classified according to the author's descriptions and varied considerably among studies: ten used multi-modal interventions (cognitive and physical tasks), eleven used physical interventions, five used cognitive interventions, and two used AAC. Characteristics of studies are presented in Tables 1 and 2.

Table 1. Summary of Interventions with an Impact on Cognitive Functions in Cerebral Palsy of Studies with a Higher Quality.

Reference	LOE	Participants	Intervention	Cognitive Outcomes
Authors (year)	n	n = (IG/CG) Age range (IG: QoL ± SD/CG: mean ± SD) Type CP (n) Motor ability	**Name** (*type of intervention*) Description of intervention IG: time per day, times per week, number of weeks (total dose) CG: type of Control Group	$Test_1$: $result_1$ ↑ (p, d / η_p^2: effect size reported by authors [a], d_{ppc2}: effect size calculated) $Test_2$: $result_2$ ↓ $Test_3$: $result_3$ =
Piovesana et al. (2017); **James et al.** (2015b)	2	n = 102, 1 abandoned (51/50) 8-18 years (IG: 11.6 ± 2.3/CG: 11.9 ± 2.5) Spastic unilateral (102) GMFCS I (45), II (56) MACS I (24), II (76), III (1)	**Mitii** (*multi-modal intervention*) A multi-modal web-based program: upper limb, cognitive, visual perceptual and physical activity training IG: 20-30 minutes per day, six times per week, 20 weeks (60 hours) CG: standard care	IG compared with CG WISC-IV: Digit span backwards: = (p=.2) Coding: = (p=.07) Symbol search: = (p=.08) D-KEFS: Inhibition, color-word interference subtest: = (p=.17) TMT number letter sequencing: = (p=.35) Tower test: = (p=.28) TVPS-3: Overall: ↑↑ (p<001, d_{ppc2}=.49) Visual discrimination: ↑↑ (p=.017, d_{ppc2}=.41) Visual memory: = (p=.11) Spatial relations: ↑↑ (p=.01, d_{ppc2}=.32) Form constancy: = (p=.07) Sequential memory: = (p=.07) Figure ground discrimination: = (p=.07) Visual closure: ↑↑ (p=.03, d_{ppc2}=.34) BRIEF-Parents[1]: Behaviour regulation index: = (p=.24) Metacognition index: = (p=.07) Global executive: = (p=.34)

Table 1 (continued).

Reference	LOE	Participants	Intervention	Cognitive Outcomes
Aran et al. (2020)	2	n = 90 (45/45) 7-12 years (IG: 11.18 ± 3.37/CG: 11.06 ± 3.24) Spastic unilateral (90) GMFCS I (59), II (31) MACS I (26), II (55), III (9)	**Virtual reality intervention** (*multi-modal intervention*) An interactive computerized gaming that includes racing, boxing, air diving and penalty shootout games IG: 45 minutes per day, twice per week, 10 weeks + traditional occupation therapy (15 hours) CG: traditional occupation therapy	IG compared with CG DOTCA-Ch: Orientation: ↑↑ (p=.04, d_{ppc2} =.02) Spatial perception: ↑↑ (p <.001, d_{ppc2}=.39) Praxis: ↑↑ (p <.001, d_{ppc2}=.50) Visuomotor construction: ↑↑ (p <.001, d_{ppc2}=.26) Thinking operations: ↑↑ (p=.04, d_{ppc2}=.02)
Ahn et al. (2021)	2	n = 47, 1 abandoned (23/23) 6-13 years (IG: 7.78 ± 1.68/CG: 7.30 ± 1.61) Type CP n.a. Motor ability n.a.	**Equine-assisted activities program** (*physical intervention*) IG: group therapy, 40 minutes per day, twice per week, 16 weeks (21.3 hours) CG: standard care	IG compared with CG CPT-II: Inattention, hit RT commissions: = (p=.35) Inattention, hit RT omissions: = (p=.65) Inattention, hit RT standard error: = (p=.13) Inattention, hit RT detectability RT for target vs non-target: = (p=.35) Inattention, hit RT: = (p=.22) Vigilance, perseverations: ↑↑ (p=.02, d_{ppc2}=.57) ARS parents[1]: Inattention: = (p=.89) Hyperactivity: = (p=.59) Total: = (p=.71)

Table 1 (continued).

Reference	LOE	Participants	Intervention	Cognitive Outcomes
Alwhaibi et al. (2020)	2	n = 45 (15/15/15) 5-8 years (Group A: 6.7 ± 0.8/Group B: 6.6 ± 0.7/Group C: 6.4± 0.8) Spastic unilateral (45) Motor ability n.a. MACS I-II (45)	**Augmented biofeedback and physical training** (*multi-modal intervention*) Group A, physical therapy intervention: exercises facilitating hand-eye coordination and fine motor skills Group B, augmented biofeedback training: E-Link Upper Limb Exerciser (computerized graded interactive system) Group C, physical therapy intervention and augmented biofeedback training IG: 60 minutes per day, three times per week, 3 months (36 hours)	Group C compared with Group A and B BEERY of VMI: Group C vs A Visual motor integration: ↑↑ (p=.001, d_{ppc2}=5.3) Visual perception: ↑↑ (p=.001, d_{ppc2}=6.00) Group C vs B Visual motor integration: ↑↑ (p=.04, d_{ppc2}=2.6) Visual perception: ↑↑ (p=.03, d_{ppc2}=1.6)
Mak et al. (2018; 2020)	2	n = 42 (21/21) 6-16 years (IG: 9 ± 3.2/CG: 9.6 ± 2.1) Spastic: unilateral (16), bilateral diplegia (26) GMFCS I (22), II (12), III (8)	**MiYoga** (*multi-modal intervention*) Mindfulness movement programme based on hatha yoga principles IG: group therapy, 90 minutes per day, once per week, 6 weeks; individual therapy, 2 weeks at home (12.5 hours) CG: standard care	Pre vs post IG compared with CG WISC-IV: Symbol search: = (p=.63) Digit span: = (p=.66) CPT-II: Inattention, hit RT commissions: = (p=.25) Inattention, hit RT omissions: = (p=.22) Inattention, hit RT standard error: ↑↑ (p=.04, η_p^2 [a]=.01, d_{ppc2}=.02) Inattention, hit RT detectability RT for target vs non-target: = (p=.86) Inattention, variability of RT: = (p=.19) Vigilance, perseverations: ↑↑ (p=.04, η_p^2 [a] =.13, d_{ppc2}=.97) Vigilance, response style: = (p=.89) Vigilance, RT interstimulus interval change: = (p=.52)

Table 1 (continued).

Reference	LOE	Participants	Intervention	Cognitive Outcomes
Mak et al. (2018; 2020) *continued*	2	n = 42 (21/21) 6-16 years (IG: 9 ± 3.2/CG: 9.6 ± 2.1) Spastic: unilateral (16), bilateral diplegia (26) GMFCS I (22), II (12), III (8)	**MiYoga** (*multi-modal intervention*) Mindfulness movement programme based on hatha yoga principles IG: group therapy, 90 minutes per day, once per week, 6 weeks; individual therapy, 2 weeks at home (12.5 hours) CG: standard care	Sustained attention, Hit RT block change: = (p=.52) D-KEFS: TMT: = (p=.79) Colour-word interference: = (p=.62) BRIEF[1]: = (p=.93) Pre vs follow-up (6 months after intervention) WISC-IV: Symbol search: = (p=.51) Digit span: = (p=.51) CPT-II: Inattention, hit RT commissions: = (p=.87) Inattention, hit RT omissions: = (p=.19) Inattention, hit RT standard error: = (p=.41) Inattention, hit RT detectability RT for target vs non-target: = (p=.31) Inattention, variability of RT: = (p=.52) Vigilance, perseverations: = (p=.94) Vigilance, response style: = (p=.80) Vigilance, RT interstimulus interval change: = (p=.35) Sustained attention, Hit RT block change: = (p=.40) D-KEFS: TMT: = (p=.05) Colour-word interference: ↑↑ (p=.004, d_{ppc2}=.19) BRIEF[1]: = (p=.6)

Table 1 (continued).

Reference	LOE	Participants	Intervention	Cognitive Outcomes
Morgan et al. (2016)	2	n = 30 (15/15) (IG: 15.7 ± 4.8/CG: 20.1 ± 5.1 weeks) Type CP n.a. Motor ability n.a.	**GAME** (*multi-modal intervention*) Active motor learning, family centred care, parent coaching and environmental enrichment IG: 30-90 minutes per day, 18-30 appointments (until 12 months corrected age) (216 ± 87.3 hours) CG: standard care	IG compared with CG BSID-III (one year of life) Cognition: ↑↑ (p=.03)
Teixeira-Machado et al. (2017)	2	n = 26 (13/13) (IG: 17.1 ± 2.4/CG: 18 ± 3.5) 15-29 years Spastic (26) GMFCS II (9), III (8), IV (7), V (2)	**Dance intervention** (*physical intervention*) Coordination-movements of upper and lower limbs, body image-interaction between subject and environment, skill and agility-sequential components of the movement and trunk and head movements for spatial orientation and equilibrium IG: 60 min per day, twice per week, 3 months (24 hours) CG: kinesiotherapy exercises (active control)	IG compared with CG FIM Cognitive function[1]: ↑↑ (p=.0001, d_{ppc2}=5.9)

Table 1 (continued).

Reference	LOE	Participants	Intervention	Cognitive Outcomes
Sajan et al. (2017)	2	n = 20 (10/10) 5-20 years (IG: 10.6 ± 3.8/CG: 12.4 ± 4.9) Spastic bilateral: diplegia (12), triplegia (5), quadriplegia (3) GMFCS I (1), II (3), III (13), IV (3)	**Nintendo Wii™** (*physical intervention*) Interactive video gaming that includes tennis and boxing activities IG: 45 minutes per day, six times per week, 3 weeks (13.5 hours) CG: standard care	IG compared with CG TVPS-3: = (p=.94)
Di Lieto et al. (2021)	2	n = 19 (10/9) 4-13 years (IG: 6.7 ± 1.7/CG: 8 ± 3) Spastic diplegia (19) GMFCS II (11), III (6), IV (2) MACS I (4), II (10), III (5)	**CogMed working memory training** (*cognitive intervention*) A web-based computerized program with working memory exercises IG: 20-45 minutes per day, five times per week, 5 weeks (8.3 – 18.8 hours)	IG compared with CG NEPSY-II[a]: Visual attention: = (p=.09) Response set: = (p=.07) Inhibition speed: ↑↑ (p=.001, d [a]=.3) Phonological processing: ↑↑ (p=.003, d [a]=.1) Imitating hand positions: = (p=.13) Speed in visuo-motor precision: = (p=.20) Accuracy in visuo-motor precision: = (p=.92) Memory for designs immediate: =' (p=.02, d [a]=.3) Memory for designs delayed: = (p=.16) Block construction: ↑↑ (p=.001, d [a]=.7) Geometric puzzles: =' (p=.007) Route finding: = (p=.23)

Table 1 (continued).

n.a., not available; ↑↑, statistical significance increase; ↓↓, statistical significance decrease; =, no differences; =' no differences after Bonferroni's correction applied by authors ($p<.004$); d, Cohen's d; d_{ppc2}, effect size estimate using pooled pre-test SD; η_p^2, partial eta-squared.

Abbreviations. ARS, Attention Deficit Hyperactivity Disorder Rating Scale; BRIEF, Behavior Rating Inventory of Executive Function; BSID-III, Bayley Scales of Infant and Toddler Development-Third Edition; BEERY of VMI, Beery-Buktenica of Visual-Motor Integration; CG, Control Group; CPRS-48, Conners' Parent Rating Scale; CPT-II, Continuous Performance Test-Second Edition; D-KEFS, Delis-Kaplan Executive Function System; DOTCA-Ch, Dynamic Occupational Therapy Cognitive Assessment for Children; FIM, Functional Independence Measure; GMFCS, Gross Motor Function Classification System; IG, Intervention Group; KCPT, Conners's Attention Test for Children; MACS, Manual Ability Classification System; Mitii, Move It To Improve It; NEPSY-II, Developmental NeuroPSYchological Assessment-Second Edition; RT, Reaction Time; TMT, Trail Making Test; TVPS-3, Test of Visual Perceptual Skills-Third Edition; WISC-IV, Wechsler Intelligence Scale for Children-Fourth Edition.

Table 2. Summary of Interventions with an Impact on Cognitive Functions in Cerebral Palsy of Studies with a Lower Quality.

Reference	LOE	Participants	Intervention	Cognitive Outcomes
Authors (year)	n	n = (IG/CG) Age range (IG: mean ± SD/CG: mean ± SD) Type CP (n) Motor ability	**Name** (*type of intervention*) Description of intervention IG: time per day, times per week, number of weeks (total dose) CG: type of Control Group	Test_1: result_1 ↑ (p, d: effect size calculated) Test_2: result_2 ↓ Test_3: result_3 =
Abuin-Porras et al. (2019)	3	n = 10 (5/5) 6-16 years (12, SD n.a.) Spastic bilateral quadriplegia (10) GMFCS ≥ III (10)	**Bobath therapy** (*physical intervention*) Reduction of the increased tone, training of trunk and head control in a sitting position, assisted weight-shifting from one hip to another while seating, assisted rotation of the trunk and voluntary reach with upper limbs IG: 45 min CG: stretching of the upper and lower limbs in a supine position (active control)	IG compared with CG KCPT: Stimulous-response interval: = Omission error: =
Cho et al. (2015)	4	n = 56 4-7 years (mean n.a., SD n.a.) Spastic: unilateral (20), bilateral diplegia (36) Motor ability n.a.	**Frosting developmental program in visual perception** (*cognitive intervention*) Visual-motor coordination, figure-ground perception, perceptual constancy and position in space and spatial relationship IG: 30 min per day, three times per week, 8 weeks (12 hours) NCG	Pre vs post VMI: ↑↑ (d=1.8) WeeFIM, social cognition[1]: ↑↑ (d=1.2)

Table 2 (continued).

Reference	LOE	Participants	Intervention	Cognitive Outcomes
Ramkumar & Gupta (2016)	4	n = 30 4-12 years (mean n.a., SD n.a.) Spastic unilateral (8) and bilateral: diplegia (14), quadriplegia (8) Motor ability n.a.	**Occupational therapy intervention** (*multi-modal intervention*) Cognitive perceptual and motor perceptual training with puzzles, shadow puzzles and memory games IG: 60 minutes per day, 5 times per week, 6 weeks (22.5 hours) NCG	Pre vs post MVPT: Raw score: ↑↑ (p<.001, d=.79) Perceptual age: ↑↑ (p<.001, d=1.0) (no differences between type of CP)
Yildirim et al. (2021)	4	n = 20 Range age n.a. (12.5 ± 2.5 years) Spastic: unilateral (11), bilateral diplegia (9) Motor ability n.a.	**Leap motion based exergame therapy** (*physical intervention*) A combination of 6 weeks of structured therapy-based hand rehabilitation with 6 weeks of leap motion based exergame therapy IG: 40 minutes per day, twice per week, 12 weeks (16 hours) NCG	Pre vs post During intervention (6 weeks) WCST: Categories completed: = (p=.44) Correct responses: = (p=.40) Perseverative responses: = (p=.82) Perseverative errors: = (p=.35) Non perseverative errors: = (p=.49) Total errors: = (p=.49) Post-intervention (12 weeks) WCST: Categories completed: ↑↑ (p<.001, d=1.4) Correct responses: = (p=.82) Perseverative responses: = (p=.18) Perseverative errors: ↑↑ (p=.012, d=.55) Non perseverative errors: ↑↑ (p=.002, d=.79) Total errors: ↑↑ (p=.005, d=1.2)

Table 2 (continued).

Reference	LOE	Participants	Intervention	Cognitive Outcomes
Pereira et al. (2019)	4	n = 15 8-12 years (10.53 ± 1.69) Spastic (10), dyskinetic (2), ataxic (3) Motor ability n.a.	**The Incredible Adventures of Anastácio, the Explorer** (*cognitive intervention*) Narrative intervention program to promote children's autonomy for activities of daily life, school trajectories and their life project IG: Individual and group therapy 60 min per week, 18 weeks (18 hours) NCG	Pre vs post D-KEFS, tower test: ↑↑
Muriel et al. (2014)	4	n = 15 4-16 years (8.8 ± 2.51) Spastic unilateral (7) and bilateral: diplegia (5), quadriplegia (3) GMFCS I (6), II (4), III (2), V (3)	**Guttmann, NeuroPersonalTrainer®** (*cognitive intervention*) A web-based computerized program with memory, attention and executive function exercises IG: 30 minutes per day, twice per week, 8 weeks (16 hours) NCG	Pre vs post WISC-IV: Verbal comprehension index: = (p=.62) Perceptual reasoning index: ↑↑ (p=.03 d=.40) Working memory index: = (p=.31) Processing speed index: = (p=.11) IQ total score: = (p=.21) CPT-II: = (p=.51) CTRS-28: = CPRS-48: = BRIEF[1]: =

Table 2 (continued).

Reference	LOE	Participants	Intervention	Cognitive Outcomes
Sørensen et al. (2014)	4	n = 14 2-4 years (3.3, SD n.a.) Spastic: unilateral (7), bilateral diplegia (7) GMFCS I-III (14)	**Program of intensified habilitation** (*multi-modal intervention*) A multi-modal program focusing on strengthening motor, communication and executive functions IG: a year (-) NCG	Pre vs post BRIEF-P Mothers[1]: Inhibitory self-control: = (p=.66) Flexibility: = (p=.30) Emergent metacognition: = (p=.70) Global executive composite: = (p=.93) BRIEF-P Fathers[1]: Inhibitory self-control: = (p=.31) Flexibility: = (p=.21) Emergent metacognition: ↑↑ (p=.02) Global executive composite: = (p=.16) BRIEF-P preschool teachers[1]: Inhibitory self-control: = (p=.23) Flexibility: ↑↑ (p=.04) Emergent metacognition: = (p=.21) Global executive composite: = (p=.17)
Hsieh et al. (2017)	4	n = 14 3-8 years (7.03 ± 1.56) Spastic diplegia (4), spastic quadriplegia (6), dyskinetic (2), ataxic (2) GMFCS I (2), III (4), IV (4), V (4)	**Hippotherapy** (*physical intervention*) IG: 30 min per week, 12 weeks (6 hours) Group A (GMFCS I-III) and Group B (IV-V) NCG	Pre vs post Group A ICF-CY checklist[1,2]: Global cognitive functions: = Attention functions: = Memory functions: = Group B ICF-CY checklist[1,2]: Global cognitive functions: = Attention functions: = Memory functions:

Table 2 (continued).

Reference	LOE	Participants	Intervention	Cognitive Outcomes
Hsieh et al. (2017) *continued*	4	n = 14 3-8 years (7.03 ± 1.56) Spastic diplegia (4), spastic quadriplegia (6), dyskinetic (2), ataxic (2) GMFCS I (2), III (4), IV (4), V (4)	**Hippotherapy** (*physical intervention*) IG: 30 min per week, 12 weeks (6 hours) Group A (GMFCS I-III) and Group B (IV-V) NCG	Pre vs follow-up (12 weeks after intervention) Group A ICF-CY checklist[1,2]: Global cognitive functions: = Attention functions: = Memory functions: = Group B ICF-CY checklist[1,2]: Global cognitive functions: = Attention functions: = Memory functions: =
Shin & Song (2016)	4	n = 11 Range age n.a. (127.9 ± 32.4 months) Paraplegia (11) GMFCS I (4), II (2), III (5)	**Kinesiotherapy** (physical intervention) Warming up, neck and trunk stabilization, posture and warm-down exercises IG: 45 minutes per day, twice a week, 8 weeks (12 hours) NCG	Pre vs post K-DTVP-2: ↑↑ (d=.82)
Martiny & Aggerholm (2016)	4	n = 11 14-18 years (mean n.a., SD n.a.) Spastic (11) GMFCS I-II	**Winter sports camp** (multi-modal intervention) Embodied Cognition based model of intervention with alpine skiing, snow rafting, dog sledding and indoor social activities IG: group therapy 3-week pre-defined physical training and 5-day winter camp (-) NCG	Pre vs post Qualitative interview, self control[1,2]: ↑

Table 2 (continued).

Reference	LOE	Participants	Intervention	Cognitive Outcomes
Christensen et al. (2017)	4	n = 11[a] 11-13 years (11.6 ± 0.8) Spastic: unilateral (1), bilateral (10) GMFCS I (10), II (1)	**Climbing** (*physical intervention*) A climbing gym with walls and routes up to 12 m of height IG: 2.5 hours per day, three times per week, 3 weeks (22.5 hours) NCG	Pre vs post Cogstate: Visuo-motor skill test, CHASE: = (p=.14) Visuo-spatial learning and memory test, PAL: = (p=.18) Groton maze learning test, MAZE: = Delay recall of the groton maze learning test, MAZE-Delay: = RT test, DETECT: = (p=1.0) Two-choice reaction time, IDENT: = (p=1.0) Working memory, 1-BACK: = (p=.99)
Cherriere et al. (2020)	4	n = 10 10-17 years (14.1 ± 1.8) Spastic unilateral (3), spastic diplegia (4), dyskinetic (1), ataxic (1), unknown (1) GMFCS I (4), II (3), III (3)	**Dance intervention** (*physical intervention*) A variance of dance styles with an emphasis on balance movements IG: 60 minutes per day, twice per week, 10 weeks (20 hours) NCG	Pre vs post Tea-Ch: Score !: = Score DT: =
Bilde et al. (2011)	4	n = 9 6-12 years (10.3, SD n.a.) Spastic GMFCS I (8), II (1) MACS I (4), II (5)	**Mitii** (*multi-modal intervention*) A multi-modal web-based program: cognitive, perceptual and motor training IG: 30 minutes per day, every day, 20 weeks (73.6 ± 8 hours) NCG	Pre vs post TVPS: Visual figure ground: ↑↑ Visuo-spatial relationship: = Visual discrimination: = Visual memory: = Visual sequence memory: = Visual closure: = Visual constancy: =

Table 2 (continued).

Reference	LOE	Participants	Intervention	Cognitive Outcomes
Lakes et al. (2019)	4	n = 8 9-14 years (mean n.a., SD n.a.) Spastic unilateral and bilateral (8) Motor ability n.a.	**Ballet intervention** (*physical intervention*) Warm-up, stretching, barre and centre floor exercises IG: 60 minutes per day, three times per week, 6 weeks (≥16 hours) NCG	Pre vs follow-up (4-5 weeks after intervention) The Hearts & Flowers Executive Function tasks: Accuracy, congruent trial: = (p=.86) RT, congruent trial: = (p=.95) Accuracy, incongruent trial: ↑↑ (p=.03, d=.74) RT, incongruent trial: ↑↑ (p<.001, d=.78) Accuracy, mixed trial: = (p=.05) RT, mixed trial: = (p=.64)
Peny-Dahlstrand et al. (2018)	4	n = 5[b] 19-28 years (23.8 ± 4.2) Spastic unilateral (2), spastic bilateral (2), dyskinetic (1) GMFCS I (1), II (3), III (1) MACS II (5)	**Cognitive Orientation to daily Occupational Performance (CO-OP)** (*cognitive intervention*) Participant identifies three activity goals that he or she wants to achieve IG: 60 minutes per day, once or twice per week, 10 sessions (10 hours) NCG	Pre vs follow-up (6 months after intervention) D-KEFS, tower test: ↑ (p=.005) DEX[1]: = (p=.10)
Lins et al. (2019)	4	n = 5 4-7 years (mean n.a., SD n.a.) Spastic: unilateral (4), bilateral diplegia (1) Motor ability n.a.	**Robot assisted therapy** (*multi-modal intervention*) Robot game that includes motor coordination, memory and attention exercises IG: twelve weeks NCG	Pre vs post Qualitative interview, attention (↑ 5/5): ↑

Table 2 (continued).

Reference	LOE	Participants	Intervention	Cognitive Outcomes
Soto & Clarke (2018)	4	n = 4 14-18 years (15.5 ± 1.7) Spastic bilateral quadriplegia (3), ataxic (1) Motor ability n.a.	**AAC** Conversation based therapy between the clinician and participant IG: 40-50 minutes per day, twice per week, 12 weeks (16 – 20 hours) NCG	Pre vs post [c] Verbs (↑ 2/4)[1,2]: = Pronouns (↑ 2/4)[1,2]: = Bound morphemes (↑ 2/4)[1,2]: = Spontaneous clauses (↑ 2/4)[1,2]: =
Heathcock et al. (2015)	4	n = 2 19 and 21 months Spastic bilateral quadriplegia (2) GMFCS V (2)	**Physical therapy** (*physical intervention*) Intensive physical therapy to enhance gross motor skills using toys or other motivators IG: 2 hours per day, 5 times per week, 4 weeks (40 hours) NCG	Pre vs post [c] BSID-III: Cognition (↑ 1/2): =

Table 2 (continued).

Reference	LOE	Participants	Intervention	Cognitive Outcomes
Desai et al. (2014)	4	n = 1 13 years Motor ability n.a.	GoTalk Now (AAC) Communication application with vocabulary layouts and grids IG: twice per week, 8 weeks (5.3 hours) NCG	Pre vs post Cognitive/Behavioural (SFA)[1]: Safety: ↑ Personal care awareness: = Behaviour regulation: ↑ Positive interaction: ↑ Task behaviour/completion: ↑ Compliance with adult directives and school rules: ↑ Following social conventions: ↑ Memory: ↑ Understanding and functional communication: ↑

Notes. [a] The sample included typically developing children, but only data for children with CP were included; [b] The sample included children with spina bifida, but only data for children with CP were included; [c] If individual results were reported, differences were considered if >50% of the total sample changed score; [1] Rating scale; [2] Non-validated measure. n.a., not available; ↑, increase in studies with no statistical analysis; ↑↑, statistical significance increase; ↓, decrease in studies with no statistical analysis; ↓↓, statistical significance decrease; =, no differences; d, Cohen's d.

Abbreviations. AAC, Augmentative and Alternative Communication; ARS, Attention Deficit Hyperactivity Disorder Rating Scale; BRIEF, Behavior Rating Inventory of Executive Function; BRIEF-P, Behavior Rating Inventory of Executive Function-Preschool Version; BSID-III, Bayley Scales of Infant and Toddler Development-Third Edition; CG, Control Group; CPRS-48, Conners' Parent Rating Scale; CPT-II, Continuous Performance Test-Second Edition; CTRS-28, Conners' Teacher Rating Scale; DEX, Dysexecutive Questionnaire; D-KEFS, Delis-Kaplan Executive Function System; GMFCS, Gross Motor Function Classification System; ICF-CY, International Classification of Functioning, Disability and Health for Children and Youth; IG, Intervention Group; KCPT, Conners's Attention Test for Children; K-DTVP-2, Korean Developmental Test of Visual Perception-Second Edition; MACS, Manual Ability Classification System; Mitii, Move It To Improve It; MVPT, Motor-Free Visual Perception Test; NCG, No Control Group; PAL, Paired Association Learning; RT, Reaction Time; SFA, School Function Assessment; TEA-Ch; Test of Everyday Attention for Children; TVPS, Test of Visual Perceptual Skills; VMI, Visual-Motor Integration; WCST, Wisconsin Card Sorting Test; WeeFIM, Wee Functional Independent Measure; WISC-IV, Wechsler Intelligence Scale for Children-Fourth Edition.

Table 3. Demographic and Clinical Data.

Gender, n (%)	Female: 312 (46.6) Male: 328 (48.9) Unknown: 30 (4.5)
Motor distribution, n (%)	Spastic CP (85.4): Unilateral: 315 (47) Bilateral: 193 (28.8) Unilateral/Bilateral: 64 (9.6) Dyskinetic CP: 4 (0.6) Ataxic CP: 5 (0.7) Unknown: 89 (13.3)
GMFCS (by level), n (%)	I: 162 (24.2) II: 136 (20.3) III: 50 (7.5) IV: 16 (2.4) V: 11 (1.6) I-II: 11 (1.6) I-III: 24 (3.6) Unknown: 260 (38.8)
MACS (by level), n (%)	I: 58 (8.7) II: 151 (22.5) III: 15 (2.2) I-II: 45 (6.7) Unknown: 401 (59.9)

Abbreviations. CP: Cerebral Palsy; GMFCS: Gross Motor Function Classification System; MACS: Manual Ability Classification System.

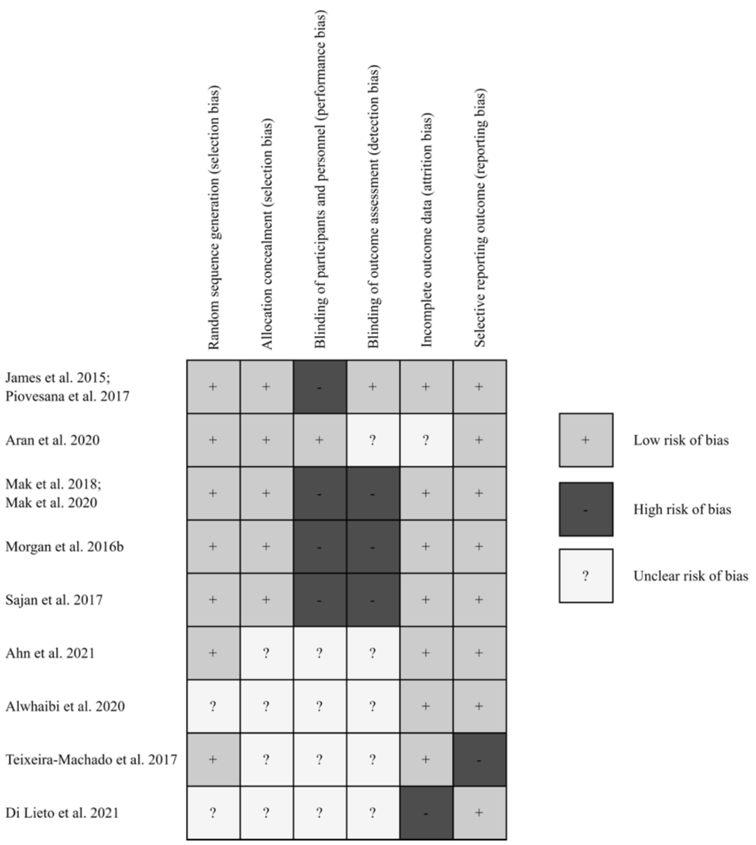


Figure 2. Summary of Risk of Bias Within Studies. Analysis is based on the Cochrane Risk of Bias Tool.

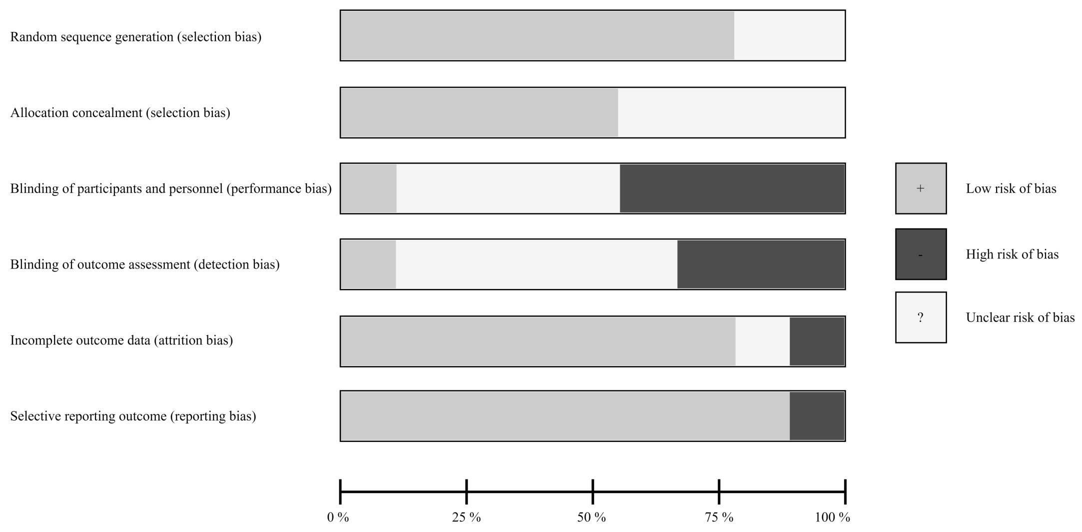


Figure 3. Risk of Bias Among Studies. Analysis is based on the Cochrane Risk of Bias Tool.

Multi-Modal intervention

Five of the ten multi-modal intervention studies were categorized as level 2 evidence (Alwhaibi et al., 2020; Aran et al., 2020; Mak et al., 2018; Morgan et al., 2016b; Piovesana et al., 2017) and five as level 4 evidence (Bilde et al., 2011; Lins et al., 2019; Martiny & Aggerholm, 2016; Ramkumar & Gupta, 2016; Sørensen et al., 2016). These types of interventions included cognitive as well as physical training, but the majority of studies did not specify the percentage of cognitive and physical tasks.

The duration of multi-modal interventions was less than 8 weeks in three studies (Mak et al., 2018; Martiny & Aggerholm, 2016; Ramkumar & Gupta, 2016), 10–12 weeks in three (Alwhaibi et al., 2020; Aran et al., 2020; Lins et al., 2019), 20 weeks in two (Bilde et al., 2011; Piovesana et al., 2017), 3–6 months in one (Morgan et al., 2016b) and 1 year in one study (Sørensen et al., 2016). The total intervention dose ranged from 12 to 216 hours.

Regarding studies with high quality, a study with low risk of bias used the Move It To Improve It (Mitii) program (Piovesana et al., 2017). Mitii is a web-based multi-modal intervention in which the child must analyze visual information, solve a cognitive problem, and respond with a motor act. Virtual reality (Aran et al., 2020) and an intervention consisting of augmented biofeedback plus physical training (Alwhaibi et al., 2020) were also used. MiYoga is a hatha yoga-based program that includes mindfulness exercises (Mak et al., 2018). Finally, Goals, Activity and Motor Enrichment (GAME) therapy was used, combining goal-oriented intensive motor training, parent education, and strategies to enrich a child's motor learning environment (Morgan et al., 2016b).

In relation to studies with low quality, interventions included puzzles or memory games as cognitive-perceptual and perceptual-motor activities (Ramkumar & Gupta, 2016) and robot-assisted games with motor coordination, memory, and attention exercises (Lins et al., 2019). A winter sport camp for physical and social activities (Martiny & Aggerholm, 2016) and a multi-modal intervention focusing on motor, communication and executive functions (Sørensen et al., 2016) were used. The effects of Mitii were also investigated in studies with low quality (Bilde et al., 2011).

Multi-modal interventions comprise components intended to work cognitive and physical aspects, and half of the studies included computerized programs (Alwhaibi et al., 2020; Aran et al., 2020; Bilde et al., 2011; Lins et al., 2019; Piovesana et al., 2017). Although there was certain variability in types of interventions, it seems that physical activity and cognitive training together produced significant improvements in general cognitive functioning (Morgan et al., 2016b), visual perception (small to large effect size) (Alwhaibi et al., 2020; Aran et al., 2020; Piovesana et al., 2017) and specific executive function domains (small and large effect size) (Mak et al., 2018). Studies with low quality also reported associations with visual perception (Bilde et al., 2011; Ramkumar & Gupta, 2016) and executive functions (Lins et al., 2019; Martiny & Aggerholm, 2016; Sørensen et al., 2016).

Only one study reported long-term effects (Mak et al., 2020). Mak et al. (2020) found improvements in a specific executive function domain (cognitive flexibility) 6 months after MiYoga program.

Cognitive intervention

Only one study of interventions focused specifically on cognition, and it was categorized as level 2 evidence (Di Lieto et al., 2021). Four studies were categorized as being of low quality (level 4 evidence) (Cho et al., 2015; Muriel et al., 2014; Peny-Dahlstrand et al., 2018; Pereira et al., 2019).

Cognitive interventions lasted for 5 weeks (Di Lieto et al., 2021), 8 weeks (Cho et al., 2015; Muriel et al., 2014) or 18 weeks (Pereira et al., 2019) depending on the study. The number of total weeks of intervention was unknown in one study (Peny-Dahlstrand et al., 2018). Total doses were similar between studies, ranging from 8 to 19 hours.

In relation to the study with high quality, Di Lieto et al. (2021) used CogMed working memory training, a home-based videogame that includes working memory exercises. Regarding studies with low quality, one study used Cognitive Orientation to daily Occupational Performance intervention (CO-OP) (Peny-Dahlstrand et al., 2018), another combined memory, attention and executive function training (Muriel et al., 2014), and the remaining two used visual perception (Cho et al., 2015) and executive function (Pereira et al., 2019) training.

Cognitive interventions produced significant changes in visual perception (medium effect size), working memory, and inhibitory control (small effect size) in one high quality study (Di Lieto et al., 2021). Studies with a lower quality also found associations with visual perception, social cognition (Cho et al., 2015), planning (Peny-Dahlstrand et al., 2018; Pereira et al., 2019), and reasoning (Muriel et al., 2014). No significant association in general executive function was reported (Muriel et al., 2014; Peny-Dahlstrand et al., 2018). The study by Peny-Dahlstrand et al. (2018) did not include immediate post-intervention assessment and only reported outcomes 6 months after the intervention; an association with planning skills was shown.

Augmentative and alternative communication

Two studies evaluated the effect of AAC on cognitive functions (Desai et al., 2014; Soto & Clarke, 2018). Both were single case studies categorized as level 4 evidence. Better performance in general cognitive functioning, memory and inhibitory control was associated with 8 weeks of ACC use (Desai et al., 2014), but no association was found in language after 12 weeks of AAC (Soto & Clarke, 2018).

Physical intervention

There were eleven studies about physical interventions. Three were categorized as level 2 evidence (Ahn et al., 2021; Sajan et al., 2017; Teixeira-Machado et al., 2017), one as level 3 evidence (Abuin-Porras et al., 2019) and six as level 4 (Cherriere et al., 2020; Christensen et al., 2017; Heathcock et al., 2015; Hsieh et al., 2017; Lakes et al., 2019; Shin & Song, 2016; Yildirim et al., 2021).
Interventions ranged from one session (Abuin-Porras et al., 2019) to multiple sessions over 3–4 weeks (Christensen et al., 2017; Heathcock et al., 2015; Sajan et al., 2017), 6–8 weeks (Lakes et al., 2019; Shin & Song, 2016) and 10–12 weeks (Cherriere et al., 2020; Hsieh et al., 2017; Teixeira-Machado et al., 2017; Yildirim et al., 2021) or 16 weeks (Ahn et al., 2021). Total doses ranged from 45 minutes to 40 hours. The types of physical intervention were also variable. Studies of high quality included dance (Teixeira-Machado et al., 2017), video gaming (Sajan et al., 2017) and hippotherapy (Ahn et al., 2021). Studies with low quality

included dance (Cherriere et al., 2020; Lakes et al., 2019), hippotherapy (Hsieh et al., 2017), climbing (Christensen et al., 2017), kinesiotherapy (Shin & Song, 2016), high-intensity training (Heathcock et al., 2015), leap motion based exergame (Yildirim et al., 2021) and Bobath therapy (Abuin-Porras et al., 2019).

Studies with high quality reported significant changes in general cognitive functioning (large effect size) (Teixeira-Machado et al., 2017) and inhibitory control (medium effect size) (Ahn et al., 2021) but not in visual perception (Sajan et al., 2017). The remaining studies, categorized as level 4 evidence, offered more varied results. Although some were associated with significant changes in visual perception (Shin & Song, 2016) and executive functions (Lakes et al., 2019; Yildirim et al., 2021), others reported no association with general cognitive functioning (Heathcock et al., 2015; Hsieh et al., 2017), visual perception (Christensen et al., 2017), memory (Hsieh et al., 2017) or executive functions (Cherriere et al., 2020; Christensen et al., 2017).

Lakes et al. (2019) did not report cognitive outcomes after the intervention finished, including only a follow-up assessment 4 weeks after the intervention. No effects of the physical intervention were found in this study. Hsieh et al. (2017) also found no cognitive changes 12 weeks after the intervention.

3.5. Characteristics of the interventions

General cognitive functioning was evaluated in six studies. Specific cognitive domains were also analyzed among the included studies: eighteen assessed executive functions, ten assessed visual perception, four assessed memory, and one assessed language. Figures 4 and 5 summarize the results for domain-specific efficacy.

General cognitive functioning

Estimates of general cognitive functioning were included in six studies. Three of them used direct measures of neuropsychological assessment, namely the Bayley Scales of Infant and Toddler Development, Third Edition (BSID-III) **(Heathcock et al., 2015; Morgan et al., 2016b)** and the Wechsler Intelligence Scale for Children, Fourth Edition (WISC-IV) (Muriel et al., 2014). The other three used rating scales or checklists to evaluate general cognitive functioning **(Desai et al., 2014; Hsieh et al., 2017; Teixeira-Machado et al., 2017)**. The two studies with high quality found significant improvements: Morgan et al. (2016) used the GAME program (a multi-modal intervention until 12 months of age) and Teixeira-Machado (2017) used a dance intervention (over 3 months, with a total dose of 24 hours) (large effect size).

Considering the studies with lower quality, one single case study found association with significant changes in general cognitive functioning after 8 weeks (16 sessions) of AAC **(Desai et al., 2014)**. However, others failed to show that physical functioning (Heathcock et al., 2015; Hsieh et al., 2017) and cognitive interventions (Muriel et al., 2014) were significantly associated with general cognitive functioning. A follow-up analysis 12 weeks after Hsieh et al. (2017) finished their intervention still found no significant differences.

Visual perception

Performance tasks were used to assess the efficacy of interventions on visual perception in seven studies (Alwhaibi et al., 2020; Aran et al., 2020; Cho et al., 2015; Christensen et al., 2017; Di Lieto et al., 2017; Ramkumar & Gupta, 2016; Shin & Song, 2016). Three of them used the Test of Visual Perceptual Skills (TVPS) (Bilde et al., 2011; Piovesana et al., 2017; Sajan et al., 2017).

Visual perception improved in all multi-modal and cognitive interventions that assessed this domain (small to large effect size) (Alwhaibi et al., 2020; Aran et al., 2020; Di Lieto et al., 2021; Piovesana et al., 2017). Studies with low quality also associated multi-modal and cognitive intervention with improvements in visual perception (Bilde et al., 2011; Cho et al., 2015; Ramkumar & Gupta, 2016). Total dose ranged from 8 to 60 hours over an intervention period of 5–20 weeks. Only one of the three physical interventions (Christensen et al., 2017; Sajan et al., 2017; Shin & Song, 2016), that by Shin & Song (2016), was associated with significant changes.

Executive functions

Eighteen studies included executive functions. Performance task tests and rating scales were combined in the assessments of four (Mak et al., 2018; Muriel et al., 2014; Peny-Dahlstrand et al., 2020; Piovesana et al., 2017), performance task tests alone were used in nine (Abuin-Porras et al., 2019; Ahn et al., 2021; Aran et al., 2020; Cherriere et al., 2020; Christensen et al., 2017; Di Lieto et al., 2017; Lakes et al., 2019; Pereira et al., 2019; Yildirim et al., 2021), and rating scales alone were used in five studies (Desai et al., 2014; Hsieh et al., 2017; Lins et al., 2019; Martiny & Aggerholm, 2016; Sørensen et al., 2016). The findings of the eighteen studies are summarized in Figure 5.

Five studies included a rating scale to assess global executive function performance (Mak et al., 2018; Muriel et al., 2014; Peny-Dahlstrand et al., 2018; Piovesana et al., 2017; Sørensen et al., 2016) but no significant changes were reported. The Behavior Rating Inventory of Executive Function (BRIEF) was used as a general measure of executive functions in four studies (Mak et al., 2018; Muriel et al., 2014; Piovesana et al., 2017; Sørensen et al., 2016), of which two had a high quality intervention (Mak et al., 2018; Piovesana et al., 2017). However, these studies with a low of bias found no significant changes after a multi-modal intervention (Mak et al., 2018; Piovesana et al., 2017). Studies of low quality also found no associations with multi-modal (Sørensen et al., 2016) and cognitive interventions (Muriel et al., 2014).

Different subdomains of executive function were assessed across studies according to those proposed by Diamond (2013): core (working memory, cognitive flexibility and inhibitory control) and higher-order (reasoning, problem solving, and planning) executive functions. Working memory improved in one of the two studies with high quality (Di Lieto et al., 2021; Mak et al., 2018), in which significant changes were found after a computerized program that includes working memory games (Di Lieto et al., 2021). However, working memory did not improve after the MiYoga multi-modal program (Mak et al., 2018). Moreover, no association was found in studies with low quality, which included a cognitive intervention delivered via a computer program (NeuroPersonalTrainer) (Muriel et al., 2014) and a physical intervention based on climbing (Christensen et al., 2017). Lakes et al. (2019) did not report an immediate post-intervention assessment, but they found no improvements in working memory by 4–5 weeks after a dance training.

Cognitive flexibility was assessed in three studies with high quality that trained through multi-modal and cognitive interventions: MiYoga (Mak et al., 2018), Mitii (Piovesana et al., 2017) and CogMed working memory training (Di Lieto et al., 2021). None of the studies observed significant changes. Although Mak et al. (2018) did not find improvements in cognitive flexibility just after intervention, delayed effects were found 6 months later (Mak et al., 2020). Moreover, associations with cognitive flexibility were also found in studies with low quality (Sørensen et al., 2016; Yildirim et al., 2021). Better performance in the Wisconsin Card Sorting Test (WCST) was found after a physical intervention of 12 weeks that consisted of leap motion based exergame therapy (Yildirim et al., 2021). Sørensen et al. (2016) found that teachers reported improvements in the Cognitive Flexibility Subscale of the BRIEF-Preschool (BRIEF-P) after multi-modal training for 1 year (level 4 evidence); however, parents did not observe changes in the same scale.

Inhibitory control was assessed in thirteen studies (Abuin-Porras et al., 2019; Ahn et al., 2021; Cherriere et al., 2020; Desai et al., 2014; Di Lieto et al., 2021; Hsieh et al., 2017; Lakes et al., 2019; Lins et al., 2019; Mak et al., 2018; Martiny & Aggerholm, 2016; Muriel et al., 2014; Piovesana et al., 2017; Sørensen et al., 2016). Three (Ahn et al., 2021; Di Lieto et al., 2021; Mak et al., 2018) of four studies graded as level 2 evidence (Ahn et al., 2021; Di Lieto et al., 2021; Mak et al., 2018; Piovesana et al., 2017) found significant improvements in inhibitory control. Specifically, Mak et al. (2018) and Ahn et al. (2021) reported a significant enhancement in the same outcome (perseverations) of Conner's Attention Test for Children (CPT) after MiYoga and hippotherapy interventions (medium to large effect size), respectively. Nevertheless, improvements in inhibitory control were not maintained in follow-up analysis 6 months after MiYoga intervention (Mak et al., 2020). Regarding cognitive interventions, significant improvements in Visual Attention and Inhibition Speed tests from Developmental NEuroPSYchological Assessment, Second Edition (NEPSY-II) were found after 5 weeks of CogMed working memory training (small effect size) (Di Lieto et al., 2021). However, a study with high quality and low risk of bias found no changes using the Mitii program (Piovesana et al., 2017). Changes in inhibitory control were also associated in studies with level 4 evidence (Desai et al., 2014; Lakes et al., 2019; Lins et al., 2019; Martini & Aggerholm et al., 2016). Better performance in The Hearts & Flowers Executive Function tasks was associated with 20 weeks of a dance intervention (Lakes et al., 2019), while a single case study found an association with significant changes in the School Function Assessment (SFA), behavior regulation scale, after 8 weeks of an AAC intervention (Desai et al., 2014). Another study found changes in a rating score scale after 2 months of robot-assisted therapy (Lins et al., 2019), and finally, one study reported an association with better self-control perception score after a winter sports camp for 1 week (Martiny & Aggerholm, 2016). However, the remaining studies with low quality did not find any association in this domain after using a multi-modal intervention (Sørensen et al., 2016), the NeuroPersonalTrainer cognitive intervention (Muriel et al., 2014) and physical interventions by means of either dance therapy (Cherriere et al., 2020) or Bobath therapy (Abuin-Porras et al., 2019).

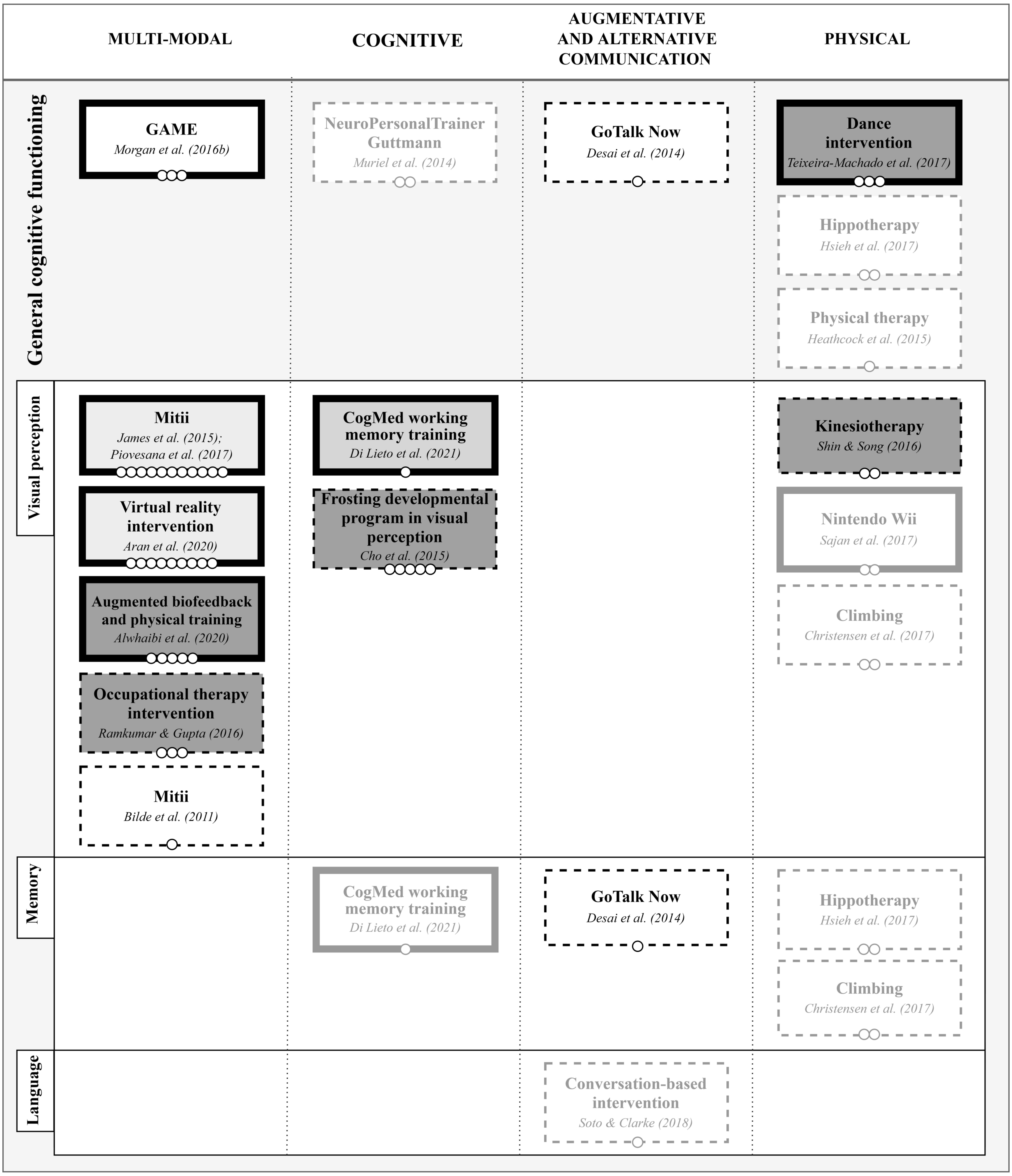


Figure 4. Summary of Interventions with an Impact on Cognitive Functioning in Cerebral Palsy.

Notes. Gray line box = interventions that no improve cognitive function, black line box = interventions that improve cognitive function; line width = methodological quality (level 2 evidence = thick line, level 4 evidence = dashed line), gray coloured box = effect size (small effect size = light gray; medium effect size = mid gray; large effect size = dark gray), white box = effect size no available; circle = 10 participants.

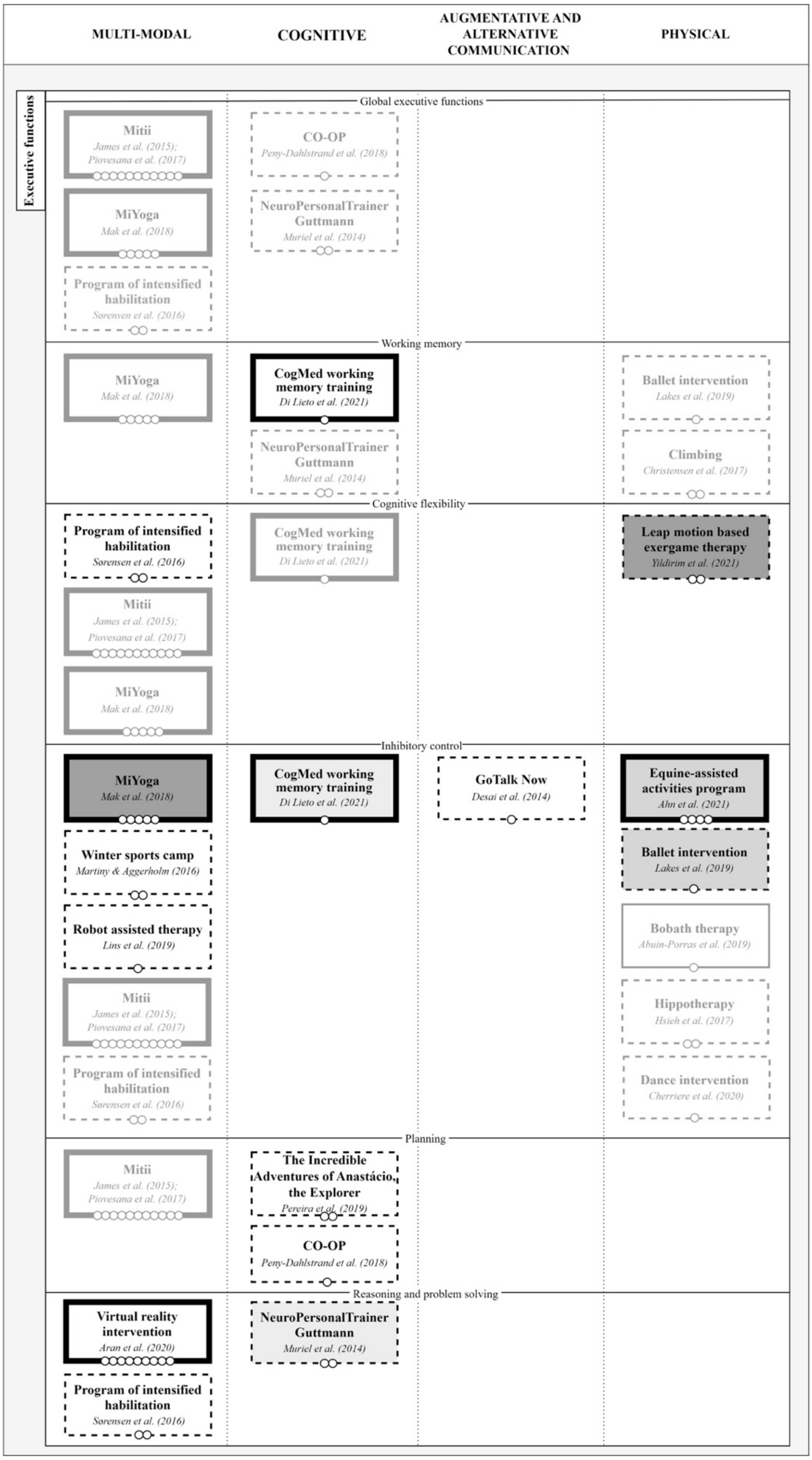


Figure 5. Summary of Interventions with an Impact on Executive Function in Cerebral Palsy.

Notes. Gray line box = interventions that no improve cognitive function, black line box = interventions that improve cognitive function; line width = methodological quality (level 2 evidence = thick line, level 3 evidence = thin line, level 4 evidence = dashed line); gray coloured box = effect size (small effect size = light gray; medium effect size = mid gray; large effect size = dark gray), white box = effect size no available; circle = 10 participants. Abbreviations. CO-OP, Cognitive Orientation to Daily Occupational Performance.

Reasoning was assessed in two studies (Aran et al., 2020; Muriel et al., 2014), and only one of them considered as high quality and low risk of bias (Aran et al., 2020). Improvements were found in thinking operations of Dynamic Occupational Therapy Cognitive Assessment for Children (DOTCA-Ch) after 10 weeks of multi-modal intervention through virtual reality (Aran et al., 2020). However, a study with low quality reported an association with better scores on perceptual reasoning index (WISC-IV) after a cognitive intervention with the NeuroPersonalTrainer for 8 weeks, and a total dose of 16 hours (Muriel et al., 2014). Better performance in problem solving, as measured by the emergent metacognition subscale of the BRIEF-P (relating to working memory and plan and organize problem-solving), was also reported in one study level 4 evidence after a year of intensive habitation (Sørensen et al., 2016), but this only included fathers (not mothers or teachers).

Planning was assessed in three studies (Peny-Dahlstrand et al., 2018; Pereira et al., 2019; Piovesana et al., 2017). A study with high quality and low risk of bias showed no benefit with a multi-modal intervention (Piovesana et al., 2017), but studies of lower quality were associated with significant changes in the tower test (Delis-Kaplan Executive Function System, D-KEFS) after a cognitive intervention lasting 10–18 hours (Peny-Dahlstrand et al., 2018; Pereira et al., 2019). One study did not include cognitive outcomes just after intervention, relying instead on assessment at 6 months follow-up (Peny-Dahlstrand et al., 2018).

Memory

Memory was assessed in four studies (Christensen et al., 2017; Desai et al., 2014; Di Lieto et al., 2021; Hsieh et al., 2017) but only one was graded as level 2 evidence (Di Lieto et al., 2021). Di Lieto et al. (2021) found no changes in visual memory after a home-based working memory. Only a single case study about 8 weeks of an ACC intervention, categorized as level 4 evidence, was associated with a better performance on the SFA, memory scale (Desai et al., 2014). However, there were no changes in learning or memory after climbing (Christensen et al., 2017) or hippotherapy interventions (Hsieh et al., 2017). Only one study included a follow-up assessment, and this identified no delayed effects after 12 weeks (Hsieh et al., 2017).

Language

Only one study assessed language skills (Soto & Clarke, 2018). This study included only two participants and their results were reported individually. One participant showed improved performance after a 12-week AAC intervention, whereas the second participant did not improve in any of the language subdomains that were assessed.

5. Discussion

This systematic review aimed to provide a greater understanding and a detailed description of specific benefits of interventions in cognitive functions for people with CP. In the present article we reviewed the findings of nine RCTs and nineteen non-randomized studies. Results of best available evidence revealed that general cognitive functioning, visual perception, working memory and inhibitory control improve after an intervention (Ahn et al., 2021; Alwhaibi et al., 2020; Aran et al., 2020; Di Lieto et al., 2021; Morgan et al., 2016b; Piovesana et al., 2017; Teixeira-Machado et al., 2017). Specifically, general cognitive functioning was improved by multi-modal (cognitive and physical tasks) and physical interventions (Morgan et al., 2016b; Teixeira-Machado et al., 2017). Even though no studies with high quality have investigated the effect of cognitive interventions on general cognitive functioning, one study with low quality reported post-intervention changes after a computerized program (Muriel et al., 2014). Another important finding of this review is that studies with high quality support the effectiveness of computerized multi-modal and cognitive interventions for improving visual perception (Alwhaibi et al., 2020; Aran et al., 2020; Di Lieto et al., 2021; Piovesana et al., 2017). However, a computerized physical intervention did not find changes in this cognitive function (Sajan et al., 2017). Taking together, this could indicate that the cognitive component of multi-modal and cognitive interventions, through a computerized program, could be a resource to produce changes in visual perception.

Concerning executive functions, beneficial effects on inhibitory control were found after multi-modal, cognitive and physical interventions (Ahn et al., 2021; Di Lieto et al., 2021; Mak et al., 2018). Although it seems that any type of intervention may improve this specific core executive function domain, only cognitive intervention also produced improvements in other core executive function domains such as working memory (Di Lieto et al., 2021). Higher-order executive functions (planning, reasoning and problem solving) play an important role in daily life, but no beneficial effects were reported on planning and problem solving after a multi-modal intervention (Aran et al., 2020; Piovesana et al., 2017).

Associations between cognitive intervention and planning (Peny-Dahlstrand et al., 2018; Pereira et al., 2019) and reasoning (Muriel et al., 2014) were found in studies with low quality and future RCT cognitive intervention should include higher-order executive function assessment.

The results of this systematic review reveal that the effect of interventions on specific cognitive functions, such as language and memory, has been insufficiently studied. Memory was explored only in a study of high quality (Di Lieto et al., 2021). Di Lieto et al. (2021) found no changes in visual memory, but the lack of studies with high quality about other types of interventions and including verbal memory prevents from drawing clear conclusions. Similarly, language was explored in only one single case study (Soto & Clarke, 2018), and further research is needed to identify an efficient intervention for this cognitive function.

This review reports long-term outcomes findings just in four studies (Hsieh et al., 2017; Lakes et al., 2019; Mak et al., 2020; Peny-Dahlstrand et al., 2018). Only one of them with high quality (Mak et al., 2020). Specifically, this study (Mat et al., 2020) reported a delayed effect in cognitive flexibility improvements 6 months after a multi-modal intervention, albeit without a control group for comparison. Long-term-effects on cognitive and physical interventions were analyzed in studies with low quality and results were inconclusive (Hsieh et al., 2017; Lakes et al., 2019; Peny-Dahlstrand et al., 2018). For this reason, long-term effects of interventions should be included in studies to know if improvements persist or even if delayed effects appear.

Some methodological issues should be noted due to the wide variety in experimental designs, sample sizes, assessment, frequencies, doses, types, and duration of interventions. Regarding experimental design, only nine studies were RCTs, considered of high quality and reaching level 2 evidence. The remaining nineteen studies were of low methodological quality, including 64% graded as level 4 evidence. Moreover, most had small sample sizes, with twenty-five studies including fewer than 50 participants and three including fewer than 5 participants, risking a lack of power to reach significance. Another aspect of methodological quality refers to outcome assessment because some studies used performance-based tests and others used behavioral rating scales, making it difficult to compare results among studies. Moreover, reliability properties were only reported in seven studies (Christensen et al., 2017; Di Lieto et al., 2021; Mak et al., 2018; Peny-Dahlstrand et al., 2018; Pereira et al., 2019; Piovesana et al., 2017; Sørensen et al., 2016) and practice effects of assessment should be considered. This underlies the need to unify the tools used for cognitive assessment in CP. Regarding the type of interventions, although multi-modal interventions combining physical and cognitive tasks seem to generate changes in cognition, results should be taken with caution due to the high diversity of interventions. Heterogeneous methodologies hinder the possibility of determining the optimal frequency and duration of interventions required to improve cognition with different interventions.

Regarding participants' characteristics, 75% of the included participants showed mild motor severity (GMFCS I-II) and 98% had spastic CP in those studies where this data was available. Previous papers indicate that cognitive performance is associated with motor ability and the type of CP (Ballester-Plané et al., 2018; Gabis et al., 2015; Laporta-Hoyos et al., 2019; Pirila et al., 2007). Future research should therefore include participants across the whole spectrum of motor ability to explore potential differences in effectiveness. Studies focused on children and only three studies included young adults. Despite the importance of cognition in middle-aged and elderly adults with CP, there have been no reports of specific interventions in this age group. Additionally, the prevalence of females (49%) and males (51%) reported in the selected studies of cognitive interventions was comparable, but this is not representative of CP population. Previous epidemiological studies have reported a 16 – 34% higher incidence of CP in males, probably due to genetic factors, hormone differences and biological vulnerability (Chounti et al., 2013; Gough et al., 2008; Romeo et al., 2016). The effects of sex differences on cognitive intervention have not yet been tested, but its influence on the effectiveness of motor interventions is known (Gough et al., 2008; Romeo et al., 2016).

Another issue is the understanding of the neuroplastic mechanisms underlying behavioral change after cognitive interventions. Neuroplasticity is key to understanding clinical improvement in CP, with the potential for neuroimaging to clarify how and for whom rehabilitation is effective (Reid et al., 2015). After cognitive intervention, changes in connectivity have been described both in general (Astle et al., 2015; Chen et al., 2016) and in neurological populations (Galetto & Sacco, 2017). Thus, it is important to measure brain changes when exploring the effect of interventions on cognition in CP.

Findings of this systematic review should be interpreted considering some limitations. First, an electronic search was conducted in specific databases and period of publication. This could be excluding some studies of interest that were published before or in other databases. Second, ACC techniques are commonly used to facilitate communication in CP. Studies about these techniques as interventions focused mainly on the motor aspects of language and the effects on cognitive functioning were not determined in several studies. Finally, the heterogeneous methodologies and the lack of RCTs precluded meta-analysis and permitted only a systematic review. Despite this, important information about those interventions considered to improve cognition in people with CP has been summarized.

6. Conclusions

In general, the methodological qualities and evidence levels of studies to improve cognitive functions in CP were low. The results of this systematic review suggest that there is evidence supporting the use of multi-modal and physical interventions to improve general cognitive functioning. Multi-modal and cognitive interventions have beneficial effects on visual perception. Both interventions, together with physical intervention, improve inhibitory control but only cognitive interventions improved other executive function domains such as working memory. No RCT assessed the effects of all executive function domains. It remains unknown which interventions affect memory and language. Future research should focus on performing high quality RCTs that consider aspects such as age, sex differences, and clinical heterogeneity.

7. References

(see thesis references)

Supplementary Material 1. Summary of Non-cognitive Function Outcomes in Interventions with an Impact on Cognitive Functions in Cerebral Palsy

Reference	LOE	Participants	Intervention	Other Outcomes
Authors (year)	n	n = (IG/CG) Age range (IG: mean ± SD/CG: mean ± SD) Type CP (n) Motor ability	**Name** (type of intervention) Description of intervention IG: time per day, times per week, number of weeks (total dose) CG: type of Control Group	$Test_1$: $result_1$ ↑ $Test_2$: $result_2$ ↓ $Test_3$: $result_3$ =
Piovesana et al. (2017); **James et al.** (2015b)	2	n = 102, 1 abandoned (51/5(8-18 years (11.6 ± 2.3/11.9 ± 2.5) Spastic unilateral (102) GMFCS I (45), II (56) MACS I (24), II (76), III (1)	**Mitii** (*multi-modal intervention*) A multi-modal web-based program: upper limb, cognitive, visual perceptual and physical activity training IG: 20-30 minutes per day, six times per week, 20 weeks (60 hours) CG: standard care	IG compared with CG AMPS Motor skills: ↑↑ Process skills: ↑↑ AHA: = MUUL: = COPM: Performance: ↑↑ Satisfaction: ↑↑ JTTHF: Dominant upper limb: ↑↑ Impaired upper limb: ↑↑
Ahn et al. (2021)	2	n = 47, 1 abandoned (23/23) 6-13 years (IG: 7.78 ± 1.68/CG: 7.30 ± 1.61) Type CP n.a. Motor ability n.a.	**Equine-assisted activities program** (*physical intervention*) IG: group therapy, 40 minutes per day, twice per week, 16 weeks (21.3 hours) CG: standard care	IG compared with CG PdsQL: Physical: = Emotional: = Social: = Academics: =

Supplementary Material 1 (continued).

Reference	LOE	Participants	Intervention	Other Outcomes
Alwhaibi et al. (2020)	2	n = 45 (15/15/15) 5-8 years (6.7 ± 0.8/6.6 ± 0.7/6.4± 0.8) Spastic unilateral (45) 1 and 1+ Modified Ashworth Scale MACS I-II (45)	**Augmented biofeedback and physical Training** (*multi-modal intervention*) Group A, physical therapy intervention: exercises facilitating hand-eye coordination and fine motor skills Group B, augmented biofeedback training: E-Link Upper Limb Exerciser (computerized graded interactive system) Group C, physical therapy intervention and augmented biofeedback training IG: 60 minutes per day, three times per week, 3 months (36 hours)	Group C compared with Group A and B Motor coordination: ↑↑

Supplementary Material 1 (continued).

Reference	LOE	Participants	Intervention	Other Outcomes	Reference
Mak et al. (2018, 2020)	2	n = 42 (21/21) 6-16 years (9 ± 3.2/9.6 ± 2.1) Spastic unilateral (16), bilateral diplegia (26) GMFCS I (22), II (12), III (8)	**MiYoga** (*multi-modal intervention*) Mindfulness movement programme based on hatha yoga principles IG: group therapy, 90 minutes per day, once per week, 6 weeks; individual therapy, 2 weeks at home (6 ± 1.86 hours) CG: standard care	IG compared with CG Child and adolescent mindfulness measure: = Strengths and difficulties questionnaire: = CP QoL-Child / Adolescent: = Wong-Baker faces pain rating scale: = Physical outcome measures: = Lateral set-up: = Sit-to-stand: = Half-kneel to stand: = 6-minute walk test (m): = Sit and reach test: = Mobility questionnaire 28: =	Pre vs follow-up (6 months after intervention) Child and adolescent mindfulness measure: = Strengths and difficulties questionnaire: = CP QoL-Child / Adolescent: = Wong-Baker faces pain rating scale: = Physical outcome measures: = Lateral set-up: ↑↑ Sit-to-stand: ↑↑ Half-kneel to stand: = 6-minute walk test (m): ↑↑ Sit and reach test: = Mobility questionnaire 28: =

Supplementary Material 1 (continued).

Reference	LOE	Participants	Intervention	Other Outcomes	Reference
Morgan et al. (2016)	2	n = 30 (15/15) (15.7 ± 4.8/20.1 ± 5.1 weeks) Not applicable	**GAME** (*multi-modal intervention*) Active motor learning, family centred care, parent coaching and environmental enrichment IG: 30-90 minutes per day, 18-30 appointments (until 12 months corrected age) (-) CG: standard care	IG compared with CG During intervention (16 weeks) PDMS-2: Raw score: ↑↑ Total motor quotient: = COPM: Performance: ↑↑ Satisfaction: = DASS-21: Total score: = Depression: = Stress: = Anxiety: =	Post-intervention (one year of life) PDMS-2: Raw score: ↑↑ Total motor quotient: ↑↑ COPM: Performance: = Satisfaction: ↑↑ DASS-21: Total score: = Depression: = Stress: = Anxiety: = GMFM-66: ↑↑ DASS-21: =
Teixeira-Machado et al. (2017)	2	n = 26 (13/13) (17.1 ± 2.4/18 ± 3.5) 15-29 years Spastic (26) GMFCS II (9), III (8), IV (7), V (2)	**Dance intervention** (*physical intervention*) Coordination-movements of upper and lower limbs, body image-interaction between subject, and environment, skill and agility-sequential components of the movement and trunk and head movements for spatial orientation and equilibrium IG: 60 min per day, twice per week, 3 months (24 hours) CG: kinesiotherapy exercises (active control)	IG compared with CG FIM: Independence function: ↑↑ Mobility: ↑↑ Communication: ↑↑ Total score: ↑↑ WHODAS 2.0: Body function: ↑↑ Activity: ↑↑ Participation: ↑↑	

Supplementary Material 1 (continued).

Reference	LOE	Participants	Intervention	Other Outcomes
Sajan et al. (2017)	2	n = 20 (10/10) 5-20 years (10.6 ± 3.8/12.4 ± 4.9) Spastic bilateral: diplegia (12), triplegia (5), quadriplegia (3) GMFCS I (1), II (3), III (13), IV (3)	**Nintendo Wii™** (*physical intervention*) Interactive video gaming that includes tennis and boxing activities IG: 45 minutes per day, six times per week, 3 weeks (13.5 hours) CG: standard care	IG compared with CG Sway velocity-eyes open: = Sway velocity-eyes closed: = Box and block test: = PBS: = QUEST: Grasp domain: = Dissociated movements domain: = Walking speed: = Walking endurance: =
Cho et al. (2015)	4	n = 56 4-7 years (mean n.a.) Spastic unilateral (20), bilateral diplegia (36) Motor ability n.a.	**Frosting developmental program in visual perception** (*cognitive intervention*) Visual-motor coordination, figure-ground perception, perceptual constancy, and position in space and spatial relationship IG: 30 min per day, three times per week, 8 weeks (12 hours) NCG	Pre vs post WeeFIM: Raw Score: ↑↑ Self-care: ↑↑ Sphincter control: = Mobility: ↑↑ Locomotion: = Communication: =

Supplementary Material 1 (continued).

Reference	LOE	Participants	Intervention	Other Outcomes
Pereira et al. (2019)	4	n = 15 8-12 years (10.53 ± 1.69) Spastic (10), dyskinetic (2), ataxic (3) Motor ability n.a.	**The Incredible Adventures of Anastácio, the Explorer** (*cognitive intervention*) Narrative intervention program to promote children's autonomy for activities of daily life, school trajectories, and their life project IG: Individual and group therapy 60 min per week, 18 weeks (18 hours) N	Pre vs post SE questionnaire: Behavioural engagement: ↑↑ Emotional engagement: ↑↑
Hsieh et al. (2017)	4	n = 14 3-8 years (7.03 ± 1.56) Spastic diplegia (4), spastic quadriplegia (6), dyskinetic (2), ataxic (2) GMFCS I (2), III (4), IV (4), V (4)	**Hippotherapy** (*physical intervention*) IG: 30 min per week, 12 weeks (6 hours) Group A (GMFCS I-III) and Group B (IV-V) NCG	Pre vs post Group A ICF-CY: Sensory functions and pain: ↑↑ Voice and speech: = Functions of the cardiovascular, haematological, immunological, and respiratory systems: ↑↑ Functions of the digestive, metabolic, and endocrine systems: = Genitourinary and reproductive functions: = Neuromusculoskeletal and movement related functions: ↑↑ Functions of the skin and related structures: = Learning and applying knowledge: ↑↑ General tasks and demands: = Communication: ↑↑ Mobility: ↑↑ Self-care: ↑↑

Supplementary Material 1 (continued).

Reference	LOE	Participants	Intervention	Other Outcomes
Hsieh et al. (2017) *continued*	4	n = 14 3-8 years (7.03 ± 1.56) Spastic diplegia (4), spastic quadriplegia (6), dyskinetic (2), ataxic (2) GMFCS I (2), III (4), IV (4), V (4)	**Hippotherapy** (*physical intervention*) IG: 30 min per week, 12 weeks (6 hours) Group A (GMFCS I-III) and Group B (IV-V) NCG	Domestic life: = Interpersonal interactions and relationships: = Major life areas: ↑↑ Community, social, and civic life: = Group B ICF-CY: Sensory functions and pain: = Voice and speech: = Functions of the cardiovascular, haematological, immunological, and respiratory systems: = Functions of the digestive, metabolic, and endocrine systems: = Genitourinary and reproductive functions: = Neuromusculoskeletal and movement related functions: ↑↑ Functions of the skin and related structures: = Learning and applying knowledge: General tasks and demands: = Communication: = Mobility: ↑↑ Self-care: = Domestic life: = Interpersonal interactions and relationships: = Major life areas: ↑↑ Community, social, and civic life: =

Supplementary Material 1 (continued).

Reference	Other Outcomes	
Hsieh et al. (2017) *continued*	Pre vs follow-up (12 weeks after intervention)	
	Group A ICF-CY: Sensory functions and pain: = Voice and speech: = Functions of the cardiovascular, haematological, immunological, and respiratory systems: = Functions of the digestive, metabolic, and endocrine systems: = Genitourinary and reproductive functions:= Neuromusculoskeletal and movement related functions: = Functions of the skin and related structures: = Learning and applying knowledge: = General tasks and demands: = Communication: = Mobility: = Self-care: = Domestic life: = Interpersonal interactions and relationships: = Major life areas: ↑↑ Community, social and civic life: =	Group B ICF-CY: Sensory functions and pain: = Voice and speech: = Functions of the cardiovascular, haematological, immunological, and respiratory systems: = Functions of the digestive, metabolic, and endocrine systems: = Genitourinary and reproductive functions: = Neuromusculoskeletal and movement related functions: = Functions of the skin and related structures: = Learning and applying knowledge: = General tasks and demands: = Communication: ↓↓ Mobility: ↓↓ Self-care: ↓↓ Domestic life: = Interpersonal interactions and relationships: = Major life areas: = Community, social, and civic life: =

Supplementary Material 1 (continued).

Reference	LOE	Participants	Intervention	Other Outcomes
Shin & Song (2016)	4	n = 11 Range age n.a. (127.9 ± 32.4 months) Paraplegia CP (11) GMFCS I (4), II (2), III (5)	**Kinesiotherapy** (*physical intervention*) Warming up, neck, and trunk stabilization, posture and warm-down exercises IG: 45 minutes per day, twice a week, 8 weeks (12 hours) NCG	Pre vs post JTTHF: Writing: Stimulated page turning: ↑↑ Lifting small object: ↑↑ Stimulated feeding: = Stacking: = Lifting large, lightweight object: ↑↑ Lifting large, heavy object: ↑↑
Christensen et al. (2017)	4	n = 11[a] 11-13 years (11.6 ± 0.8) Spastic unilateral (1), bilateral (10) GMFCS I (10), II (1)	**Climbing** (*physical intervention*) A climbing gym with walls and routes up to 12 m of height IG: 2.5 hours per day, three times per week, 3 weeks (22.5 hours)	Pre vs post Pinch precision task: ↑↑ Pinch strength task: = Pinch rate-of-force-development: = The test of whole hand strength: = Test of ankle coordination: = Test of ankle stiffness: = Test of ankle range of motion: ↑↑ Test of ankle dorsiflexion strength: = Romberg 30 s balance test: = Sit-to-stand test: ↑↑ Sådan er jeg questionnaire: Overall: = Physical abilities: = Skills and abilities: = Mental well-being: = Relationship to parents: = Relationship to others: =

Supplementary Material 1 (continued).

Reference	LOE	Participants	Intervention	Other Outcomes
Cherriere et al. (2020)	4	n = 10 10-17 years (14.1 ± 1.8) Spastic unilateral (3), spastic diplegia (4), dyskinetic (1), ataxic (1), unknown (1) GMFCS I (4), II (3), III (3)	**Dance intervention** (*physical intervention*) A variance of dance styles with an emphasis on balance movements IG: 60 minutes per day, twice per week, 10 weeks (20 hours) NCG	Pre vs post PBS: Dynamic balance: ↑↑ Static balance: ↑↑ Total score: ↑↑ Static balance (force platform): Max AP Amplitude of COF: = Max ML Amplitude of COF: = Max AP Speed of COF: = Max ML Speed of COF = PRT: Total COF shiftings on force platform: ↑↑ Total score: = Waling velocity: = Rythmic trial (Stamback): ↑↑ Tip pinch strength: = Right side strength: = Left side strength: =
Bilde et al. (2011)	4	n = 9 6-12 years (10.3, SD n.a.) Spastic GMFCS I (8), II (1) MACS I (4), II (5)	**Mitii** (*multi-modal intervention*) A multi-modal web-based program: cognitive, perceptual, and motor training IG: 30 minutes per day, every day, 20 weeks (73.6 ± 8 hours) NCG	Pre vs post AMPS: ↑↑ AHA: = Isometric muscle test: ↑↑ Sit-to-stand test: ↑↑ Frontal and lateral test: ↑↑ Romberg test: = Bruce tradmill test (Gait test): ↑↑ 6 minutes walking test: =

Supplementary Material 1 (continued).

Reference	LOE	Participants	Intervention	Other Outcomes
Lakes et al. (2019)	4	n = 8 9-14 years (mean n.a., SD n.a.) Spastic unilateral and bilateral (8) Motor ability n.a.	**Ballet intervention** (*physical intervention*) Warm-up, stretching, barre, and centre floor exercises IG: 60 minutes per day, three times per week, 6 weeks (≥16 hours) NCG	Pre vs post Body mass index: = Dual X-ray absorptiometry: = SCALE: = Time of ambulation (gait): ↑↑ Actigraph GT3X, habitual physical activity: = Pre vs follow-up (4-5 weeks after intervention) Body mass index: = Dual X-ray absorptiometry: = SCALE: = Time of ambulation (gait): ↑↑ Actigraph GT3X, habitual physical activity: =
Peny-Dahlstrand et al. (2018)	4	n = 5[b] 19-28 years (23.8 ± 4.2) Spastic unilateral (2), bilateral (2), dyskinetic (1) GMFCS I (1), II (3), III (1) MACS II (5)	**Cognitive Orientation to daily Occupational Performance** (*CO-OP*) (*cognitive intervention*) Participant identifies three activity goals that he or she wants to achieve IG: 60 minutes per day, once or twice per week, 10 sessions (10 hours) NCG	Pre vs post [c] COPM: Performance (↑ 15/15 goals): ↑ Satisfaction (↑ 15/15 goals): ↑ OSA, Swedish version (↑ 2/4): = AMPS: Motor skills (↑ 0/5): = Process skills (↑ 2/5): = Pre vs follow-up [c] (6 months after intervention) COPM Performance (↑ 15/15 goals): ↑ Satisfaction (↑ 15/15 goals): ↑ OSA, Swedish version (↑ 1/4): = AMPS: Motor skills (↑ 0/5): = Process skills (↑ 1/5): =

Supplementary Material 1 (continued).

Reference	LOE	Participants	Intervention	Other Outcomes
Heathcock et al. (2015)	4	n = 2 19 and 21 months Spastic bilateral quadriplegia (2) GMFCS V (2)	**Physical therapy** (*physical intervention*) Intensive physical therapy to enhance gross motor skills using toys or other motivators IG: 2 hours per day, 5 times per week, 4 weeks (40 hours) NCG	Pre vs post [c] BSDI-III Gross motor (↑ 2/2): ↑ Fine motor (↑ 1/2): = Expressive language (↑ 0/2): = Receptive language (↑ 2/2): ↑ GMFM-66 (↑ 2/2): ↑ GMFM-88 (↑ 2/2): ↑
Desai et al. (2014)	4	n = 1 13 years Motor ability n.a.	**GoTalk Now** (*AAC*) Communication application with vocabulary layouts and grids IG: twice per week, 8 weeks (5.3 hours) NCG	Pre vs post Communication matrix: ↑ GAS: ↑ SFA, physical: Computer/Equipment use: ↑ SFA, task supports Adaptations: = Assistance: ↑ SFA, participation: ↑

Supplementary Material 1 (continued).

Notes. [a] The sample included typical developing children, but only data for children with CP were included; [b] The sample included children with spina bifida, but only data for children with CP were included; [c] If individual results were reported, differences were considered if >50% of the total sample changed score.
n.a., not available; ↑, increase in studies with no statistical analysis; ↑↑, statistical significance increase; ↓, decrease in studies with no statistical analysis; ↓↓, statistical significance decrease; =, no differences.
Abbreviations. AHA, Assisting Hand Assessment; AMPS, Assessment of motor and process Skills; BSID-III, Bayley Scales of Infant and Toddler Development-Third Edition; CG, Control Group; COPM, Canadian Occupational Performance Measure; CP QoL, Cerebral Palsy Quality of Life Questionnaire; COF, Center of Force; DASS-21, Depression, Anxiety and Stress Scales-21; FIM, Functional Independence Measure; GAS, Goal Attainment Scaling; GMFCS, Gross Motor Function Classification System; GMFM, Gross Motor Function Measure; ICF-CY, International Classification of Functioning, Disability and Health for Children and Youth; IG, Intervention Group; JTTHF, Jebsen-Taylor Test of Hand Function; MACS, Manual Ability Classification System; MUUL, Melbourne Assessment of Unilateral Upper Limb Function; Mitii, Move It To Improve It; NCG, No Control Group; OSA, Occupational Self-Assessment; PBS, Pediatric Berg's Balance Scale; PDMS-2, Peabody Developmental Motor Scale-Second Edition; PdsQL, Pediatric Quality of Life Inventory 4.0 Genetic Core Scale; PRT, Pediatric Reach Test; QUEST, Quality of Upper Extremity Skills Test; SCALE, Selective Control Assessment of the Lower Extremity; SE, School Engagement Questionnaire; SFA, Student's School Function; WeeFIM, Wee Functional Independent Measure; WHODAS, World Health Organization Disability Assessment Schedule.

STUDY 2

Factors Related to Quality of Life in Children with Cerebral Palsy

Pediatric Neurology (2023)

Blasco, M., García-Galant, M., Laporta-Hoyos, O., Ballester-Plané, J., Jorba-Bertran, A., Caldú, X., Miralbell, J., Alonso, X., Meléndez-Plumed, M., Toro-Tamargo, E., Gimeno, F. & Pueyo, R.

ABSTRACT

Background

We investigated the influence of relevant demographic, clinical, neuropsychological, and psychosocial variables on the proxy-reported quality of life (QoL) of children with cerebral palsy (CP).

Methods

The proxy-reported Cerebral Palsy Quality of Life-Child questionnaire (CP QoL-Child) was completed by 58 children with CP (mean age = 10.22 years, SD = 1.67). Relationships between QoL scores and demographic, clinical, neuropsychological, and psychosocial variables were assessed. CP QoL scores and other variables that correlated significantly were introduced into a multiple linear regression model.

Results

Executive functioning and motor functional status were explanatory variables for the CP QoL total score. Executive functions explained three specific QoL domains: Social Well-being and Acceptance, Feelings about Functioning, and Emotional Well-being and Self-esteem. Parental stress also explained Social Well-being and Acceptance. Motor functional status and visual perception were explanatory variables for the Access to Services domain. Finally, autism spectrum disorder (ASD) traits were an explanatory variable for the Participation and Physical Health domain.

Conclusion

Executive functioning and motor functional status importantly influence QoL of children with CP. Visual perception, ASD symptoms, and parental stress variables are related with specific QoL domains. These findings demonstrate that interventions targeting cognitive functions in children with CP may positively influence QoL.

Highlights

- Executive functioning and motor functional status are explanatory variables of QoL total score in CP
- Visual perception skills and ASD symptoms influence specific domains of QoL in CP
- Parental stress also affects the QoL of children with CP

1. Introduction

Cerebral palsy (CP) describes a group of permanent disorders of movement and/or posture attributed to nonprogressive disturbances that occurred in the developing fetal or infant brain. Motor disorders are often accompanied by alterations in cognition, sensation, communication, perception, and behavior (Rosenbaum et al., 2007). CP is a chronic condition that may have negative implications on quality of life (QoL) through life span (Colver et al., 2014). The World Health Organization (WHO) defines QoL as "an individual's perception of their position in life in the context of the culture and values systems in which they live and in relation to their goals, expectations, standards and concerns" (WHOQOL GROUP, 1995). The International Classification of Functioning, Disability and Health (ICF) model proposed by the WHO encourages the consideration of the impact of several biopsychosocial factors in daily life. The ICF framework suggests that QoL may be influenced by different domains that are interrelated: body function and structure, activities, participation, and contextual and personal factors (World Health Organization, 2007).4 Considering this framework, it is essential to identify the different factors that affect QoL in CP and that should be included in interventions. Motor functioning is one of the most studied factors influencing QoL in CP. Several studies have explored associations between QoL and gross (Badia et al., 2016; Böling et al., 2016; Power et al., 2020; Rapp et al., 2017) and manual (Böling et al., 2016; Laporta-Hoyos et al., 2017; Park, 2017) motor functions, type of CP, and motor distribution (Böling et al., 2016; Jiang et al., 2016, 2016). Research also indicates that clinical (epilepsy, pain, or communication) (Böling et al., 2016; Giray et al., 2018; Jiang et al., 2016; Laporta-Hoyos et al., 2017; Omura et al., 2018; Rapp et al., 2017) and demographic (age, sex, and socioeconomic status) (Das et al., 2017; Jiang et al., 2016; Laporta-Hoyos et al., 2017; Omura et al., 2018; Power et al., 2020; Türkoğlu et al., 2016) variables influence QoL of people presenting CP.

Despite the importance of cognitive functions in CP, little is known about their impact on QoL. The few available studies exploring the association between cognitive functions and QoL have mainly focused on general intellectual functioning (Badia et al., 2016; Böling et al., 2016; Jiang et al., 2016; Laporta-Hoyos et al., 2017; Rapp et al., 2017) which is impaired in 50% of children with CP (intellectual quotient [IQ] < 70) (Novak et al., 2012; Påhlman et al., 2021; Stadskleiv, 2020).

Children with CP also present specific cognitive impairments. Concretely, visual perception and executive functions are the most affected cognitive domains in CP (Ego et al., 2015; Pagliano et al., 2007; Pueyo et al., 2009). Nevertheless, research about the association between QoL and visual perception or executive functions is scarce (Laporta-Hoyos et al., 2017; Mitry et al., 2016). Very few studies have described memory skills in people presenting with CP (Ballester-Plané et al., 2018; Østensjø et al., 2003; Pueyo et al., 2009; Toomela, 2012), and two of them report difficulties (Pueyo et al., 2009; Toomela, 2012). Previous studies have demonstrated the importance of memory in children due to its role in learning and acquisition of knowledge in academic, leisure, and social contexts (Smith, 2009) but association with QoL in CP has not been explored.

As for behavioral problems, associations have been explored between QoL and both prosocial behavior and psychopathology in children and adolescents with CP (Colver et al., 2015; Dang et al., 2015). Autism spectrum disorder (ASD) traits in children with CP are higher than in typically developing children, with an estimated prevalence raised up to 30% (Påhlman et al., 2021). No study to date has explored the association between ASD traits and QoL in children with CP. Considering these results, it is of special interest to conduct a study including all these neuropsychological variables to identify the best determinants of QoL. Moreover, psychosocial variables such as type of schooling (Badia et al., 2016; Power et al., 2020), participation (Burak & Kavlak, 2019; Omura et al., 2018), and parental stress (Rapp et al., 2017) have been associated with QoL in children with CP.

Taking into account the biopsychosocial model proposed by the ICF, the aim of the present study was to investigate the influence of demographic, clinical, neuropsychological, and psychosocial variables on QoL of children with CP.

2. Materials and Methods

2.1. Participants

Participants were recruited from the Sant Joan de De´u-Barcelona Children's Hospital, Vall d’Hebron University Hospital, and Fundacio´ ASPACE Catalunya in Barcelona. Ethical approval was obtained from the University of Barcelona's Institutional Ethics Committee, Institutional Review Board (IRB 00003099, assurance number: FWA00004225). The research was conducted in accordance with the Helsinki Declaration. Written informed consent was obtained by all parents or legal guardians of participants. The inclusion criteria were (1) clinical diagnosis of CP; (2) children aged between 8 and 12 years; (3) being able to understand instructions assessed by the Screening Test of Spanish Grammar (Toronto, 1973); and (4) presence of an intelligible yes/no response system. The presence of severe hearing or visual difficulties that precluded neuropsychological assessment was considered as an exclusion criterion.

2.2. Assessments

2.2.1. QoL

QoL was measured using the parent-proxy version of the Cerebral Palsy Quality of Life-Child (CP QoL-Child) questionnaire. CP QoL-Child is a specific questionnaire designed for children with CP and based on the ICF. This questionnaire considers seven QoL domains: Social Well-being and Acceptance, Participation and Physical Health, Feelings about Functioning, Emotional Well-being and Self-Esteem, Pain and Impact of Disability, Access to Services, and Family Health. CP QoL-Child scores were converted to values between 0 and 100, and the mean for each domain was calculated. A CP QoL total score was also computed by adding all domains. Higher scores indicate better QoL except in Pain and Impact of Disability domain, where lower scores indicate better QoL (Waters et al., 2007).

2.2.2. Demographic data

Participants' demographic data were obtained through parent's interview, including age, sex, and socioeconomic status (Estudio General de Medios, 2016).

2.2.3. Clinical data

Clinical information, such as motor CP type, distribution of the motor impairment, motor functional status, communication, gestational age, presence of epilepsy (Fisher et al., 2014) and pain was extracted from clinical history and proxy-reported questionnaires.

Motor functional status

Gross motor function was assessed by the Gross Motor Function Classification System (GMFCS) (Palisano et al., 2008). The GMFCS classifies children with CP based on their functional abilities and limitations. In addition, the Manual Abilities Classification System (MACS) (Eliasson et al., 2006) and the Bimanual Fine Motor Function (BFMF) system (Elvrum et al., 2016) were used to categorize manual ability. The three scales contain five levels of classification, and higher scores indicate lower levels of motor functioning.

Communication

Everyday communication abilities were assessed by the Communication Function Classification System (CFCS) (Hidecker et al., 2011), which contains five levels. Speech production was measured by the Viking Speech Scale (VSS) (Pennington et al., 2013), which has four levels. Higher scores in both scales indicate higher difficulties.

Pain

Pain was assessed by the Bodily Pain and Discomfort Scale of The Child Health Questionnaire (Landgraf, 2020). This questionnaire considers the presence of pain, frequency, and intensity during the last month. The frequency score was used in all analyses, and higher scores indicate higher frequency of pain.

2.2.4. Neuropsychological assessment

Participants completed a neuropsychological assessment to evaluate general intellectual functioning, visual perception, executive functions, and memory. Raw scores were converted into standardized scores to correct for age. Parents of participants completed questionnaires to assess psychological adjustment and ASD traits.

General intellectual functioning

General intellectual functioning was measured using the Raven's Coloured Progressive Matrices (RCPM) (Raven et al., 2011). RCPM is a standardized easy-to-administer tool in people with CP (Ballester-Plané et al., 2016; Pueyo et al., 2008). Higher scores in RCPM indicate better performance.

Visual perception

Visual perception was evaluated by the Facial Recognition Test (FRT) (Benton 1994) and the Arrows subtest of the Developmental NEuroPSYchological Assessment-Second Edition (NEPSY-II) (Korkman et al., 2014). Higher scores in both tests indicate a better performance.

Executive functions

According to Diamond's model (Diamond, 2013) both core (inhibitory control, working memory, and cognitive flexibility) and higher-order (planning) executive functions were assessed. Inhibitory control was assessed by the Digits total score from Wechsler Intelligence Scale for Children-Fifth Edition (WISC-V) (Wechsler et al., 2015) and the Auditory Attention subtest of the NEPSY-II (Korkman et al., 2014). Working memory was assessed by using Backward Digit Span from WISC-V (Wechsler et al., 2015) Cognitive flexibility was assessed by the Response Set subtest of the NEPSY-II (Korkman et al., 2014), and planning was assessed by using the Tower Test of the Delis-Kaplan Executive Function System (D-KEFS) (Delis et al., 2001). Social cognition was assessed using the Theory of Mind subtest of the NEPSY-II (Korkman et al., 2014). Higher scores in all these tests indicate a better performance.

To assess behavioral manifestations of executive functioning in everyday life, the parent-proxy version of the Behavior Rating Inventory of Executive Function-Second Edition (BRIEF-2) was used (Gioia et al., 2000). This scale comprises four indexes: Behavioral Regulation, Emotional Regulation, Cognitive Regulation, and Global Index of Executive Function. Higher T scores indicate worst performance.

Memory

Verbal and visual memory were measured using the Word Selective Reminding subtest of the Test of Memory and Learning (TOMAL) (Reynolds, 1998) and the Memory for Designs subtest of the NEPSY-II (Korkman et al., 2014), respectively. Higher scores indicate a better performance.

Psychological adjustment

The Strengths and Difficulties Questionnaire (SDQ) (Goodman, 1997) completed by the parents was used to measure psychological adjustment including emotional, behavioral, and socialization problems. The total difficulties score, a measure of overall psychological adjustment, was used in all analyses. Higher scores indicate more presence of behavioral problems.

Autism spectrum disorder traits

The Autism Spectrum Screening Questionnaire (ASSQ) was used for the screening of ASD traits (Ehlers et al., 1999). Higher scores on ASSQ indicate the presence of more ASD traits.

2.2.5. Psychosocial data

Psychosocial data included type of schooling, participation, and parental stress

Type of schooling

Type of schooling was obtained through parents' interview, indicating mainstream school, mainstream with support class, mainstream school in special classroom, and special school.

Participation

Participation was evaluated by the Participation and Environment Measure for Children and Youth (PEM-CY) (Coster et al., 2011); it examines the level of participation at home, school, and community settings, and higher scores indicate better participation.

Parental stress. Parental Stress Scale (PSS) was used to assess self-perceived stress from participants' parents (Berry & Jones, 1995). Higher scores on the PSS scale indicate greater stress levels.

2.3. Statistical analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences (IBM SPSS V.25). Assumptions of normality, linearity, and homoscedasticity were examined using the Kolmogorov-Smirnov test, scatterplots, and histograms. Pearson, Spearman, and Kendall bivariate correlations between the CP QoL scores and demographic, clinical, neuropsychological, and psychosocial variables were performed. Significance was set at $P < 0.05$ and corrected for multiple comparisons (Holm-Bonferroni). Those variables that correlated significantly after applying the Holm-Bonferroni correction were introduced into multiple linear regression models (stepwise method) to identify the best explanatory models of CP QoL scores. The assumption conditions of multiple linear regression model were checked. One participant was identified as an outlier in several scores of the neuropsychological assessment and was removed from correlation and regression analyses. The r and R2 values were interpreted as measures of effects size, for correlation and regression models, respectively. Cohen's interpretative criteria (Cohen, 1988) were applied considering r/R^2 effects as small $r \geq 0.10/R^2 \geq 0.01$, medium $r \geq 0.30/R^2 \geq 0.09$, and large $r \geq 0.50/R^2 \geq 0.25$. The significance level was set at P value <0.05.

The present study includes 58 participants with CP age ranging from 8 to 12 (mean age = 10.22 years, SD = 1.67). Half of the sample was female, and most of the participants were diagnosed with spastic CP (91.4%) Only 29.3% of participants had epilepsy, and most participants reported experiencing pain (82.0%). Demographic and clinical information of the sample are summarized in Tables 1 and 2, respectively. The descriptive statistics for neuropsychological and psychosocial variables are presented in Tables 3 and 4. The mean CP QoL total score was 72.37 (SD = 9.94), and the highest scores were observed in the Emotional Well-being and Self-Esteem (mean age = 81.11, SD = 14.58) domains (Table 5).

Table 1. Descriptive statistics for demographic data.

Age, mean (SD) / range	10.22 (1.67) / 8-12
Sex, n (%)	Female: 29 (50)
	Male: 29 (50)
Socioeconomic status (monthly income), n (%)	A1 (>€3,005): 6 (10.3)
	A2 (€2,452 – €3,005): 23 (39.7)
	B (€2,146 – €2,451): 7 (12.1)
	C (€1,603 – €2,145): 9 (15.5)
	D (€1,313 – €1,602): 9 (15.5)
	E1 (€745 – €1,312): 4 (6.9)

Abbreviations. SD, Standard Deviation.

Table 2. Descriptive statistics for clinical data.

Type of CP, n (%)	Spastic: 53 (91.4)
	Dyskinetic:4 (6.9)
	Unknown: 1 (1.7)
Distribution of motor impairment, n (%)	Diplegia: 11 (19)
	Hemiplegia: 36 (62.1)
	Triplegia: 2 (3.4)
	Tetraplegia: 9 (15.5)
Motor functional status	
GMFCS, n (%)	I: 34 (58.6)
	II: 16 (27.6)
	III: 6 (10.3)
	IV: 2 (3.5)
MACS, n (%)	I: 24 (41.4)
	II: 28 (48.3)
	III: 6 (10.3)
BFMF, n (%)	I: 31 (53.5)
	II: 20 (34.4)
	III: 6 (10.3)
	IV: 1 (1.8)
Communication	
CFCS, n (%)	I: 35 (60.3)
	II: 18 (31)
	III: 3 (5.2)
	IV: 2 (3.5)
VSS, n (%)	I: 43 (74.1)
	II: 11 (19)
	III: 4 (6.9)
Gestational age (in weeks), n (%)	<37 w: 36 (62.1)
	≥ 37 w: 17 (29.3)
	Unknown: 5 (8.6)
Epilepsy, n (%)	No epilepsy:41 (70.7)
	Active: 17 (29.3)
Pain, n (%) [b]	Never: 24 (41.4)
	Once or twice: 14 (24.2)
	A few times: 8 (13.8)
	Fairly often: 5 (8.6)
	Very often:1 (1.7)
	Every day or almost every day: 1 (1.7)
	Unknown: 5 (8.6)

Abbreviations. BFMF, Bimanual Fine Motor Function; CFCS, Communication Function Classification System; CP, Cerebral Palsy; GMFCS, Gross Motor Function Classification System; MACS, Manual Ability Classification System; VSS, Viking Speech Scale.

Table 3. Descriptive statistics for neuropsychological assessment.

Neuropsychological variable	n	Mean (SD)	Range
IQ			
RCPM (IQ)	58	97.67 (12.57)	75-125
Visual perception			
FRT (z)	58	0.49 (1.50)	-2.90 to 4.33
NEPSY-II, Arrows (z)	58	-1.13 (1.22)	-3.00 to 1.67
Executive functions			
Inhibition			
WISC-V, Digits total score (z)	57[a]	-1.19 (0.97)	-3.00 to 0.67
NEPSY-II, Auditory Attention (z)	58		
Working memory			
WISC-V, Digit Span Backwards (z)	57[a]	-0.90 (1.39)	-4.40 to 1.44
Cognitive flexibility			
NEPSY-II, Response Set (z)	58		
Planning			
D-KEFS, Tower Test (z)	57[b]	-0.77 (1.09)	-3.00 to 2.00
Social cognition			
NEPSY-II, Theory of Mind (z)	57[c]	-1.03 (1.02)	-2.19 to 1.50
Executive functions in daily life			
BRIEF-2, Behavioral Regulation Index (T)	58	61.79 (11.70)	42-90
BRIEF-2, Emotional Regulation Index (T)		64.00 (11.49)	42-89
BRIEF-2, Cognitive Regulation Index (T)		64.09 (10.87)	36-86
BRIEF-2, Global Index of Executive Function (T)		65.64 (11.12)	44-90
Memory			
Verbal			
TOMAL, Word Selective Reminding (z)	56[a]	-0.04 (1.00)	-2.33 to 1.33
Visual			
NEPSY-II, Memory for Designs (z)	55[c]	-1.47 (1.30)	-3.00 to 1.00
Psychological adjustment			
SDQ, total difficulties score	56[d]	13.77 (5.76)	2.-32
ASD traits			
ASSQ	52[d]	10.06 (9.42)	0-36

Abbreviations. ASD, Autism Spectrum Disorder; ASSQ, Autism Spectrum Screening Questionnaire; BRIEF-2, Behavior Rating Inventory of Executive Function-Second Edition; D-KEFS, Delis-Kaplan Executive Function System; FRT, Facial Recognition Test; IQ, Intelligence Quotient; NEPSY-Second Edition, A Developmental NEuroPSYchological Assessment-II; RCPM, Raven's Coloured Progressive Matrices; SD, Standard Deviation; SDQ, Strengths and Difficulties Questionnaire; TOMAL, Test of Memory and Learning; WISC-V, Wechsler Intelligence Scale for Children-Fifth Edition.

Reasons for missing data: [a] very slow communication system that preclude to use an appropriate response system for the test used; [b] severe motor impairment that made it difficult to complete the task; [c] being not able to complete the test due to fatigue; [d] not answered by the parents.

Table 4. Descriptive statistics for psychosocial data.

Neuropsychological variable		n	n (%) / mean (SD)	Range
Type of schooling (n)				
	Mainstream school	58	29 (50.0)	
	Mainstream school with support class		21 (36.2)	
	Mainstream school in special classroom		3 (5.2)	
	Special school		5 (8.6)	
Participation	(mean)			
	PEM-CY, frequency home	54[a]	5.56 (0.83)	2.80-6.70
	PEM-CY, frequency school		4.26 (1.13)	1.75-6.20
	PEM-CY, frequency community		2.61 (1.00)	0.50-5.30
Parental stress (mean)				
	PSS	55[a]	25.56 (7.68)	13-45

Abbreviations. PEM-CY, Participation and Environment Measure for Children and Youth; PSS, Parental Stress Scale.

Reasons for missing data: [a] not answered by the parents.

Table 5. Descriptive statistics for CP QoL domains.

CP QoL domains	n	Mean (SD)	Range
CP QoL total score	58	72.37 (9.94)	35.25-92.11
Social Well-being and Acceptance	58	80.93 (11.74)	52.08-100
Feelings about Functioning	58	72.94 (12.75)	31.25-94.79
Participation and Physical Health	58	67.51 (15.50)	13.64-88.64
Emotional Well-being and Self-Esteem	58	81.11 (14.58)	8.33-100
Access to Services	58	67.06 (18.35)	18.75-100
Pain and Impact of Disability	58	65.57 (13.86)	21.88-89.06
Family Health	58	70.76 (14.76)	37.50-100

Abbreviations. CP QoL, Cerebral Palsy Quality of Life Questionnaire.

3. Results

3.1. Correlation analysis

Significant correlation coefficients between the demographic, clinical, neuropsychological, and psychosocial variables and the CP QoL scores after Holm-Bonferroni correction are presented in Table 6.

Table 6. Significant bivariate correlations between CP QoL domains score and explanatory variables after Holm-Bonferroni correction.

CP QoL total score	$r_p/r_s/r^T$	p
Motor status		
Gross motor function: GMFCS	-0.40^T	<0.001
Executive functions in daily life		
BRIEF-2, Emotional Regulation Index	-0.44_s	0.001
BRIEF-2, Cognitive Regulation Index	-0.42_s	0.001
BRIEF-2, Global Index of Executive Function	-0.48_s	<0.001
Psychological adjustment		
SDQ, total difficulties score	-0.44_s	0.001
ASD traits: ASSQ	-0.53_s	<0.001
Social Well-being and Acceptance		
Executive functions in daily life		
BRIEF-2, Emotional Regulation Index	-0.54_p	<0.001
BRIEF-2, Cognitive Regulation Index	-0.42_p	0.001
BRIEF-2, Behavioral Regulation Index	-0.50_p	<0.001
BRIEF-2, Global Index of Executive Function	-0.55_p	<0.001
Psychological adjustment		
SDQ, total difficulties score	-0.49_p	<0.001
Parental stress: PSS	-0.45_p	0.001
Feelings about Functioning		
Executive functions in daily life		
BRIEF-2, Cognitive Regulation Index	-0.42_p	0.001
BRIEF-2, Behavioral Regulation Index	-0.44_p	0.001
BRIEF-2, Global Index of Executive Function	-0.50_p	<0.001
Participation and Physical Health		
ASD traits: ASSQ	-0.46_s	0.001
Emotional Well-being and Self-Esteem		
Executive functions in daily life		
BRIEF-2, Emotional Regulation Index	-0.52_p	<0.001
BRIEF-2, Behavioral Regulation Index	-0.44_p	0.001
BRIEF-2, Global Index of Executive Function	-0.46_p	<0.001
Psychological adjustment		
SDQ, total difficulties score	-0.43_s	0.001
Access to Services		
Motor functional status		
Gross motor function: GMFCS	-0.38^T	<0.001
Visual perception: FRT	0.45_p	<0.001

Abbreviations. ASD, Autism Spectrum Disorder; ASSQ, Autism Spectrum Screening Questionnaire; BRIEF-2, Behavior Rating Inventory of Executive Function-Second Edition; CP QoL, Cerebral Palsy Quality of Life Questionnaire; FRT, Facial Recognition Test; GMFCS, Gross Motor Function Classification System; PSS, Parental Stress Scale; SDQ, Strengths and Difficulties Questionnaire.

r_p Pearson correlation, r_s Spearman correlation, r^T Tau-Kendall correlation.

3.1.1. CP QoL total score

Gross motor function, executive functions in daily life, psychological adjustment, and ASD symptomatology scores were significantly and negatively correlated with the CP QoL total score (large and medium effect size). Demographic and psychosocial variables were not statistically associated with the CP total score.

3.1.2. Specific CP QoL domains

Demographic variables did not correlate with any specific domain. Regarding clinical variables, gross motor function (GMFCS) correlated negatively (medium effect size) with the scores in the Access to Services domain of the CP QoL questionnaire. No statistically significant correlation was found between the manual ability (MACS and BFMF) and communication (CFCS and VSS) scores and scores in any specific CP QoL domain.

In relation with neuropsychological variables, visual perception scores correlated positively (medium effect size) with Access to Services. The executive functions in daily life scale (BRIEF-2) scores were associated with scores in different CP QoL domains. Specifically, scores in four BRIEF-2 indexes (including the Global Index) were negatively associated with Social Well-being and Acceptance domain (large and medium effect size). Similarly, three BRIEF-2 indexes were negatively associated (large and medium effect size) with Feelings about Functioning and Emotional Well-being and Self-Esteem scores. Executive function performance-based test scores did not correlate significantly with any QoL domain. No association was found between IQ and memory with any of the CP QL domains.

Psychological adjustment, as assessed by the SDQ total difficulties score, correlated negatively (medium effect size) with Social Well-being and Acceptance and Emotional Well-being and Self-Esteem domains. ASD symptoms (ASSQ) correlated negatively (medium effect size) with scores in the Participation and Physical Health domain.

Among psychosocial variables, parental stress (PSS) scores were significantly negatively associated with scores in the Social Well-being and Acceptance domain.

Any of the demographic, clinical, neuropsychological, and psychosocial variables considered in the present study were not significantly correlated with Pain and Impact of Disability, and Family Health domains.

3.2. Regression analysis

The multiple linear regression models are presented in Table 7.

3.2.1. CP QoL total score

Clinical and neuropsychology variables were significant explanatory variables for CP QoL total score model. The multiple linear regression model for CP QoL total score indicated that motor functional status (GMFCS) and executive function in daily life (Global Index of Executive Function, BRIEF-2) were more impaired, CP QoL total score decreased.

3.2.2. Specific CP QoL domains

Clinical, neuropsychological, and psychosocial variables were significant explanatory variables for CP QoL domains in multiple linear regression models. According to effect size (from larger to smaller) for each multiple linear regression model, behavioral manifestations of executive functioning in everyday life (Global Index of Executive Function, BRIEF-2) together with parental stress (PSS) were related to Social Well-being and Acceptance domain (large effect size). Gross motor function (GMFCS) and visual perception (FRT) explained the variance in Access to Services domain (large effect size). Executive functions in daily life were also the only explanatory variables of two QoL domains: Feelings about Functioning and Emotional Well-being and Self-Esteem (large effect size). Finally, ASD symptomatology (ASSQ) alone was an explanatory variable (large effect size) for Participation and Physical Health domain model.

Table 7. Multiple linear regression analysis between CP QoL domains and potential explanatory variables that correlated with CP QoL.

CP QoL domains	R^2	β	t
CP QoL total score			
Motor status: GMFCS	0.50	-0.50	-4.76***
Executive functions in daily life			
BRIEF-2, Global Index of Executive Function		-0.52	- 4.94***
Social Well-being and Acceptance			
Executive functions in daily life			
BRIEF-2, Global Index of Executive Function	0.38	-0.45	-3.63***
Parental stress: PSS		-0.28	-2.31*
Feelings about Functioning			
Executive functions in daily life			
BRIEF-2, Cognitive Regulation Index	0.25	-0.50	-4.24***
Participation and Physical Health			
ASD traits: ASSQ	0.13	-0.36	-2.67**
Emotional Well-being and Self-Esteem			
Executive functions in daily life			
BRIEF-2, Emotional Regulation Index	0.25	-0.50	-4.07***
Access to Services			
Motor functional status			
Gross motor function: GMFCS	0.33	-0.38	-3.27**
Visual perception: FRT		0.33	2.86**

Abbreviations. ASD, Autism Spectrum Disorder; ASSQ, Autism Spectrum Screening Questionnaire; BRIEF-2, Behavior Rating Inventory of Executive Function-Second Edition; CP QoL, Cerebral Palsy Quality of Life Questionnaire; FRT, Facial Recognition Test; GMFCS, Gross Motor Function Classification System; PSS, Parental Stress Scale.

* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$.

4. Discussion

This is the first study to investigate the association between QoL and a broad range of relevant variables including demographic, clinical, neuropsychological, and psychosocial variables in children with CP. Moreover, this research considers some variables that have not been studied previously in CP (such as VSS, memory, and ASD traits). Our results highlight that executive functions and motor functional status are key factors affecting QoL of children with CP. Visual perception, ASD traits and parental stress variables are related with specific QoL domains.

Taken together, a range of executive function components are associated with both QoL total score and with specific QoL domains. The BRIEF-2 Global Index seems to be a good predictor for the CP QoL total score and for the scoring in the Social Well-being and Acceptance domain in multiple linear regression models. The BRIEF-2 Cognitive Regulation Index was related with the Feelings about Functioning domain scores. In other words, this association indicates that problem-solving skills, as measured by Cognitive Regulation Index, play a role in individuals' feelings about their independence in daily activities. In addition, better emotion regulation skills, assessed by BRIEF-2 Emotional Regulation Index, were related with feeling good about oneself, as is described Emotional Well-being and Self-Esteem QoL domain. The importance of executive functions in QoL in people with CP through life span is ratified by our results and previous studies (Laporta-Hoyos et al., 2017).

Performance-based tests used in the present study to assess executive functions did not show any significant correlation with any QoL domain; this may due to the fact that performance-based tests have lower ecological validity than rating scales, as they assess aspects of executive functions that are required in everyday home and/or school settings (Krivitzky et al., 2019).

Visual perception skills were the other neuropsychological variable with significant impact on specific domains of QoL, such as the Access to Services domain; this may be due to the fact that children with visual perceptual impairments require more adaptations, such as special equipment and additional community services. However, difficulties to access these assistive technology resources decrease their individual's functioning and independence, consequently affecting their well-being. Visual perception was not significantly associated with the CP QoL total score in our sample. To date, only one study has investigated the association between visual perceptual impairments and QoL (Mitry et al., 2016). Mitry et al. (2016) found that visual perception was an explanatory variable of overall QoL in a sample similar to ours, with children aged between 6 and 11 years. The inconsistency between our findings and Mitry's et al. (2016) could be due to the differences in motor severity between samplesdour study did not include participants with severe motor impairment (GMFCS V). Accordingly, the rate of visual perceptual impairments was around 12% in our sample, whereas in Mitry et al.'s (2016) sample 53% of participants presented these impairments. Another explanation for the different results between studies could be that the tool used to measure QoL was different between studies. Mitry et al. (2016) assessed QoL through a generic questionnaire, whereas in the present study a questionnaire designed specifically to assess QoL in CP population was used (Waters et al., 2007).

The lack of significant associations between QoL and general intellectual functioning in our study as an explanatory variable is consistent with Laporta-Hoyos et al.'s results (Laporta-Hoyos et al., 2017). However, other studies suggest that children with higher IQ tend to have better QoL (Badia et al., 2016; Böling et al., 2016; Jiang et al., 2016; Rapp et al., 2017). The inconsistency between these findings and ours may be due to the tools used to measure IQ (Jiang et al., 2016; Rapp et al., 2017) or due to the fact that people with low IQ were also included in previous studies (Badia et al., 2016; Böling et al., 2016). The mean IQ in our study was higher, and this might have influenced our results.

Memory skills were not associated with QoL in our sample. Pediatric studies exploring the association between memory and QoL are scarce. Only one study has found that verbal memory plays an important role in QoL in children with epilepsy (Hrabok et al., 2013),56 which was not a common comorbidity in our sample.

The present study is the first one to explore the association between ASD symptoms and QoL in children with CP. Interestingly, only ASD symptoms explained the scoring in the Participation and Physical Health domain in the multiple linear regression model. This association is not surprising, as social communication difficulties can undermine participation in school, sporting, and community activities. Finally, it is important to highlight that ASD symptoms were significantly univariably correlated with the CP QoL total score, even though such association did not remain significant in the multiple linear regression model.

Psychological adjustment, as measured by the SDQ, was significantly and univariably associated with two QoL domains (Social Well-being and Acceptance and Emotional Well-being and Self-Esteem) and the CP QoL total score. Psychological adjustment, however, did not feature in any multiple linear regression model for QoL. These results agree with those of Power et al. (2020) who found that SDQ scores were significantly univariably correlated with specific QoL domains.

Regarding motor functional status variables, aligning with previous findings (Badia et al., 2016; Böling et al., 2016; Power et al., 2020; Rapp et al., 2017), GMFCS was associated with the total QoL in our study. Conversely, manual ability did not exert an impact on QoL. Consistently, Burak and Kavlav (2019) did not find any association between manual ability and QoL in a sample including participants with similar MACS levels (I to III) to our sample. Previous studies including participants with greater levels of manual impairment, however, report significant associations between manual ability and QoL (Böling et al., 2016; Laporta-Hoyos et al., 2017; Park, 2017). Similarly, other clinical variables (type of CP, distribution of motor impairment, communication, prematurity, and epilepsy) were not associated with QoL. Taken together, the results of the present and previous studies seem to indicate that these variables are associated with QoL when samples include children with severe communication difficulties, motor distribution impairment (Jiang et al., 2016), or more comorbidities (Türkoğlu et al., 2016).

Concerning psychosocial variables, parental stress is associated with Social Well-being and Acceptance domain, which measures social network and personal relationships. These findings reinforce the idea that parental stress plays an important role in specific domains of QoL in children with CP.5,8 In contrast to early findings (Badia et al., 2016; Burak & Kavlak, 2019; Omura et al., 2018; Power et al., 2020), type of schooling and participation were not associated with QoL in our study.

Finally, it is important to mention that two QoL domains (Pain and Impact of Disability, and Family Health) were not associated with any of the variables considered (demographic, clinical, neuropsychological, and psychosocial). Pain and Impact of Disability domain was perceived as the least satisfactory domain, as in previous findings (Böling et al., 2016).

This is the first study exploring the association between QoL and a wide range of biopsychological variables considering the ICF framework for children with CP, but some limitations should be considered. First, sample size is moderate, and future studies including larger samples will provide further understanding about which factors influence QoL. Second, our sample included children with mild manual motor impairments (MACS I to III). Although there is a lack of participants with severe motor impairments to cover the whole spectrum, our results reinforce the effect of some variables in QoL in mild cases. Finally, we relied on parental reports to measure QoL. Previous studies indicate that the perception of QoL may differ between self-reports and proxy reports, as caregivers tend to underestimate the QoL of children and adolescents with CP (Dang et al., 2015; Sentenac et al., 2021). However, the biopsychological approach of our study allows a comprehensive understanding of variables that may impact QoL.

In conclusion, our study identified that executive functions, motor functional status, visual perception functions, ASD symptoms, and parental stress were significant explanatory variables in multiple linear regression models for QoL. Importantly, executive functions were significant explanatory variables in several QoL domains, highlighting their key role in QoL. Given their influence in QoL, cognitive functions, especially executive and visual perception functions, together with ASD traits should be targets for intervention in children with CP.

5. References

(see thesis references)

STUDY 3

Far Transfer Effects of a Home-Based Computerized Executive Function Intervention in Children with Cerebral Palsy: a Randomized Controlled Trial.

Working paper under review in Developmental Medicine & Child Neurology

Blasco, M., García-Galant, M., Ballester-Plané, J., Laporta-Hoyos, O., Caldú, X., Leiva, D., Boyd, R., Ortibus, E., & Pueyo, R.

ABSTRACT

Aims

To evaluate far transfer effects of a home-based computerized executive function intervention on non-targeted cognitive functions (visual perception and memory), as well as quality of life and participation in children with CP. This study also aims to determine whether these improvements, if any, were maintained 9 months after the intervention.

Methods

Sixty children with CP (8-12 years old) were randomly allocated into intervention or waitlist control groups. The intervention group underwent a home-based executive function intervention program for 30 minutes per day, 5 days a week for 12 weeks. All participants were assessed before the intervention, immediately and 9 months after the intervention finished.

Results

After the intervention finished, immediate verbal memory, verbal learning and visual perception (object recognition) performance were significantly better in the intervention group compared to the waitlist group. No improvements were found in visual memory, visual spatial perception, quality of life and participation after the intervention. Follow-up scores showed beneficial effects were not maintained 9 months after the intervention finished.

Interpretation

A home-based computerized executive function intervention produces short-term far transfer effects on memory and visual perception in children with CP.

What this paper adds

- A home-based computerized executive function intervention improves other non-target cognitive functions (memory and visual perception) in children with CP.
- Improvements were not maintained 9 months after the intervention finished.

1. Introduction

Cerebral palsy (CP) is the leading cause of physical disability during childhood with an estimated prevalence of around 1.6 per 1000 live births (McIntyre et al., 2022). The term CP refers to a group of permanent movement and/or posture development disorders due to brain injury during the antenatal, perinatal or early postnatal period that persists through the lifespan. These motor symptoms are often accompanied by disturbances of sensation, communication, perception, behavior, epilepsy and cognition (Rosenbaum et al., 2007).

Visual perception and executive function impairments are two of the most described cognitive impairments in CP (Fluss & Lidzba, 2020). Executive function impairments have been reported in both core (inhibitory control, working memory, and cognitive flexibility) and higher-order (planning, reasoning and problem-solving) executive functions (Di Lieto et al., 2017; Freire & Osório, 2020). Memory impairments have been also reported in CP, which are associated with learning and academic performance during childhood (Baddeley et al., 2003; Pueyo et al., 2009). It is of special interest to develop interventions addressed to cover these cognitive functions (Baddeley et al., 2003).

Children with CP may need to undergo diverse interventions to address the wide range of motor and non-motor impairments. The need to optimise resources to reduce time and costs leads intervention research to not only focus on effects on those abilities addressed by the intervention (near transfer effects) but also on changes in non-targeted abilities (far transfer effects) (Bombonato et al., 2023; Oldrati et al., 2020). Prior studies about intervention in CP have mainly focused on physical interventions (Blasco et al., 2022). These interventions seem to produce beneficial effects on general cognitive functioning and executive functions (Ahn et al., 2021; Teixeira-Machado et al., 2017). Nevertheless, no improvements have been reported in visual perception (Teixeira-Machado et al., 2017). To date no studies have explored the potential effects of these interventions on memory skills.

Contrary to physical interventions, multi-modal interventions (combining physical and cognitive tasks) improved visual perception (Alwhaibi et al., 2020; Aran et al., 2020), although non target by these interventions. Moreover, these multi-modal interventions had also beneficial effects on general cognitive functioning and executive functions (Aran et al., 2020; Morgan et al., 2016b). As in the case of physical interventions, no studies about multi-modal interventions have investigated the effects on memory skills. Considering this, it is of special interest to investigate the role of cognitive interventions, whose aim is to improve specific cognitive functions.

Research about the effectiveness of cognitive interventions for people with CP is, however, scarce. Only far transfer effects in visual perception improvements have been demonstrated after a home-based executive intervention in children with CP (Di Lieto et al., 2021). Studies in other populations have proved the potential of executive function intervention to enhance memory skills in children (Acosta et al., 2019). Di Lieto et al. (2021) did not find visual memory improvements and no study to date has explored the potential benefits of cognitive intervention on verbal memory. Among different types of cognitive interventions, those targeting executive function should be prioritized due to its development during childhood and adolescence. In this way, greater cognitive effects after an executive function intervention, even in non-targeted cognitive functions, compared with other cognitive intervention types (Zelazo & Carlson, 2012). Moreover, executive functions have been associated with quality of life along the lifespan in people with CP (Blasco et al., 2023; Laporta-Hoyos et al., 2017). In addition, considering the need to optimise resources, research has prioritized home-based computerized interventions in people with CP (Brown et al., 2010). Therapy schedules together with mobility barriers, may be a burden for children with CP and their families. Home-based computerized programs allow flexibility about when and where interventions can take place, which results into greater motivation and adherence (Ballantyne et al., 2019; Chen et al., 2013).

The main purpose of this study was therefore to explore whether a home-based computerized executive function intervention for children with CP has far transfer effects on memory, visual perception, quality of life and participation. A second aim was to determine whether these far transfer effects, if any, would be maintained at 9-months post-intervention.

2. Materials and methods

The present study is a single-blind randomized controlled trial (RCT). The CONSORT Statement was followed in the design, implementation and reporting of this study (Moher et al., 2001). The protocol was registered on ClinicalTrials.gov (NCT04025749) and published (García-Galant et al., 2020). Ethics approval was obtained from the University of Barcelona's Institutional Ethics Committee, Institutional Review Board (IRB 00003099, assurance number: FWA00004225; http://www.ub.edu/recerca/comissiobioetica.htm) and Sant Joan de Déu-Barcelona Children's Hospital Ethics Committee (PIC-45-20). The research was conducted in accordance with the Helsinki Declaration. Written informed consent was obtained from all participants' parents or legal guardians.

2.1. Participants

Participants were recruited from the Sant Joan de Déu-Barcelona Children's Hospital, Vall d'Hebron University Hospital and Fundació ASPACE Catalunya in Barcelona. Participants were also recruited from our project website and a previous study (Laporta-Hoyos et al., 2019). The inclusion criteria were: (1) having a clinical diagnosis of CP; (2) being between 8 and 12 years old; (3) Manual Ability Classification System (MACS) from I to III (Eliasson et al., 2006); (4) being able to understand simple instructions as assessed by the Screening Test of Spanish Grammar (Toronto, 1973); (5) referring availability to participate in the study for a year; (6) having internet access at home. The exclusion criteria were having severe and/or visual difficulties that precluded cognitive assessment and intervention.

2.2. Study design and procedure

Participants were matched in pairs based on age bands (8-10.5/10.6-12 years), sex, MACS level (I-II/III) and intelligence quotient (<80/≥80) (Raven et al., 2011). Each one of the paired participants were randomly allocated to one of the two groups (intervention or waitlist control). Randomization was performed by an in-house program written in R software. Participants were informed of group allocation after baseline assessment. The researcher who conducted neuropsychological assessment was blinded to the group status of participants until data collection finished.

2.1.1. Intervention group

Participants randomized to the intervention group performed a computerized home-based executive function intervention using NeuronUP (www.neuronup.com). Intervention was specifically composed for this research project by a careful selection of the tasks, according to the main executive function domains. The difficulty level for each task was gradually adjusted automatically depending on the child's level of performance during each session. Executive intervention included core executive function (inhibitory control, working memory and cognitive flexibility), higher-order executive function (planning) and social cognition tasks. Intervention consisted of 15 minutes per session, and 10 sessions per week for 12 weeks (total dose = 30 hours). Adherence was monitored by a health professional using website reports after each intervention session.

2.1.1. Waitlist control group

Participants randomized to the waitlist control group maintained their usual care.

2.2. Assessment

2.2.1. Neuropsychology assessment

A comprehensive neuropsychological assessment was carried out before the intervention (T0, baseline), immediately after the intervention finished (T1, post-intervention) and 9 months post-intervention (T2, follow-up). Standard paper and pen neuropsychological tests were used to assess memory and visual perception skills. Raw scores were converted into standardized scores (Z scores). Reliability was good across the different neuropsychological tests (García-Galant et al., 2020). Verbal and visual immediate memory skills were assessed using the Digit Forward Span from the Wechsler Intelligence Scale for Children-Fifth Edition (WISC-V) (Wechsler et al., 2015) and the Spatial Forward Span from the Wechsler Non-Verbal Scale of Ability (WNV) (Wechsler & Naglieri, 2006), respectively. Verbal learning and long-term memory skills were evaluated by the Word Selective Reminding of the Test of Memory and Learning (TOMAL) (Reynolds, 1998). Visual learning and visual long-term memory were assessed by the Memory for Designs from the Developmental Neuropsychological Assessment-Second Edition (NEPSY-II) (Korkman et al., 2014). Regarding visuoperceptual dimensions (Ben Itzhak et al., 2021), object recognition and visual spatial perception were assessed by Facial Recognition Test (FRT) (Benton 1994) and Arrows (NEPSY-II)) (Korkman et al., 2014), respectively.

2.2.2. Quality of life and participation assessment

Proxy-reported questionnaires about quality of life and participation were completed by the parents at the same 3 points as the neuropsychological assessment (T0, T1 and T2). Quality of life was measured by the Cerebral Palsy Quality of Life-Child (CP QoL-Child) questionnaire (Waters et al., 2007). A CP QoL total score was calculated by adding the seven domains. Participation was assessed using the Participation and Environment Measure for Children and Youth (PEM-CY) questionnaire (Coster et al., 2011), including level of participation at home, school and community settings.

2.3. Potential covariates assessment

Variables that could influence the effectiveness of intervention were considered potential covariates: pain, autism spectrum disorder traits, psychological adjustment, family quality of life and parental stress. Physical pain was measured by the Bodily Pain and Discomfort Scale of the Child Health Questionnaire (Landgraf, 2020). Autism spectrum disorders traits were assessed using the Autism Spectrum Screening Questionnaire (Ehlers et al., 1999). Psychological adjustment was examined by Strengths and Difficulties Questionnaire (Goodman, 1997). Family quality of life and parental stress were measured using the Beach Center Family Quality of Life Scale (Hoffman et al., 2006) and the Parental Stress Scale (Berry & Jones, 1995).

2.4. Statistical analysis

Statistical Package for the Social Sciences (IBM SPSS V.27) was used for the statistical analysis. Graphs were generated with R 4.2.2. Analysis of covariance (ANCOVAs), with neuropsychology, quality of life and participation baseline scores (T0) as covariates and group as factor, were performed to assess group differences in performance gains right after finishing the intervention (T1) and 9 months post-intervention (T2). In order to ensure that the estimated effects of the executive interventions were fully independent from the effects of other variables, pain, autism spectrum disorder traits, psychological adjustment, family quality of life and parental stress were considered as potential covariables. Before ANCOVA analyses, bivariate correlations (Pearson, Spearman and Kendall) between baseline outcomes and potential covariates were performed applying Bonferroni's correction (p=0.01). Those potential covariates that correlated significantly with baseline outcomes were introduced, together with baseline outcome, as covariates. Estimated marginal means of each variable were calculated considering covariates included in each specific analysis. The significance level was set at p-value < 0.05. Effect size for the ANCOVA was assessed by partial eta-square (η_p^2), considering effects as small ≥ 0.01; medium ≥ 0.06 and large ≥ 0.14 (Cohen, 1988).

In addition to per-protocol analysis, intention-to-treat (ITT) analyses were performed with R (version 4.2.2 R Core Team 2022). ITT analysis included all those participants with baseline measure of each outcome (Genolini et al., 2013, 2016).

3. Results

3.1. Participants

Of the 63 participants who completed the baseline assessment, 60 were assessed at post-intervention and follow-up post-intervention (Figure 1). There were no significant group differences in terms of demographic and clinical characteristics (Table 1). Descriptive statistics for potential covariates are shown in Table 2. No significant group differences in potential covariates were found. Neuropsychological, quality of life and participation scores at T0, T1 and T2 are presented in Supplementary Material (S1). The mean attendance and total dose were 114 sessions (106-120 sessions) and 28.35 hours (range 26.30 – 30 hours).

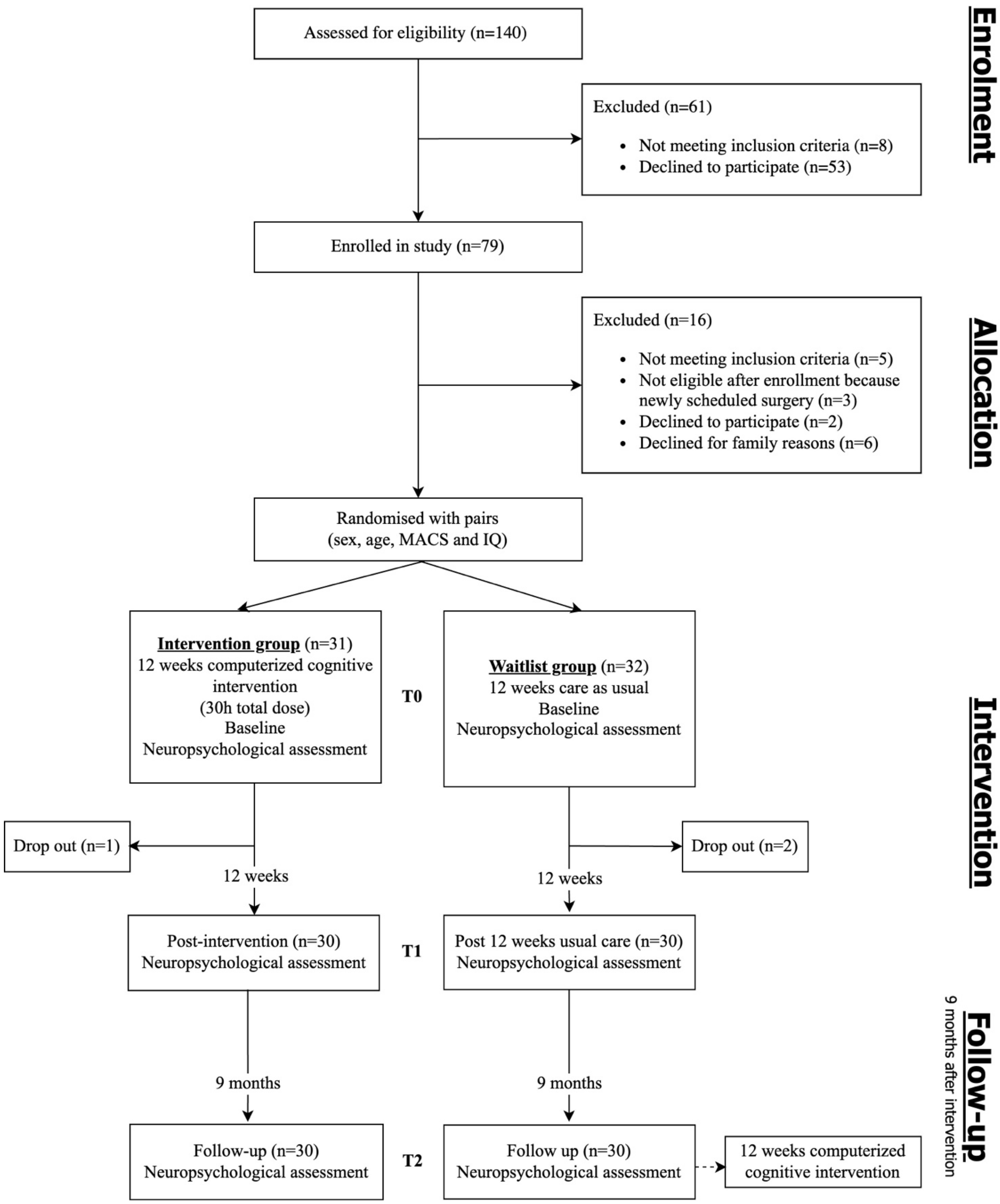


Figure 1. Consort flow chart.

Abrreviations. MACS = Manual Ability Classification System; IQ= Intelligence quotient.

Table 1. Descriptive statistics for demographic and clinical data.

Demographic and clinical variables		Intervention group (n = 30)	Waitlist control group (n = 30)
Age, mean ± SD (range)		10.30 ± 1.66 (8.08-12.92)	10.01 ± 1.73 (8.00-12.92)
Sex, n (%)			
	Female	15 (50.0)	15 (50.0)
	Male	15 (50.0)	15 (50.0)
Gestational Age (in weeks), n (%)			
	<37 w	14 (46.7)	20 (66.7)
	≥ 37 w	12 (40.0)	8 (26.7)
	Unknown	4 (13.3)	2 (6.6)
Epilepsy, n (%) [a]			
	No epilepsy	24 (80.0)	18 (60.0)
	Active	6 (20.0)	12 (40.0)
Type of CP, n (%)			
	Spastic	27 (90.0)	27 (90.0)
	Dyskinetic	3 (10.0)	2 (6.7)
	Unknown	0 (0.0)	1 (3.3)
Motor Distribution, n (%)			
	Unilateral	24 (80.0)	24 (80.0)
	Bilateral	6 (20.0)	6 (20.0)
GMFCS, n (%)			
	I	20 (66.7)	14 (46.7)
	II	6 (20.0)	12 (40.0)
	III	4 (13.3)	2 (6.7)
	IV	0 (0.0)	2 (6.7)
MACS, n (%)			
	I	11 (36.7)	14 (46.7)
	II	16 (53.3)	13 (43.3)
	III	3 (10)	3 (10)
BFMF, n (%)			
	I	18 (60.0)	14 (46.7)
	II	8 (26.7)	12 (40.0)
	III	3 (10.0)	4 (6.7)
	IV	1 (3.3)	0 (0.0)
CFCS, n (%)			
	I	20 (66.7)	16 (53.3)
	II	9 (30.0)	10 (33.3)
	III	1 (3.3)	2 (6.7)
	IV	0 (0.0)	2 (6.7)
VSS, n (%)			
	I	26 (86.7)	18 (60.0)
	II	3 (10.0)	9 (30.0)
	III	1(3.3)	3 (10.0)
IQ, mean ± SD (range)		100.42 ± 15.17 (75-125)	95.88 ± 9.33 (75-110)

Notes. [a] The International League Against Epilepsy criteria (58) was used to determine epilepsy status.

Abbreviations. BFMF, Bimanual Fine Motor Function; CFCS, Communication Function Classification System; CP, Cerebral Palsy; GMFCS, Gross Motor Function Classification System; IQ, Intelligence Quotient; MACS, Manual Ability Classification System; VSS, Viking Speech Scale

3.2. Performance in groups post-intervention and follow-up

Immediately post-intervention (T1) scores for each group and ANCOVA per protocol results are presented in Table 3. The intervention group performed significantly better on immediate verbal memory (Digit Span Forward, WISC-V) and verbal learning (Word Selective Reminding, TOMAL) than the waitlist control group at post-intervention, with large (F=13.79, p=<0.001, η_p^2=0.20) and medium (F=7.36, p=0.009, η_p^2=0.12) effect sizes, respectively. No significant verbal long-term memory (Word Selective Reminding Delayed, TOMAL) differences were found between groups after the intervention. No significant differences between groups were found in terms of visual memory. More specifically, no differences were found in terms of immediate memory (Spatial Span Forward, WNV), learning and long-term memory (Memory for Designs, NEPSY-II).

Object recognition (FRT) was significantly improved after the intervention, with a medium effect size (F=4.14, p=0.047, η_p^2=0.07). Visual spatial perception, however, did not improve significantly (Arrows, NEPSY-II). There were no post-intervention differences between groups for quality of life (CP QoL) and participation (PEM-CY).

Follow-up post-intervention scores (T2) for each of the two groups and ANCOVA results are presented in Table 4. No significant differences between the intervention and waitlist control groups were found for any of the outcomes. Tables S2 and S3 present ITT analysis. Significant differences between groups in the ITT analysis are the same as the ones found in the ANCOVA per protocol analysis.

3.3. Graphical representation of results

Participant's performance is graphically presented in Figures 2-4. Estimated marginal differences between groups at immediate post-intervention (T1) and 9 months follow-up post-intervention (T2) are represented in boxes. Estimated marginal differences are differences between the groups' estimated marginal means. As can be seen in the graphical representation, although differences between groups were not statistically significant in all neuropsychological outcomes 9 months follow-up post-intervention (T2), the intervention group showed higher performance than the waitlist control group (estimated marginal differences above zero). It is noteworthy that participation and quality of life scores did not increase in the intervention group in comparison with waitlist control group.

Table 2. Descriptive statistics for potential covariates.

Covariates	Intervention group	Waitlist control group
Frequency of Pain, n (%)		
Never	8 (26.7)	16 (29.1)
A few times	14 (46.7)	10 (18.2)
Often	4 (13.3)	3 (5.4)
Unknown	4 (13.3)	1 (1.8)
ASSQ, median (range)	5 (0-36)	9 (0-25)
SDQ, mean ± SD	13.9 ± 6.2	13.7 ± 5.2
FQoL, mean ± SD	3.8 ± 0.7	3.8 ± 0.6
PSS, median (range)	22 (13-43)	25 (17-45)

Abbreviations. ASSQ, Autism Spectrum Screening Questionnaire; FQoL, Beach Center Family Quality of Life Scale; PSS, Parental Stress Scale; SDQ, Strengths and Difficulties Questionnaire.

Table 3. Analysis of covariance comparing intervention and waitlist control groups on post-intervention.

Outcomes	Intervention group	Waitlist control group	ANCOVA Post-intervention (T1)		
	Estimated marginal mean (SD)		F	p	η_p^2
Learning and memory					
Immediate memory					
Verbal: Digit Span Forward (WISC-V)	-0.53 (0.11)	-1.13 (0.12)	13.79	<0.001	0.20
Visual: Spatial Span Forward (WNV)	-0.79 (0.21)	-0.85 (0.21)	0.04	0.853	<0.01
Learning					
Verbal: Word Selective Reminding (TOMAL)	0.32 (0.19)	-0.44 (0.20)	7.36	0.009	0.12
Visual: Memory for Designs (NEPSY-II)	-0.68 (0.19)	-0.87 (0.19)	0.47	0.496	0.01
Long-term memory					
Verbal: Word Selective Reminding Delayed (TOMAL)	0.14 (0.12)	0.08 (0.13)	0.15	0.697	<0.01
Visual: Memory for Designs Delayed (NEPSY-II) [a]	-0.89 (0.18)	-1.00 (0.18)	0.23	0.634	0.01
Visual perception					
FRT	0.81 (0.24)	0.14 (0.24)	4.14	0.047	0.07
Arrows (NEPSY-II)	-0.95 (0.13)	-1.16 (0.13)	1.26	0.267	0.02
Quality of life					
CP QoL Total Score [a,b,c]	73.77 (1.24)	70.97 (1.21)	2.50	0.121	0.05
Participation					
Home (PEM-CY) [b,d]	5.76 (0.12)	5.59 (0.12)	0.91	0.346	0.02
School (PEM-CY)	4.00 (0.24)	4.19 (0.24)	0.28	0.596	0.01
Community (PEM-CY)	2.96 (0.18)	2.76 (0.18)	0.29	0.572	0.01

Notes. Covariates: [a] ASSQ, [b] PSS, [c] SDQ, [d] FQoL.

Abbreviations. ASSQ, Autism Spectrum Screening Questionnaire; CP QoL, Cerebral Palsy Quality of Life Questionnaire; FQoL, Beach Center Family Quality of Life Scale; FRT, Facial Recognition Test; NEPSY-II, A Developmental NEuroPSYchological Assessment- Second Edition; PEM-CY, Participation and Environment Measure for Children and Youth; PSS, Parental Stress Scale; SD, Standard Deviation; SDQ, Strengths and Difficulties Questionnaire; TOMAL, Test of Memory and Learning; WISC- V, Wechsler Intelligence Scale for Children-Fifth Edition; WNV, Wechsler Non-Verbal Scale of Ability.

Table 4. Analysis of covariance comparing intervention and waitlist control groups on follow-up.

Outcomes	Intervention group	Waitlist control group	ANCOVA Follow-up (T2)		
	Estimated marginal mean (SD)		F	p	η_p^2
Learning and memory					
Immediate memory					
Verbal: Digit Span Forward (WISC-V)	-0.52 (0.16)	-0.85 (0.16)	2.11	0.152	0.04
Visual: Spatial Span Forward (WNV)	-0.78 (0.16)	-0.87 (0.16)	0.15	0.699	<0.01
Learning					
Verbal: Word Selective Reminding (TOMAL)	0.38 (0.22)	0.35 (0.23)	0.01	0.936	<0.01
Visual: Memory for Designs (NEPSY-II)	-0.32 (0.22)	-0.51 (0.22)	0.38	0.540	0.01
Long-term memory					
Verbal: Word Selective Reminding Delayed (TOMAL)	0.51 (0.11)	0.33 (0.12)	1.21	0.276	0.02
Visual: Memory for Designs Delayed (NEPSY-II) [a]	0.09 (0.27)	-0.76 (0.27)	3.06	0.087	0.06
Visual perception					
FRT	0.76 (0.22)	0.29 (0.22)	2.21	0.142	0.04
Arrows (NEPSY-II)	-1.01 (0.13)	-1.07 (0.14)	0.10	0.759	<0.01
Quality of life					
CP QoL Total Score [a,b,c]	69.30 (1.60)	72.17 (1.56)	1.60	0.213	0.03
Participation					
Home (PEM-CY) [b,d]	5.57 (0.14)	5.57 (0.14)	<0.01	0.974	<0.01
School (PEM-CY)	4.20 (0.20)	4.11 (0.20)	0.12	0.730	<0.01
Community (PEM-CY)	2.48 (0.15)	2.65 (0.15)	0.66	0.422	0.01

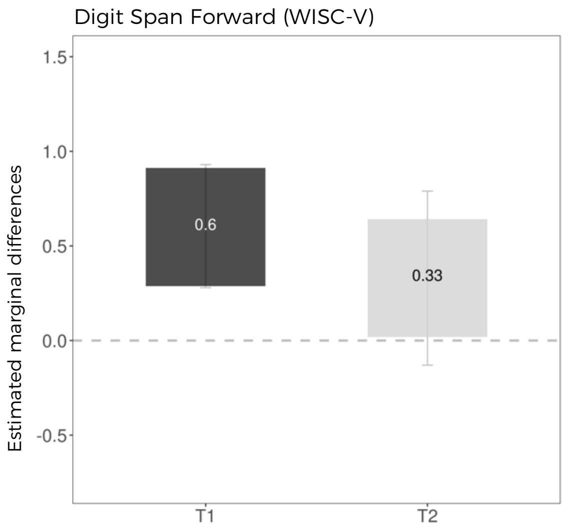
Notes. Covariates: [a] ASSQ, [b] PSS, [c] SDQ, [d] FQoL.

Abbreviations. ASSQ, Autism Spectrum Screening Questionnaire; CP QoL, Cerebral Palsy Quality of Life Questionnaire; FQoL, Beach Center Family Quality of Life Scale; FRT, Facial Recognition Test; NEPSY-II, A Developmental NEuroPSYchological Assessment-Second Edition; PEM-CY, Participation and Environment Measure for Children and Youth; PSS, Parental Stress Scale; SD, Standard Deviation; SDQ, Strengths and Difficulties Questionnaire; TOMAL, Test of Memory and Learning; WISC–V, Wechsler Intelligence Scale for Children-Fifth Edition; WNV, Wechsler Non-Verbal Scale of Ability.

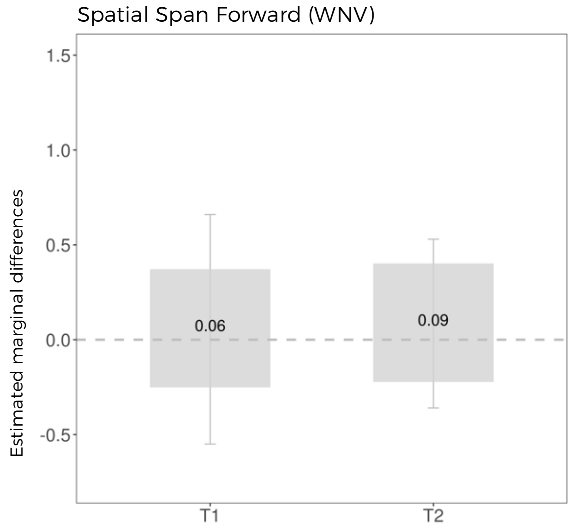
Figure 2. Graphical representation of differences between intervention and waitlist groups in learning and memory.

Immediate memory

Verbal

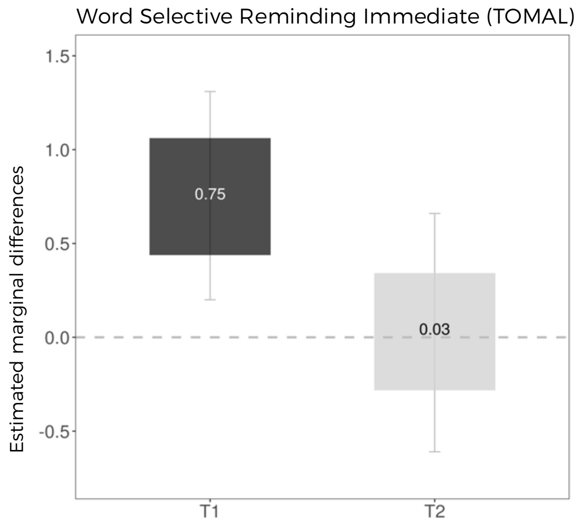


Visual



Learning

Verbal



Visual

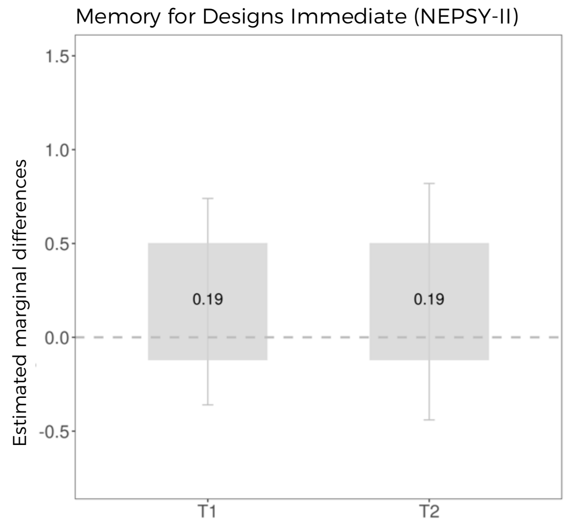
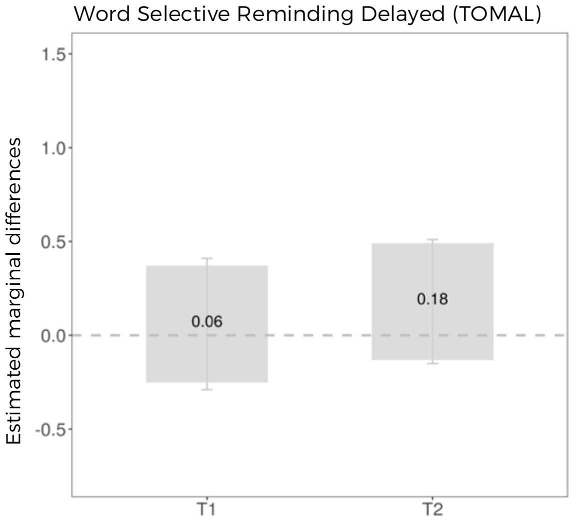


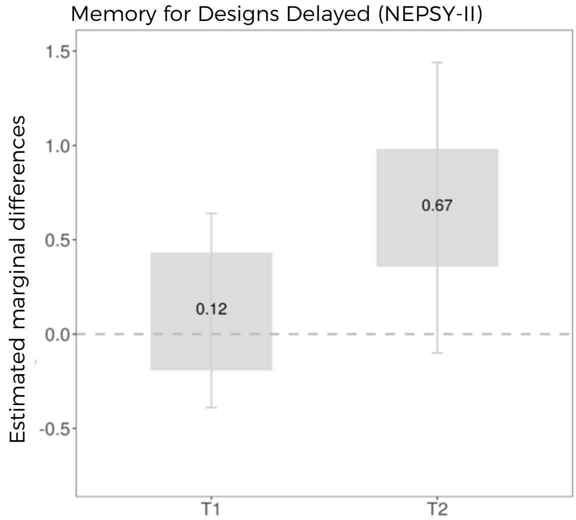
Figure 2 (continued).

Long-term memory

Verbal



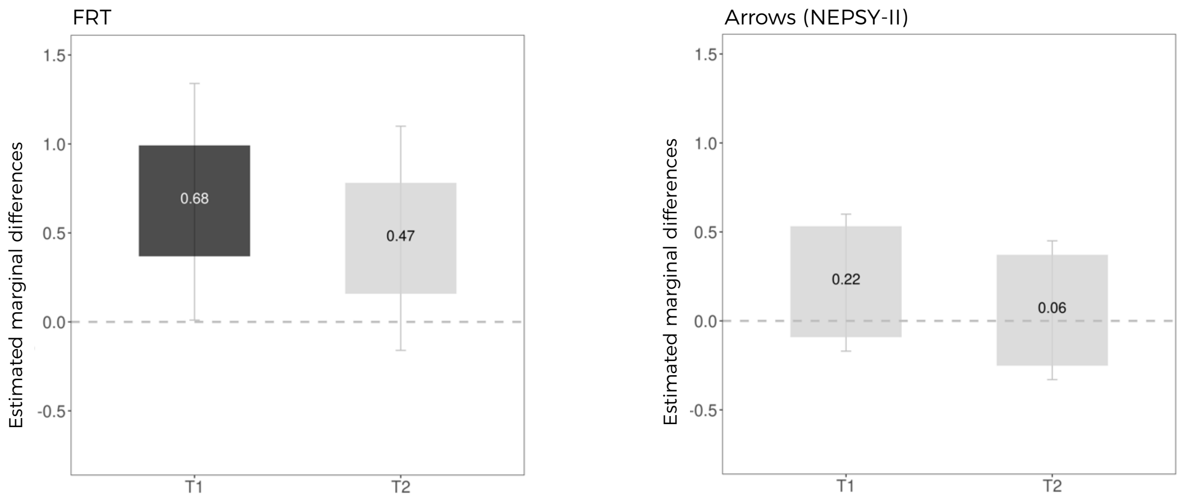
Visual



Notes. Estimated marginal differences = intervention group estimated marginal mean minus waitlist group estimated marginal mean; dark grey coloured box = significant differences, grey coloured box = non significant differences. Estimated marginal differences above zero indicate better performance in the intervention group than in the waitlist group.

Abbreviations. NEPSY-II, A Developmental NEuroPSYchological Assessment-Second Edition; TOMAL, Test of Memory and Learning; WISC-V, Wechsler Intelligence Scale for Children-Fifth Edition; WNV, Wechsler Non-Verbal Scale of Ability

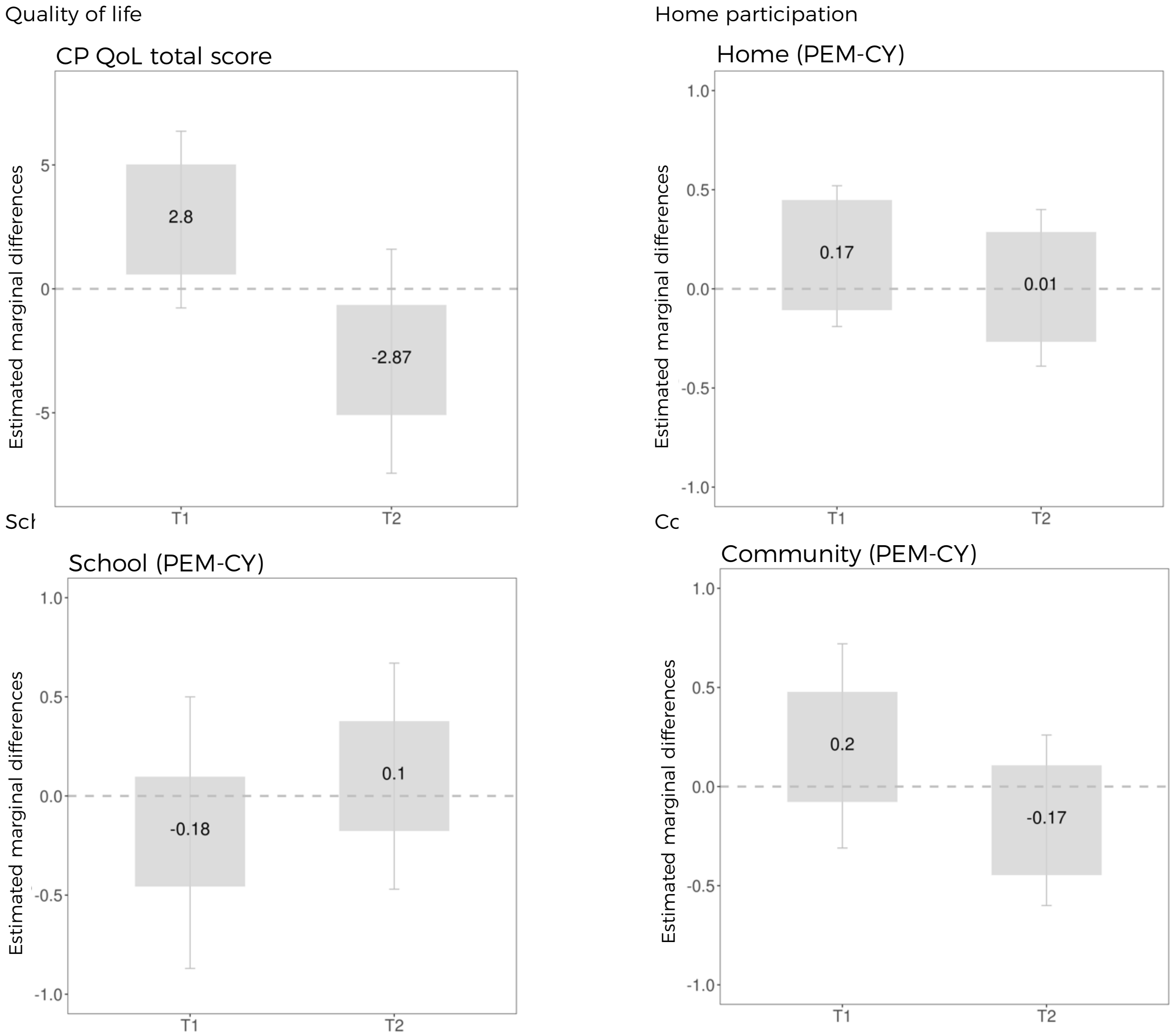
Figure 3. Graphical representation of differences between intervention and waitlist groups in visual perception.



Notes. Estimated marginal differences = intervention group estimated marginal mean minus waitlist group estimated marginal mean; dark grey coloured box = significant differences, grey coloured box = non significant differences. Estimated marginal differences above zero indicate better performance in the intervention group than in the waitlist group.

Abbreviations. FRT, Facial Recognition Test; NEPSY-II, A Developmental NEuroPSYchological Assessment-Second Edition.

Figure 4. Graphical representation of differences between intervention and waitlist groups in quality of life and participation.



4. Discussion

Children with CP who undergo a home-based computerized executive function intervention program for 12 weeks improved their verbal memory (immediate memory and learning) and visual perception (object recognition) skills immediately post-intervention (T1). The intervention did not, however, enhance visual memory, visual spatial perception skills, quality of life and participation. This is the first study to explore the effect of an intervention on verbal memory in children with CP. Our research provides evidence that immediate verbal memory and verbal learning are improved after undergoing an executive function intervention program, in accordance with the fact that memory is a cognitive function interrelated with other cognitive functions, such as executive functions (Baddeley, 2012; Rzezak et al., 2014). Additionally, our results agree with previous research about far transfer effects of executive functions interventions in memory (Acosta et al., 2019). Acosta et al. (2019) reported changes in immediate verbal memory after a working memory intervention in children with language disorders. Improvements post-intervention in immediate verbal memory and learning were also found. Nevertheless, no changes were found in long-term memory. This could be due to transferring from short to long-term is an automatic but slow process (Baddeley, 1998) and a larger intervention duration could lead to find changes in this memory domain.

The improvements found in visual perception are consistent with previous studies reporting far transfer effects on this cognitive function after cognitive and multi-modal computerized interventions in children with CP (Critten et al., 2018; James et al., 2015a). The findings of this study indicate that interventions including cognitive tasks delivered via a computerized program improve some components of object recognition, such as face processing, in children with CP. Visual perception is associated with everyday motor skills and academic performance and plays an important role in daily life activities (Critten et al., 2018; James et al., 2015a).This fact together with the high prevalence of visual perception impairments in CP (Ego et al., 2015), highlights the importance of targeting visual perception in interventions for people with CP. Research in CP seems to indicate that to obtain far transfer effects in visual perception, a weekly computerized intervention program of at least 3 months is required.

Otherwise, no improvements in visual spatial perception skills were found in our research. These results align with the research of Di Lieto et al. (2021) in which an executive function intervention, but with an inferior intervention dose, also did not induce changes in Arrows subtest (NEPSY-II). There is a wide variety of visuoperceptual functioning in children (Ben Itzhak et al., 2021). Until now, visual perception assessment in intervention research has been mainly limited to specific domains (e.g. object recognition or visual spatial perception domains) (Aran et al., 2020; Di Lieto et al., 2021) and this could difficulty to identify a global perspective of improvements based on child's visual perception profile (Ben Itzhak et al., 2021). Further studies should include an extensive visual perception battery to determine which specific dimensions improve by interventions in CP.
Regarding the absence of changes in visual spatial perception skills, no changes were also found in visual memory after the intervention in accordance with the previous study of Di Lieto et al. (2021). Specifically, none of the studies found improvements in Memory for the Designs subtest (NEPSY-II). This could indicate that no changes in visual spatial perception skills could be influencing visual memory assessment, where spatial localization are required.

Visual perception and verbal memory improvements were not maintained 9 months after the intervention finished. A previous study with the near transfer effects showed long-term effects on executive functions 9 months after this intervention (García-Galant et al., 2020). This reinforces the idea that near transfer effects occur frequently, but far transfer effects are modest (Willis et al., 2006). It would be interesting to explore whether a booster intervention helps to maintain far transfer effects in these specific cognitive functions. Booster intervention in cognitive programs have been investigated scarcely, but some studies in other populations indicate that they promote long-term effects (Willis et al., 2006). Another point of interest could be to include computerized assessment to test whether beneficial effects could be higher and/or maintained at follow-up.

No significant transfer effects were demonstrated in quality of life and participation. Moreover, no delayed effects appeared 9 months later. No previous studies have investigated specifically the effects of cognitive interventions on these variables. On the one hand, our results are in line with previous studies in CP about multi-modal and physical interventions, with no changes reported in quality of life (Ahn et al., 2021; Mak et al., 2018). Previous studies also report no significant improvements in quality of life in other children's populations after an executive function intervention (De Vries et al., 2015). On the other hand, our results for participation differ from those found in a previous study undergoing a physical intervention (Teixeira-Machado et al., 2017). Improvements were found after 12 weeks of dance intervention. Further research is needed to clarify the effectiveness of interventions with different characteristics to improve quality of life and participation in this population.

Despite the strengths of this work, some questions should be raised for future research. Firstly, children in our study comprised MACS I-III. The sample was limited to children with mild motor severity in order to homogenize the sample characteristics and the effective time of the intervention between children. Future studies should include participants representing whole spectrum of motor severity due to cognitive impairments are likely to be referred in severe motor cases of CP (56). Secondly, our study did not include an active control group. Although it could be interesting to include an active control group, it is difficult to find a computerized intervention tasks without including executive function component/domain. Added to that, COVID-19 pandemic may have affected children's responses to treatment. Recent studies indicate that children with CP discontinued their daily routines as well as the activities in special education and rehabilitation centres during the pandemic (Cankurtaran et al., 2021).This decreased general health status and functional ability during the pandemic situation, may probably affect performance in the assessment and intervention of our study.

To sum up, a home-based computerized executive function intervention can be effective to obtain far transfer effects in memory and visual perception. However, improvements were not maintained at long-term. Quality of life and participation did not improve after the intervention. Further research in the whole spectrum of CP severity is needed to identify strategies that allow maintaining these improvements over time and the possibility to transfer to daily life aspects.

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5. References

(see thesis references)

Supplementary Material 1. Outcomes descriptive data on the neuropsychological assessment tasks of intervention and waitlist groups at baseline, post-intervention and follow-up.

	Intervention group						Waitlist group					
	Baseline		Post-intervention		Follow-up		Baseline		Post-intervention		Follow-up	
	n	Mean* (SD) Median (min/max)	n	Mean* (SD) Median (min/max)	n	Mean* (SD) Median (min/max)	n	Mean* (SD) Median (min/max)	n	Mean* (SD) Median (min/max)	n	Mean* (SD) Median (min/max)
Learning and memory												
Immediate memory												
Verbal: Digit Span Forward (WISC-V)	30	-0.36 (-2.33/0.64)	30	-0.36 (-2.33/0.80)	30	-0.47* (0.95)	30	-1.22 (-2.45/3.84)	29[a]	-1.22 (-2.33/-0.11)	30	-1.00* (1.21)
Visual: Spatial Span Forward (WNV)	30	-0.84* (1.32)	30	-0.61* (1.60)	30	-0.62* (1.25)	29[a]	-1.30* (1.00)	30	-1.06* (1.32)	30	-1.08* (1.14)
Learning												
Verbal: Word Selective Reminding (TOMAL)	30	-0.58* (1.25)	30	0.42* (1.60)	30	0.17 (-3.00/3.67)	28[b]	-0.83* (1.64)	28[b]	-0.55* (1.61)	27[a,b]	-0.33 (-2.67/3.33)
Visual: Memory for Designs (NEPSY-II)[1]	29[a]	-0.67 (-3.00/2.00)	29[a]	-0.32* (1.38)	29[a]	0.33 (-3.00/2.00)	29[a]	-2.00 (-3.00/0.67)	30	-1.27* (1.48)	27	-0.67 (-3.00/2.00)
Long-term memory												
Verbal: Word Selective Reminding Delayed (TOMAL)	30	0.33 (-2.00/1.33)	30	0.33 (-2.33/1.33)	30	1.00 (-1.67/1.33)	28[b]	0.00 (-2.33/1.33)	28[b]	0.17 (-2.00/1.33)	27[a,b]	0.33 (-2.33/1.33)
Visual: Memory for Designs Delayed (NEPSY-II)	28[a]	-1.33 (-3.00/1.00)	29[a]	-0.53* (1.41)	28[a]	0.17 (-3.00/1.67)	29[a]	-2.00 (-3.00/1.00)	30	-1.42* (1.56)	26[a,c]	-1.00 (-3.00/1.67)
Visual perception												
FRT	30	0.62* (1.29)	30	0.87* (1.63)	30	0.71 (-5.63/2.91)	30	0.44* (1.68)	30	0.07* (1.69)	30	0.36 (-2.63/2.37)
Arrows (NEPSY-II)[1]	30	-0.80* (1.19)	30	-0.67 (-3.00/2.00)	30	-0.79* (1.20)	30	-1.50* (1.17)	30	-1.42 (-3.00/0.67)	28[a,c]	-1.31* (1.23)
Quality of life												
CP QOL Total Score	29[d]	75.58 (35.25/92.1)	27[d]	73.89* (10.73)	27[d]	72.25 (42.08/90.3)	29[d]	74.97 (52.02/84.11)	30	71.47* (7.19)	28[d]	73.20 (51.01/88.3)
Participation												
Home (PEM-CY)	27[d]	5.89 (2.80/6.60)	29[d]	5.67* (0.93)	26[d]	5.56* (0.97)	27[d]	5.60 (-3.80/6.70)	30	5.58* (0.60)	26[d]	5.43* (0.61)
School (PEM-CY)	27[d]	4.39* (0.96)	29[d]	3.92* (1.39)	26[d]	4.14* (1.06)	26[d]	4.12* (1.30)	29[d]	4.05* (1.17)	25[d]	3.97* (1.06)
Community (PEM-CY)	27[d]	2.66* (0.97)	29[d]	2.87* (1.03)	26[d]	2.33* (0.97)	26[d]	2.56* (1.05)	28[d]	2.74* (1.08)	26[d]	2.62* (0.92)

Notes. [1] Significant differences between intervention and waitlist groups at baseline. Reasons for missing data: [a] being not able to complete the test due to fatigue; [b] very slow communication system that precludes to use an appropriate response system for the test used; [c] lockdown precluded assessment; [d] not answered by the parents. Accommodation was applied in Memory for Designs (NEPSY-II) due to motor severity of a participant, assessor put the cards where the child indicated.

Abbreviations. CP QOL, Cerebral Palsy Quality of Life Questionnaire; FRT, Facial Recognition Test; NEPSY-II, A Developmental NEuroPSYchological Assessment Second Edition; PEM-CY, Participation and Environment Measure for Children and Youth; SD, Standard Deviation; TOMAL, Test of Memory and Learning; WISC-V, Wechsler Intelligence Scale for Children-V; WNV, Wechsler Non-Verbal Scale of Ability.

Supplementary Material 2. Intention-to-treat analysis of covariance comparing intervention and waitlist control groups on post-intervention.

Outcomes	Intervention group	Waitlist control group	ANCOVA Post-intervention (T1)		
	Estimated marginal mean (SD)		F	p	η_p^2
Learning and memory					
Immediate memory					
Verbal: Digit Span Forward (WISC-V)	-0.62 (0.12)	-1.16 (0.11)	11.05	0.002	0.16
Visual: Spatial Span Forward (WNV)	-0.83 (0.20)	-0.87 (0.20)	0.02	0.886	<0.01
Learning					
Verbal: Word Selective Reminding (TOMAL)	0.30 (0.18)	-0.44 (0.19)	7.94	0.007	0.12
Visual: Memory for Designs (NEPSY-II)	-0.77 (0.18)	-0.89 (0.17)	0.24	0.628	<0.01
Long-term memory					
Verbal: Word Selective Reminding Delayed (TOMAL)	0.10 (0.12)	0.05 (0.12)	0.08	0.774	<0.01
Visual: Memory for Designs Delayed (NEPSY-II) [a]	-0.82 (0.16)	-0.97 (0.16)	0.73	0.397	0.01
Visual perception					
FRT	0.78 (0.23)	0.12 (0.22)	4.30	0.042	0.07
Arrows (NEPSY-II)	-0.99 (0.13)	-1.19 (0.13)	1.11	0.297	0.02
Quality of life					
CP QoL Total Score [a,b,c]	74.13 (1.12)	71.18 (1.14)	3.09	0.085	0.06
Participation					
Home (PEM-CY) [b,d]	5.67 (0.11)	5.60(0.11)	0.62	0.435	0.01
School (PEM-CY)	3.91 (0.21)	4.16 (0.21)	0.69	0.410	0.01
Community (PEM-CY)	2.85 (0.16)	2.83 (0.16)	0.01	0.944	<0.01

Notes. Covariates: [a] ASSQ, [b] PSS, [c] SDQ, [d] FQoL.

Abbreviations. ASSQ, Autism Spectrum Screening Questionnaire; CP QoL, Cerebral Palsy Quality of Life Questionnaire; FQoL, Beach Center Family Quality of Life Scale; FRT, Facial Recognition Test; NEPSY-II, A Developmental NEuroPSYchological Assessment- Second Edition; PEM-CY, Participation and Environment Measure for Children and Youth; PSS, Parental Stress Scale; SD, Standard Deviation; SDQ, Strengths and Difficulties Questionnaire; TOMAL, Test of Memory and Learning; WISC-V, Wechsler Intelligence Scale for Children-Fifth Edition; WNV, Wechsler Non-Verbal Scale of Ability.

Supplementary Material 3. Intention-to-treat analysis of covariance comparing intervention and waitlist control groups on follow-up.

Outcomes	Intervention group	Waitlist control group	ANCOVA Follow-up (T2)		
	Estimated marginal mean (SD)		F	p	η_p^2
Learning and memory					
Immediate memory					
Verbal: Digit Span Forward (WISC-V)	-0.60 (0.16)	-0.96 (0.16)	2.49	0.120	0.04
Visual: Spatial Span Forward (WNV)	-0.82 (0.15)	-0.90 (0.15)	0.12	0.731	<0.01
Learning					
Verbal: Word Selective Reminding (TOMAL)	0.34 (0.21)	0.34 (0.21)	0.00	0.999	<0.01
Visual: Memory for Designs (NEPSY-II)	-0.54 (0.20)	-0.60 (0.19)	0.04	0.848	<0.01
Long-term memory					
Verbal: Word Selective Reminding Delayed (TOMAL)	0.46 (0.11)	0.32 (0.11)	0.81	0.371	0.01
Visual: Memory for Designs Delayed (NEPSY-II) [a]	-0.16 (0.24)	-0.75 (0.24)	2.12	0.152	0.04
Visual perception					
FRT	0.71 (0.22)	0.29 (0.21)	2.01	0.161	0.03
Arrows (NEPSY-II)	-1.11 (0.13)	-1.14 (0.12)	0.03	0.865	<0.01
Quality of life					
CP QoL Total Score [a,b,c]	70.07 (1.49)	71.99 (1.52)	0.34	0.561	<0.01
Participation					
Home (PEM-CY) [b,d]	5.55 (0.13)	5.50 (0.13)	0.58	0.448	0.01
School (PEM-CY)	3.96 (0.18)	4.09 (0.18)	0.23	0.632	<0.01
Community (PEM-CY)	2.33 (0.14)	2.64 (0.14)	2.55	0.116	0.04

Notes. Covariates: [a] ASSQ, [b] PSS, [c] SDQ, [d] FQoL.

Abbreviations. ASSQ, Autism Spectrum Screening Questionnaire; CP QoL, Cerebral Palsy Quality of Life Questionnaire; FQoL, Beach Center Family Quality of Life Scale; FRT, Facial Recognition Test; NEPSY-II, A Developmental NEuroPSYchological Assessment-Second Edition; PEM-CY, Participation and Environment Measure for Children and Youth; PSS, Parental Stress Scale; SD, Standard Deviation; SDQ, Strengths and Difficulties Questionnaire; TOMAL, Test of Memory and Learning; WISC-V, Wechsler Intelligence Scale for Children-Fifth Edition; WNV, Wechsler Non-Verbal Scale of Ability.

DISCUSSION

SUMMARY OF GOALS

The previous section addressed the main aim of this thesis, which was to **optimise the effects of cognitive interventions in children with CP**. The three studies conducted in this doctoral thesis adopted different approaches to achieve the general goal.

First, we described the main types of interventions used to improve cognitive functions in CP. Study 1 was a systematic review that found that **physical** and **multi-modal interventions** improved cognition in individuals with CP. However, interventions that improved cognition did not have a significant impact on QoL. Study 1 showed limited evidence regarding cognitive interventions for CP, but promising results were observed for executive function interventions. **Executive function interventions** produce **near** and **far** transfer effects of core executive functions and visual perception, respectively. Nevertheless, the far effects on specific cognitive functions, such as verbal memory and daily life (QoL and participation), as well as the maintenance of near and far effects over time, remained unknown.

Physical and multi-modal interventions did not improve the QoL. Additionally, the role of cognitive interventions in improving QoL remained unclear. Therefore, it was crucial to identify the most effective type of cognitive intervention. Study 2 addressed these issues. This study employed a cross-sectional design to investigate the relationship between QoL and cognition in children with CP along with other relevant demographic, clinical, and psychosocial variables. The results of Study 2 showed that executive functions have an impact on QoL in children with CP. Given that executive function interventions seemed to produce transfer effects on cognitive functions (Study 1) as well as the importance of executive functions on QoL (Study 2), this type of intervention should be prioritized to investigate the far transfer effects on non-trained cognitive functions and QoL in CP, while also examining the maintenance or delayed effects over time. These aims were addressed in Study 3, which, through an RCT, determined the far transfer effects of executive function interventions on visual perception and verbal memory in children with CP. However, these improvements were not maintained after nine months, and no delayed effects were observed on other cognitive domains, QoL, or participation.

The next section discusses the findings of this thesis in detail to shed light on this topic. Some aspects have been discussed previously in the discussion section of each study; however, given their importance they are examined in detail below.

TYPE OF INTERVENTIONS AVAILABLE TO ENHANCE COGNITION IN CEREBRAL PALSY

Over the past two decades, the interest in CP interventions has increased significantly, as evidenced by the growing number of publications on this topic (Klawonn et al., 2020). This increase in rehabilitation research has led to greater emphasis on summarizing and assessing existing evidence in the field, resulting in a large number of systematic reviews. Although fewer than 20 systematic reviews of CP interventions were conducted between 1992 and 2003, this number increased substantially to over 200 between 2012 and 2019 (Novak et al., 2020).

A systematic review by Novak et al. (2013) stands out as the most significant work on interventions for CP, with over 1500 citations in scientific papers. The question that arises is whether different types of symptoms receive equal attention in patients with CP. Based on the overview presented in the introduction of this thesis and recent systematic reviews published in the field of CP (Beckers et al., 2020; Cherriere, Robert, et al., 2020; Duarte Machado et al., 2023; Fandim et al., 2021; Guindos-Sanchez et al., 2020; Llamas-Ramos et al., 2022; Montoro-Cárdenas et al., 2021; Novak et al., 2020; Zanon et al., 2019), it is evident that this is not the case. Motor symptoms have been the primary focus of research since the beginning and efforts have been made to explore their treatment. As a result, interventions for CP have focused on motor impairments such as gross motor or manual ability difficulties, among others (Novak et al., 2013, 2020).

Although cognitive impairment is a common feature of CP (Fluss & Lidzba, 2020; Stadskleiv, 2020), cognitive functions have not received the same level of attention. To address this necessity comprehensively, the first two aims of this thesis were: (1) to determine the main characteristics of interventions in people with CP to obtain beneficial effects on cognitive functions; and (2) to identify gaps in the existing literature regarding interventions with an impact on cognitive functions in people with CP. Study 1 addressed these aims and revealed state-of-the-art of interventions that have an impact on cognitive function.

This systematic review provides a comprehensive overview of these interventions and offers a detailed description of their benefits for each cognitive function. Although other reviews have reported the effects of interventions on cognition, it was not the primary outcome of these studies, and no specific details on improved domains were provided (Cherriere et al., 2020; Duarte Machado et al., 2023; Fandim et al., 2021; Novak et al., 2020). Hence, to the best of our knowledge, Study 1 is the only systematic review of CP that specifically focused on cognitive functioning. Our systematic review included a total of 28 studies in the qualitative analyses. Of these, only nine were RCTs, indicating the need for studies with a higher quality of evidence. The scarcity of interventions that impact cognition is in agreement with the findings of other studies (Novak et al., 2020). Novak et al. (2020) identified 141 interventions to manage CP, but of those, only seven included cognitive function as an outcome.

Beyond the discussion by cognitive functions detailed in Study 1, the results also suggested the effectiveness of various types of interventions. Studies with high quality evidence have reported that physical (Ahn et al., 2021; Teixeira-Machado et al., 2017), multi-modal (Alwhaibi et al., 2020; Aran et al., 2020; James et al., 2015b; Mak et al., 2018, 2022; Morgan et al., 2016b; Piovesana et al., 2017), and cognitive (Di Lieto et al., 2021) interventions have positive effects on diverse cognitive functions. These interventions have been shown to enhance general intellectual functioning (Morgan et al., 2016b; Teixeira-Machado et al., 2017), visual perception (Alwhaibi et al., 2020; Aran et al., 2020; Di Lieto et al., 2021; James et al., 2015b; Piovesana et al., 2017), and executive functions (Aran et al., 2020; Mak et al., 2018).

1. Physical interventions

Physical interventions accounted for approximately 39% of the studies included in this systematic review, making them the predominant type of interventions (Abuin-Porras et al., 2019; Ahn et al., 2021; Cherriere et al., 2020; Christensen et al., 2017; Heathcock et al., 2015; Hsieh et al., 2017; Lakes et al., 2019; Sajan et al., 2017; Shin & Song, 2016; Teixeira-Machado et al., 2017; Yildirim et al., 2021). Considering that interventions for CP primarily target motor aspects, it is not surprising that research has focused on optimising these interventions by investigating their transfer effects on cognition.

These interventions vary in format including dance (Cherriere et al., 2020; Lakes et al., 2019; Teixeira-Machado et al., 2017), hippotherapy (Ahn et al., 2021; Hsieh et al., 2017), videogaming (Sajan et al., 2017), climbing (Christensen et al., 2017), kinesiotherapy (Shin & Song, 2016), high-intensity training (Heathcock et al., 2015), leap-motion-based exergame (Yildirim et al., 2021) and Bobath therapy (Abuin-Porras et al., 2019). Although physical interventions were the predominant type of intervention in our systematic review, only a small number of these studies were RCTs (n = 3) (Ahn et al., 2021; Sajan et al., 2017; Teixeira-Machado et al., 2017).

The findings of our study showed that physical interventions have the potential to improve cognition in individuals with CP. High quality studies have demonstrated our initial hypothesis regarding transfer effects on general cognitive functioning (Teixeira-Machado et al., 2017) and executive functions (inhibitory control) (Ahn et al., 2021). These improvements were demonstrated after approximately 24 hours of physical intervention (Ahn et al., 2021; Teixeira-Machado et al., 2017).

These results reinforce the idea of an interrelationship between cognition and motor functioning in individuals with CP. Previous studies have emphasized the significant influence of cognitive impairment on the effectiveness of motor interventions (Fazzi et al., 2005; Kim et al., 2006; Reid et al., 2015). In this case, the association was inverted, underscoring the noteworthy contribution of motor aspects in enhancing cognitive functions. Beyond the research on CP, the underlying mechanisms responsible for the beneficial effects of physical interventions on cognition have not yet been completely elucidated in other populations, and most studies have focused on adults (Grassmann et al., 2017; Umegaki et al., 2021). Nevertheless, from a psychological perspective, a challenging physical task can involve specific cognitive functions, such as executive functions, and consequently, activate the same brain regions used to control higher-order cognitive processes (Schmidt et al., 2020). Thus, it is more than likely that cognitive functions are trained during physical tasks, leading to notable changes. Moreover, among the various mechanisms involved in these cognitive changes, physical interventions may increase brain-derived neurotrophic factor (BDNF) levels. BDNF seems to be associated with neuronal survival, neurogenesis, and preservation of white matter structure. Furthermore, physical interventions promote an increase in brain network connectivity. Additionally, other mechanisms underlying the beneficial effects of physical interventions, particularly in the elderly population, involve the reduction of oxidative stress, inflammation, and biomarkers, such as amyloid β and hyperphosphorylated tau, which are associated with neurodegenerative processes (Umegaki et al., 2021).

Previous research in typically developing populations has shown far transfer effects of physical interventions on cognitive functions from early childhood (Carson et al., 2016; Erickson et al., 2019; Esteban-Cornejo et al., 2015) to adulthood (Erickson et al., 2019). Similarly, these far transfer effects have been observed in children with other neurodevelopmental disorders such as ASD and ADHD (Liang et al., 2022; Tan et al., 2016), which are also highly prevalent in children with CP (Påhlman et al., 2021). Nevertheless, the impact of physical interventions is not equal across cognitive functions. Among the different cognitive functions that can be improved, executive functions appear to be particularly receptive to change through physical interventions (Erickson et al., 2019; Grassmann et al., 2017; Liang et al., 2021). Core executive functions, particularly inhibitory control and cognitive flexibility, are the easiest to benefit from physical interventions (Koščak Tivadar, 2017; Liang et al., 2021; Mora-Gonzalez et al., 2019). A meta-analysis (Liang et al., 2022) revealed that children with ASD experience improvements in cognitive flexibility and inhibitory control as a result of physical interventions. These results are consistent with those of our review which showed beneficial effects in these executive function domains. In our case, while beneficial effects on inhibitory control were found in both studies of high (Ahn et al., 2021) and low (Lakes et al., 2019) quality, cognitive flexibility was only investigated and demonstrated in one study with low quality (Yildirim et al., 2021). Further high quality research is needed to determine the effects of physical interventions in both core and higher-order executive function domains.

Contrary to our expectations, our systematic review did not find studies with high quality that support the effectiveness of physical interventions on visual perception. As will be discussed more extensively later, it is necessary to include cognitive tasks to enhance this specific cognitive function.

At this point, the reader may be curious about the characteristics that require physical intervention to enhance cognition. Regarding intervention characteristics (format, intensity, and duration), remarkable variability was observed among the studies included in our systematic review. This variability allows responses to specific individual needs, motivation to be addressed, and adjusted interventions accordingly. However, diversity also makes it difficult to draw firm conclusions regarding the most effective interventions for achieving cognitive improvement. Nevertheless, among the different types of physical interventions for CP, dance has gained increasing interest, leading to an increase in the number of systematic reviews and meta-analyses assessing its effectiveness in CP (Cherriere et al., 2020; Duarte Machado et al., 2023; López-Ortiz et al., 2019). A meta-analysis (Duarte Machado et al., 2023) has reported the benefits of dance interventions on cognitive function in the CP population. However, owing to the limited number of included studies (n = 3), it was not possible to determine the specific effects of dance intervention on cognition. Duarte Machado et al. (2023) agreed that there are limited RCTs in this field and emphasized the need for further high quality research to establish a clearer understanding of the effects of dance interventions on cognitive functioning in individuals with CP.

2. Multi-modal interventions

Our systematic review identified 10 studies that investigated the effects of **multi-modal interventions** on cognitive function, half of which were RCTs. Multi-modal interventions, which encompass both cognitive and physical tasks, are of great clinical relevance in the field of CP. The complex nature of this disorder requires a multifaceted approach to address multiple symptoms, thereby integrating motor and cognitive symptomatology. Study 1 suggests that interventions combining physical and cognitive tasks have the potential to enhance **general intellectual functioning** (Morgan et al., 2016b), **executive functions** (Mak et al., 2018, 2020), and **visual perception** (Alwhaibi et al., 2020; Aran et al., 2020; James et al., 2015b; Piovesana et al., 2017) in children with CP.

The results of the best available evidence showed that general cognitive functioning improved in infants aged 12 months of age (Morgan et al., 2016b) after a multi-modal intervention that included parental coaching and environmental enrichment. However, to the best of our knowledge, multi-modal interventions have not been the primary intervention used to improve general intellectual functioning in children, and further research should be conducted in the field.

The results of our systematic review have demonstrated that research on multi-modal interventions and their effects on cognition in CP has mainly focused on executive functions. Studies of high quality included have revealed improvements in inhibitory control (Mak et al., 2018), and reasoning (Aran et al., 2020) in children with CP. Additionally, Mak et al. (2022) reported delayed effects on cognitive flexibility six months after the intervention. The findings of the present study are consistent with research conducted in other paediatric populations, indicating that multi-modal interventions enhance working memory and cognitive flexibility (Egger et al., 2019; Schmidt et al., 2020). However, relatively few studies have been published specifically on children, as most have focused on adults, particularly the elderly. Research on the adult population has reported improvements in executive functions (Dhir et al., 2021; Guo et al., 2020; Rieker et al., 2022), and, to a lesser extent, in memory skills (Ward et al., 2017).

Hence, it seems that combining cognitive and physical tasks is better for achieving improvements in executive functions. However, some clues, such as the dose, remain to be elucidated. In addition to the specific type of multi-modal intervention, the way physical and cognitive modalities are presented is another factor that needs to be clarified. Most studies have investigated dual tasks by simultaneously combining physical and cognitive tasks (Guo et al., 2020).

All studies that assessed visual perception reported improvements (Alwhaibi et al., 2020; Aran et al., 2020; Bilde et al., 2011; James et al., 2015b; Piovesana et al., 2017; Ramkumar & Gupta, 2016). Among these, three were RCTs (Alwhaibi et al., 2020; Aran et al., 2020; James et al., 2015b; Piovesana et al., 2017). Notably, two RCTs with a low risk of bias and a larger number of participants (approximately 100) (Aran et al., 2020; James et al., 2015b; Piovesana et al., 2017) showed that computerized multi-modal interventions produced beneficial effects in the CP population.

3. Cognitive interventions

Out of the 28 studies included in our systematic review, only a limited number of 5 focused specifically on **cognitive interventions**. Furthermore, among these studies, only one was an RCT (Di Lieto et al., 2021). A detailed analysis of the evidence available on near and far transfer effects, together with the results obtained by Di Lieto et al. (2021) is provided when the results of the RCT (Study 3) are discussed. However, it is remarkable that the study conducted by Di Lieto et al. (2021) found improvements in **working memory**, **inhibitory control**, **and visual perception** in a sample of children aged between 4 and 13 years, demonstrating both near and far transfer effects of a cognitive intervention.

As mentioned in the methods section, the risk of bias of RCTs was assessed using the Cochrane Collaboration Risk of Bias Tool (Higgins & Green, 2011) described in Study 1. The analysis of the risk of bias in Di Lieto et al. (2021) work reported unclear risk of bias in 4 of 6 domains (random sequence generation, allocation concealment, blinding of participants and personnel and blinding of outcome assessment), with an overall 75% of unclear risk. Nevertheless, studies of lower quality (no RCTs) have also found an association between cognitive interventions and improvements in visual perception (Cho et al., 2015), executive functions (planning and reasoning) (Peny-Dahlstrand et al., 2020; Pereira et al., 2019), and social cognition (Cho et al., 2015) in individuals with CP. Despite these promising results in cognitive interventions, the scarcity of research in the field, specifically regarding high quality studies, supports our initial hypothesis about the gap in the literature on cognitive interventions for CP. This aligns with the results reported by Novak et al. (2020), in which no cognitive interventions were identified to enhance cognitive function.

Although our systematic review does not allow for generalization, the effectiveness of cognitive interventions has been extensively explored in other paediatric populations. Numerous systematic reviews have been published on the effectiveness of executive function interventions using computerized programs (Luis-Ruiz et al., 2020; Pasqualotto et al., 2021; Robledo-Castro et al., 2023; Sala et al., 2019; Scionti et al., 2020; Shepard et al., 2022). Among these, working memory interventions are the most popular, followed by inhibitory control interventions. Existing literature suggests that cognitive interventions often result in near transfer effects. A second-order meta-analysis (Sala et al., 2019) found that working memory training enhances trained cognitive functions; however, evidence regarding far transfer effects is inconclusive and small or even null far transfer effects have been reported (Bombonato et al., 2023; Kassai et al., 2019; Luis-Ruiz et al., 2020; Melby-Lervåg & Hulme, 2013; Sala et al., 2019).

4. Which intervention is most effective for cerebral palsy: physical, multi-modal, or cognitive?

Considering the results of the systematic review, professionals in the field of CP may wonder about the most effective interventions for enhancing cognitive functions in individuals with CP. Could physical intervention be the best option? Or perhaps combining physical tasks with cognitive tasks may be more effective? Alternatively, focusing solely on cognitive tasks, may lead to produce greater effects?

Answering these questions is not as straightforward as it may initially seem, based on the current evidence. While physical interventions have been shown to enhance general intellectual functioning and working memory, they may not improve visual perception. Given that VPIs are one of the main cognitive symptoms of CP, these interventions have failed to improve them. Additionally, high quality studies investigating the effects of these interventions on memory and other core and higher-order executive functions are lacking.

On the other hand, multi-modal interventions have demonstrated improvements not only in general intellectual functioning and working memory, but also in visual perception and reasoning. However, it is important to note that the cognitive benefits obtained in multi-modal interventions often remain limited to the trained cognitive functions, rather than generalizing to other cognitive functions. This suggests that these interventions may not be the most optimised ones.

Furthermore, while both physical and multi-modal have positive effects on cognition, no RCTs have examined memory skills and all core executive function domains. Our RCT project was developed to address these gaps, later discussed, with near and far transfer effects obtained. Moreover, physical and multi-modal interventions failed to produce far transfer effects on QoL, with limited evidence of benefits.

In contrast, cognitive interventions, particularly those targeting executive functions, seem to produce changes in both trained and untrained cognitive functions. Although no previous RCT has investigated the effects of cognitive interventions on higher-order executive functions, non-RCTs indicate that changes can occur in these domains. However, gaps remain in our understanding of these cognitive interventions. It is unknown whether the improvements obtained, both near and far transfer effects, are maintained over time. Additionally, previous studies have not addressed the far transfer effects of these interventions on untrained cognitive functions, such as verbal learning and long-term memory, or on daily well-being, such as QoL and participation.

Despite these aspects requiring further clarification, cognitive interventions show promise for optimising the effects of intervention in individuals with CP. Future research, particularly RCTs of higher quality, is needed to gain a better understanding of the potential of cognitive interventions to improve cognitive functions and well-being in this population. Study 3 attempted to address these gaps and provided a comprehensive recommendation by considering the results of RCT in the final section of this discussion.

QUALITY OF LIFE IN PEOPLE WITH CEREBRAL PALSY: A BIOPHYSOCHOSOCIAL APPROACH

As reflected in the introduction of this thesis, the concept of QoL encompasses overall life satisfaction, which includes various aspects related to emotional, social, and physical well-being, self-esteem, and self-determination (Colver, 2009, 2012). Thus, identifying factors related to **QoL** can help to determine appropriate assessments and interventions to improve the daily lives of individuals with CP. Therefore, the third aim of this thesis was to explore the relationship between QoL and cognitive functions in children with CP, while also considering relevant demographic, clinical, and psychosocial variables. Study 2 is of particular relevance, as it adopts a comprehensive biopsychosocial perspective, incorporating cognitive functions, to determine which have a greater impact on QoL in CP. This knowledge is essential for targeting specific cognitive functions to optimise cognitive interventions and improve well-being in CP. The findings revealed that executive functions and visual perception are explanatory factors for QoL in children with CP. Additionally, gross motor function, ASD traits, and parental stress variables were found to be related to QoL.

1. Factors related to overall quality of life in cerebral palsy

1.1. Executive functions

As hypothesized, our results prove that executive functions are explanatory variables for overall and specific QoL domains in children with CP. Specifically, the BRIEF-2 questionnaire was a good predictor of the total QoL score and the subdomains of Social Well-being and Acceptance, Feelings about Functioning, and Emotional Well-being and Self-esteem. These results highlight the relevance of these functions in the emotional, physical, and social aspects of the QoL. Although studies examining the impact of executive functioning on individuals with CP are scarce, one study investigated the relationship between executive functioning and QoL (Laporta-Hoyos et al., 2017). Our findings are consistent with those of Laporta-Hoyos et al. (2017), who found a relationship between executive functions and QoL in adolescents and adults with dyskinetic CP. Laporta-Hoyos et al. (2017) reported that cognitive flexibility is an explanatory variable across several QoL domains. Although no prior research has investigated the effect of executive functions on QoL in children with CP, this relationship has been demonstrated in other paediatric populations, such as children with ASD (De Vries & Geurts, 2015), epilepsy (Love et al., 2016; Schraegle & Titus, 2016; Sherman et al., 2006), congenital heart disease (Sanz et al., 2018), and neurofibromatosis type 1 (Roy et al., 2021).

Our results showed no association between QoL and performance-based executive function tests. Laporta-Hoyos et al. (2017) found that different performance-based executive tests predicted various QoL domains in adolescents and adults with CP. Specifically, the Wisconsin Card Sorting Test was a predictor of total CP QoL score, General and Participation, Communication and Physical Health, Family Health, and Feelings about Functioning. In addition, the Ballon Analogue Risk Task-Youth explains Communication and Physical Health domain. In our case, the indexes of the BRIEF-2 questionnaire, a rating scale used specifically to assess executive functions in daily life, were the explanatory variables for the regression model of QoL domains. It is important to note that performance-based tests and rating scales assess different aspects of executive functions (Pino Muñoz & Arán Filippetti, 2021). While performance-based measures seem to evaluate underlying cognitive skills under controlled environmental conditions, rating measures focus on the ecological, daily, and observable aspects of executive functions in everyday home and school settings (Krivitzky et al., 2019; Pino Muñoz & Arán Filippetti, 2021). In particular, the BRIEF questionnaire is related to a child's academic performance (Pino Muñoz & Arán Filippetti, 2021). Hence, our work findings, along with previous literature, reinforce the imperative idea of conducting a comprehensive neuropsychological assessment in children with CP, including performance-based tests and rating scales, to identify those who may be at risk for lower QoL.

In other paediatric populations, studies examining the role of executive functions in children's QoL have also found a relationship between BRIEF and QoL questionnaires (De Vries & Geurts, 2015; Love et al., 2016; Sanz et al., 2018; Schraegle & Titus, 2016; Sherman et al., 2006). Love et al. (2016) demonstrated that ecological executive dysfunction (namely in this way by the own authors), measured using the BRIEF-2 questionnaire, decreased QoL levels in children and adolescents with medically refractory epilepsy. These studies have shown a notable prevalence of executive dysfunction in different populations, with T-scores ≥ 65 in more than one-third to half of the participants (Love et al., 2016; Schraegle & Titus, 2016; Sherman et al., 2006). In our work, 42% of participants showed clinical-level dysfunction in the Global Index of Executive Function (SD = 11.12). Our findings are consistent with data from previous studies, supporting the link between executive functions and QoL in children. Further research, however, should investigate the percentage of impairment to determine whether the relationship depends on executive functions difficulties.

1.2. Gross motor function

In addition to executive functions, **motor function** was identified as a significant predictor of **total QoL Score**. These findings align with the prior links between gross motor function and QoL (Badia et al., 2016; Beckung et al., 2008; Böling et al., 2016; Chen et al., 2014; Liu et al., 2009; Majnemer et al., 2007; Park, 2017; Rapp et al., 2017). Furthermore, multiple studies have emphasized the relationship between QoL and motor functioning, assessing QoL through the CP QoL questionnaire and adopting a biopsychosocial approach that considers clinical, demographic, and psychosocial variables (Badia et al., 2016; Böling et al., 2016; Chen et al., 2014; Power et al., 2020). Recently, Power et al. (2020) reinforced the idea that QoL can be explained by various clinical (hearing and speech impairment), demographic (sex), and psychosocial (type of schooling, mother's education, primary caregiver depression, and stress) factors, highlighting the role of gross motor function.

2. Factors associated with specific domains of quality of life: visual perception, Autism Spectrum Disorder, and parental stress.

Our findings indicate that executive and gross motor functions are not the only predictors of QoL. Visual perception, ASD traits, and parental stress were the explanatory variables for specific QoL domains.

2.1. Visual perception and quality of life

Our work showed that **visual perception** has a significant impact on the **Access to Services domain**. However, contrary to our initial hypothesis, we did not observe a direct association between visual perception and overall QoL. To date, only one study has investigated the relationship between visual perception and QoL in individuals with CP (Mitry et al., 2016). Interestingly, Mitry et al. (2016) reported that visual perception was an exploratory variable in the total QoL score in a sample where 53% of children had VPIs. In our study, we specifically focused on mild to moderate cases of CP, with only approximately 12% of children presenting with VPIs in the object/recognition domain and 40% in visual spatial perception. Thus, our research found a lower impairment than expected in children with CP (Ego et al., 2015; Pueyo et al., 2009). This lower prevalence in our study may explain why we did not observe a direct association between visual perception and total QoL score.

Moreover, when comparing our study with Mitry et al. (2016), it is important to note the following differences in QoL and visual perception measures. Mitry et al. (2016) assessed QoL through a generic questionnaire, while we used a QoL questionnaire specifically designed to cover well-being in the CP population. Furthermore, the visual attention and recognition/navigation domains of the Insight questionnaire were related to overall QoL in Mitry et al.' (2016) study. The domains that were related to QoL in Mitry et al.'s (2016) study differed from those assessed in our study (Tsirka et al., 2020). Nevertheless, measures similar to ours (Tsirka et al., 2020), such as the Lea Mailbox (Williams et al., 2015) and the perception of the movement domain from the Insight questionnaire (Macintyre-Beon et al., 2012), were not significant predictors of QoL.

Therefore, replicating our study with a larger sample size and encompassing the entire visual perceptual spectrum would be beneficial in determining whether the factors influencing QoL are consistent or differ across the whole spectrum of CP. As in the case of executive functions and considering evidence, it would be interesting to assess the various domains that encompass visual perception and consider rating scales as complementary to the diagnosis of VPIs, as well as its impact on QoL in each individual case.

2.2. Autism Spectrum Disorder

Our study found that **ASD traits** alone explained the **Participation and Physical Health domain,** which is a significant finding due to no previous study has explored the effects of ASD traits on the QoL of individuals with CP. These results are in line with earlier research in the field of ASD (De Vries & Geurts, 2015), which demonstrated that ASD traits can influence multiple domains of QoL, including the physical domain, as was observed in our study's observations. Consequently, difficulties in social communication may hinder participation in everyday activities at school, in sports, and within the community.

In our sample, the prevalence of ASD traits was around 16%, whereas other recent studies have estimated that it occurs in approximately 30% of CP cases (Påhlman et al., 2021). Although our sample had a lower prevalence of ASD, it is notable that ASD traits were significantly correlated with the CP QoL total score. However, when introduced into the multiple linear regression model of the Cp QoL total score, ASD traits were not a significant explanatory variable. Nevertheless, further research should investigate its role using a sample with a higher prevalence of ASD and CP.

Furthermore, considering the high prevalence of ASD in the CP population and its implications for physical well-being, it is crucial to consider and assess the presence of ASD symptomatology, especially when proposing interventions.

2.3. Parental stress

The results of this study showed that **parental stress** influences **Social Well-being and Acceptance domain**. The identification of parental stress as a factor that influences QoL in children with CP has been demonstrated in other studies (Power et al., 2020; Rapp et al., 2017). Parental stress represents the level of dysfunction in the parent-child system related to parents' functioning and its level is significantly higher in children with CP than in typically developing children (De Gaetano et al., 2022). Morever, higher levels of parental stress have been associated with lower QoL in children with CP (Harris, 2021; Sentenac et al., 2021; White-Koning et al., 2008). Previous studies (Power et al., 2020; Rapp et al., 2017), including our work, found an association between parental stress and QoL using a proxy-reported version of the CP QoL questionnaire. However, possible parent-child discrepancies in QoL ratings (Makris et al., 2021) suggest that future research should include a multi-informant approach in which both the child and their caregivers' experiences are recollected to assess QoL.

Furthermore, De Gaetano et al. (2022) showed that parental stress in children with severe neuromotor disability is correlated with the level of cognitive and behavioural disability, rather than motor severity. Considering the importance of parental stress in QoL, strategies to decrease stress levels in caregivers of children with CP should be applied because it would have beneficial effects in children and their families.

3. Neuropsychological variables without a significant role in quality of life

Contrary to our initial hypothesis, we found no significant association between general intellectual functioning and QoL in our sample of children with CP. Previous studies have found that general intellectual functioning may be an explanatory variable for CP. However, it is important to note that the results between studies are difficult to compare due to the variations in estimating the general intellectual functioning. Some studies relied on parental interviews (Badia et al., 2016; Rapp et al., 2017), whereas others utilized registry data (Jiang et al., 2016) or combined different measures, such as parent interviews and formal assessments (Arnaud et al., 2008). In addition to heterogeneity in the assessment, none of the children in our sample scored below 70, which is considered an indication of ID, and only 7% of the sample had an IQ score of 75. However, earlier studies reported that approximately half or more of participants presented with ID (Arnaud et al., 2008; Badia et al., 2016; Jiang et al., 2016; Rapp et al., 2017).

Nevertheless, our work aligns with studies that have shown no relationship between general intellectual functioning and QoL (Laporta-Hoyos et al., 2017; Power et al., 2020). These studies, with a biopsychosocial approach, including several variables found that general intellectual functioning was not related to CP QoL. The findings of Laporta-Hoyos et al. (2017) demonstrated that general intellectual functioning was not an explanatory variable of QoL in adults with dyskinetic CP. Similarly, we utilized the performance-based test Raven's Coloured Progressive Matrices, as Laporta-Hoyos et al. (2017). Although Laporta-Hoyos et al. (2017) found a positive correlation between IQ and specific subdomains of QoL, it was not an explanatory variable in multiple linear regression models. This correlation may be partially attributed to the fact that the sample in their study had lower general intellectual functioning (mean = 87.04, SD = 26.31) than ours (mean = 97.67, SD = 12.57). Notably, both studies identified executive functions as explanatory variables for several QoL measures, further supporting the importance of considering specific cognitive functions in CP, particularly executive functions.

To the best of our knowledge, no earlier studies have considered the relationship between memory and QoL. However, contrary to expectations, Study 2 did not find memory to be an explanatory variable for QoL. A previous study on children with epilepsy found a significant association between verbal memory and QoL, indicating the need for further investigation into the role of memory in the CP population. Additionally, our study only included verbal and visual long-term memory, and future work should explore the effects of immediate memory and learning on QoL in children with CP.

4. The relevance of identifying quality of life determinants

To enhance children's well-being, it is crucial to determine the factors that contribute to QoL. The identification of these factors should guide interventions and, consequently, resource prioritization. In the context of CP, it has become evident that interventions aimed at increasing QoL should primarily focus on executive functions.

This thesis highlights the importance of neuropsychological, clinical, and psychosocial variables in the QoL of children with CP. Regarding neuropsychological aspects, it is important to consider that executive functions, visual perception, and ASD traits are good predictors of QoL. Executive functions play a crucial role in the QoL of individuals with CP, impacting their lives throughout their lifespan. This emphasizes the importance of assessing and addressing executive functions in both children and adults. Research on CP has determined the influence of executive functions in children aged eight and above. However, there is a lack of evidence regarding the influence of these cognitive functions in early childhood. Therefore, further research should be conducted during early childhood to determine whether executive functions should be considered relevant from the earliest stages of life. In addition, gross motor function plays an important role in the QoL. The results also demonstrate the relevance of the biopsychosocial approach in determining the well-being of individuals with CP, and consequently, the need for multidisciplinary work to improve QoL.

The ICF framework is becoming increasingly important in the QoL field. Based on this model, Almasri and Alquaqzeh (2023) conducted a systematic review to summarize the determinants of QoL in children with CP. The authors reported several factors that influence each component of ICF: (1) body function and structure: CP type, child's behavioural difficulties, and the presence of pain, hearing, and speech impairments in the body; (2) activities: gross motor and fine motor functions, sleep difficulties, physical activity, and walking performance, or poor social interaction and communication skills; (3) participation in leisure activities and daily habits; and (4) personal factors: age, child's motivation to perform tasks, and child's comfort and emotions. Additionally, environmental factors, such as parental stress and depression levels, family coping patterns, mother's age, and education level, also influence QoL. Applying an ICF framework to classify the significant determinants of QoL with reference to the systematic review conducted by Almasri and Alquaqzeh (2023), we can add the following components that influence QoL: (1) body function and structure: executive functions, visual perception, and ASD traits; (2) activities: gross motor function; and (3) environmental factors: parental stress.

FAR TRANSFER EFFECTS OF EXECUTIVE FUNCTION INTERVENTIONS IN PEOPLE WITH CEREBRAL PALSY

The results of Studies 1 and 2 suggest the possibility of executive function intervention as a treatment for enhancing cognitive function and QoL in children with CP. However, further research is needed to optimise the effects of cognitive interventions on CP. This aim was covered by Study 3, in which the final goal was to explore the potential far transfer effects of home-based computerized executive function interventions on other cognitive functions (memory and visual perception) and various aspects of daily life (QoL and participation). Additionally, long-term effects were assessed by examining whether the intervention's benefits persisted after a nine-month period and whether any delayed effects emerged.

1. Near and far transfer effects, what are more usual

Study 3 showed **far transfer effects** on specific domains of **memory** and **visual perception** after an executive function intervention in children with CP. Specifically, verbal immediate memory, verbal learning, and object/picture recognition improved after 12 weeks of the intervention. However, no beneficial effects were reported in visual memory, visual spatial perception, or aspects of daily life such as QoL and participation.

As seen previously, this thesis is part of the ETCONNECT project, which examined the near and far transfer effects of a home-based executive function intervention in a group of children with CP. Near transfer effects have been published beyond this thesis (García-Galant et al., 2023). Before discussing the far transfer effects in detail, it is important to consider the near transfer effects. Improvements in all **core executive** functions (inhibitory control, working memory, and cognitive flexibility) were observed in the intervention group. These beneficial effects were maintained for up to nine months after the intervention. Regarding higher-order executive functions and executive functions in daily life, no improvements were observed after the intervention or at the 9-month follow-up. Alongside changes in core executive functions, **social cognition** also improved, with follow-up effects observed over the same period (García-Galant et al., manuscript in preparation).

In summary, improvements in near (core executive functions and social cognition) and far (verbal memory and visual perception) transfer effects were obtained through a home-based executive function intervention. Follow-up results indicated that whereas near transfer effects were maintained 9 months later, no far transfer effects remained. These results demonstrate that nearly all trained cognitive functions showed significant improvements and remained. The results obtained are in line with previous studies, indicating that near transfer effects are much more common than far transfer effects (Bombonato et al., 2023; Kassai et al., 2019; Luis-Ruiz et al., 2020; Melby-Lervåg & Hulme, 2013; Sala et al., 2019). Certainly, the debate on the effectiveness of cognitive interventions in achieving far transfer effects remains open. In a second-order meta-analysis, Sala et al. (2019) found that the far transfer effects were null or small. On the other hand, Bombonato et al. (2023) conducted a meta-analysis to clarify the possibility of the far transfer effect of executive function interventions in children with neurodevelopmental disorders including ADHD, ASD, and other developmental and specific learning disabilities. Five studies included in the qualitative analysis reported improvements in memory, nonverbal reasoning, and intelligence. However, only three studies were included in the meta-analysis, and no statistically significant overall effect size was found.

Although far transfer effects are less common, researchers and clinicians are interested in them, especially in populations with chronic conditions where there is multiple and heterogeneous symptomatologies, as in the case of CP. The results obtained in the present study appear to be better than those of previous systematic reviews and meta-analyses of other paediatric populations (Bombonato et al., 2023; Kassai et al., 2019; Luis-Ruiz et al., 2020; Melby-Lervåg & Hulme, 2013; Sala et al., 2019). Our results reinforce the results of the only RCT published, which, as mentioned earlier had an overall 75% unclear bias, on the effects of an executive function intervention in children with CP (Di Lieto et al., 2021). Di Lieto et al. (2021) found far transfer effects on inhibitory control, visual perception, and phonological processing.

The fact that we obtained greater far transfer effects compared to prior studies in CP and other child populations could be explained by differences among the specific executive function interventions used. Previous research has mainly focused on working memory interventions, particularly for children (Di Lieto et al., 2021; Sala et al., 2019; Strobach & Huestegge, 2017). In contrast, our intervention included working memory, inhibitory control, and cognitive flexibility tasks equally from the beginning of the intervention. Additionally, higher-order executive functions and social cognition tasks were included from week 7. Although no higher-order executive functions were improved, this type of cognitive functions implies the integration of lower-level cognitive processes such as memory and could consequently produce changes in these functions. Another aspect that should be considered is that executive function interventions seem to be more effective in children with neurodevelopmental disabilities than in those without (Oldrati et al., 2020), probably due to the presence of cognitive impairments. As mentioned earlier, a notable number of participants (42%) exhibited executive dysfunction, with cognitive flexibility (38%) and inhibitory control (35%) being the most affected domains (see Annex 1). The results analysed in relation to the number of participants who transitioned from the clinical impairment category to the unaffected were considered insufficient for drawing conclusive findings. Children in the intervention group may show significant improvement without transitioning to the unaffected group, due to their score are not situated proximal to the cut-off. Thus, using the initial Z-scores may help capture the continuous and cumulative effect of the intervention, helping us uncover any noteworthy improvements that may have occurred in intervention group compared to waitlist group.

The improvements observed in untrained cognitive functions can be explained in two ways. First, interventions for these impaired functions can lead to improvements in other cognitive functions that are not directly targeted. Second, improvements in executive functions themselves can also create transfer effects, thus benefiting these untrained functions. It is worth noting that the presence of executive dysfunction in our sample, as seen in other neurodevelopmental disabilities (Oldrati et al., 2020), may partially contribute to the promising results compared to those reported in previous studies (Kassai et al., 2019; Melby-Lervåg & Hulme, 2013; Sala et al., 2019).

In summary, the results of the RCT (Study 3) demonstrated that executive functions interventions improved non-trained cognitive functions. Thus, beneficial effects in specific domains of memory and visual perception were observed after 12 weeks of intervention. Nevertheless, these beneficial effects were not maintained 9 months after the completion of the intervention, probably due to the necessity of a booster dose or perform a more ecological intervention. The findings of Study 3 appear to address the initial objectives of this thesis, and executive interventions may offer promising treatments for optimising the effects of interventions to improve cognitive function in individuals with CP. In the following section, the obtained far transfer effects are discussed in detail.

2. Far transfer effects on memory skills

To the best of our knowledge, Study 3 is the first to examine the effects of a cognitive intervention on verbal memory in individuals with CP. Our results showed that immediate verbal memory and verbal learning improved after 12 weeks of a home-based executive function intervention in children with CP. These findings are in line with those of previous studies on other child populations (Acosta et al., 2019; Løhaugen et al., 2011).

The observed changes in **immediate verbal memory** are not surprising, considering their close association with working memory. The Baddeley et al. model (1998; 2011) emphasizes the significance of immediate memory (referred to as short-term memory in the Baddeley model) in the working memory system. The findings from the ETCONNECT project revealed results regarding the interrelationship between near and far transfer effects. Initially, no immediate improvements in verbal working memory were observed after the intervention. However, it is worth noting that an enhancement in verbal working memory was observed nine months later. In contrast, significant improvements in immediate verbal memory were evident immediately after the intervention. These findings could suggest a potential interplay between immediate memory and working memory, indicating a possible transfer effect. Gradual improvements in immediate verbal memory might enhance the mechanisms underlying working memory over time, leading to delayed effects. Considering Baddeley et al. 's model (1998; 2011) of working memory, the debate remains open regarding whether immediate verbal memory should be considered a near or far transfer effect. Certainly, the memory is not trained directly and is considered a far transfer effect. However, the interrelationship between working memory and memory is evident, and the effects obtained in immediate memory are difficult to consider at the same level of the transfer effect as in other cognitive functions. In this way, it is not so *far far* and we could think that the effects obtained are between the near and far transfer effects. Consequently, immediate memory improvements could be a ***midd* or *intermediate* transfer effect**. Although the idea of effects between near and far effects has not been explored sufficiently in cognitive interventions, some authors have used the intermediate term to categorize these effects (Melby-Lervåg et al., 2016).

Transfer effects were observed in verbal learning. These improvements are of special relevance because of the implication of this function in the acquisition of new information and knowledge and, consequently, its repercussions in school settings (Smith, 2009). Nevertheless, no changes in long-term memory have been reported. This can be explained by the fact that long-term memory is a complex and slow process that requires considerable time to produce improvement (Cowan, 2008). Executive functions, particularly working memory, play an important role in transferring information from sensory inputs to immediate memory, and are closely involved in the learning of novel information (Baddeley, 2012; Vander Linden et al., 2019). Previous studies have found that better working memory is associated with better long-term memory performance (Cotton & Ricker, 2022). Thus, it is likely that longer interventions with subsequent improvements in working memory and learning could translate to better long-term memory performance. Although no significant differences were found in long-term memory, it is notable that despite the lack of statistical significance, the intervention group showed higher scores in both verbal and visual long-term memory than the control group in follow-up assessment, and even higher than their immediate post-intervention scores. The baseline performance was considered in the statistical analysis to avoid the influence in the results. In general, cognitive performance was worse in the waitlist control group compared to the intervention group, but baseline differences were only statistically significant between groups in Arrows and Memory for Designs (NEPSY-II). Enhancing long-term memory can be a complex process, but cognitive interventions, particularly those targeting executive function, show promise as potential treatments.

3. Far transfer effects on visual perception

After 30 hours of intervention, participants showed significant enhancements in visual perception, particularly in the object/picture recognition dimension. These findings are noteworthy considering the high prevalence of VPIs in individuals with CP (Ego et al., 2015). Visual perception difficulties are associated with academic and motor problems in individuals with CP (Critten et al., 2018, 2019; James et al., 2015a). Specifically, impairments in object/picture recognition have been linked to facial expression and reading difficulties (McKillop et al., 2006; Philip & Dutton, 2014). Additionally, it is important to note that visual perception affects the QoL. As demonstrated in Study 2, the object/facial recognition domain was identified as a relevant variable within the Access to

Services domain. Mitry et al. (2016) further highlighted the influence of visual perception on the overall QoL of children with CP.

Another important aspect to consider is that the intervention was delivered through a **computerized program**. The results obtained align with those of Study 1 and previous research on computerized interventions (Oldrati et al., 2020), suggesting that cognitive tasks administered via computerized programs enhance visual perception. Technological devices have shown superior effectiveness compared with paper-based interventions in studies investigating visual perceptual interventions (Chen et al., 2013; Park & Park, 2015; Wu et al., 2022). Chen et al. (2013) found that computerized group and individual training were more effective than paper-based interventions in improving the visual perception of children with developmental delay. Similarly, Wu et al. (2022) reported significant increases in visual perceptual performance in a computerized intervention group; however, these improvements were not statistically significant in a standard rehabilitation group. This could be attributed to the more engaging experience provided by computerized interventions, which enhances participant motivation and engagement.

Visual perception encompasses a wide range of dimensions, including object/picture recognition, visual spatial perception, visual discrimination and matching, figure-ground perception, motion perception, and visual short-term memory (Ben Itzhak et al., 2021). The neuropsychological assessment performed in this study focused on object/picture recognition, visual spatial perception, and visual short-term memory, with improvements observed in object/picture recognition. These dimensions are commonly evaluated in the clinical and research settings. In fact, object/picture recognition and visual spatial perception are among the most discriminating dimensions between CVI and no CVI (Ben Itzhak et al., 2021). However, as mentioned earlier, children with CP present a **wide spectrum of visual perceptual profiles** with varying impairments in each case.

Professionals have emphasized the necessity of employing an extensive battery of visual perceptual tests to comprehensively assess the range of strengths and deficits within each child's profile (Ortibus et al., 2019). Tests such as the Test of Visual Perceptual Skills–Third Edition (TVPS-3) (Martin & Gardner, 2006), the Beery-Buktenica Developmental Test of

Visual-Motor Integration-Sixth Edition (Beery-VMI-6) (Beery, 1997) and motion perception tasks (Van der Zee et al., 2019) could be useful for targeting visual perceptual profiles. However, it should not be forgotten that assessing both near and far transfer effects on cognitive function requires extensive neuropsychological assessments.

Recently, advancements have been made in the field of visual perceptual intervention, including the development of individualized and adaptive mini-games aimed at targeting visual perceptual skills (Ben Itzhak et al., 2022). Although no results from these interventions have yet been published, these new developments will allow firm conclusions to be drawn regarding the common features with executive function interventions. Moreover, further research will provide insights into tasks that should be included in home-based executive function interventions for children with CP to enhance the multiple dimensions of visual perception and maintain improvements over time.

Improvements in visual perception were observed after the intervention, but no direct benefits were observed 9 months later in Study 3. This could be explained by the fact that the follow-up 9 months after the intervention was a long period for an intervention of 12 weeks, when no posterior booster dose was administered. Although long-term effects and potential non-cognitive improvements are discussed in detail in the next section, visual perceptual improvements could remain, including additional sessions once the intervention was completed, known as booster dose, or even including tasks more related to visual perception.

4. Far transfer effects on daily life

To the best of our knowledge, Study 3 is the first study to investigate the effects of cognitive intervention on daily life in people with CP. However, contrary to our initial assumptions, executive function intervention did not result in significant improvements in QoL of children with CP. These findings are consistent with those of previous studies conducted in different populations (De Vries et al., 2015; Dovis et al., 2015). For example, De Vries et al. (2014) found no transfer effect of executive function interventions on QoL in children with ASD, whereas Dovis et al. (2015) reported no significant post-intervention or follow-up improvements in children with ADHD. Moreover, the intervention group in our study did not show an increase in participation compared to the waitlist control group.

Nevertheless, recent studies have shown that executive function interventions can enhance QoL in paediatric populations with sustained improvements over time (Hahn-Markowitz et al., 2020; Modi et al., 2021). One possible explanation for the lack of QoL improvements could be the absence of changes in executive functions in daily life. Our cross-sectional study (Study 2) demonstrated that behavioural manifestations of executive function in everyday life were associated with QoL. However, our RCT results indicated that these behavioural manifestations of executive function in everyday life, as measured by BRIEF-2, did not improve after the intervention (García-Galant et al., 2023). Similarly, De Vries et al. (2015) found a relationship between BRIEF and QoL in children with ASD, but their subsequent RCT investigating working memory and cognitive flexibility interventions showed no improvements in BRIEF and QoL (De Vries et al., 2015). Dovis et al. (2015) also reported no improvements in BRIEF or QoL in children with ADHD in their post- and follow-up assessments.

The nature of the training tasks used in the intervention may have contributed to this lack of change. While some tasks were designed to resemble aspects of daily life, such as preparing the backpack, others were less ecologically valid, such as the space conquest task. For instance, in preparing the backpack task, the child had to prepare their backpack for school by selecting only the necessary material for that day, whereas the space conquest was a spaced-themed task involving jumping between different moving planets until arriving at the destination. The inclusion of several tasks that were less ecological may have hindered the transfer of intervention effects to daily life, including executive functions in everyday life. Thus, it is crucial to incorporate tasks that are closely related to real-life situations in order to facilitate the transfer effect to other measures. A study of an ADHD population showed that improvements in QoL were obtained with an executive function intervention supplemented by tasks related to daily activities (Hahn-Markowitz et al., 2020).

Furthermore, QoL and level of participation in children with CP are influenced by various factors. Hence, it is crucial to consider certain environmental factors, such as parental stress, because it seems they play a significant role in influencing the QoL of children with CP, as observed in Study 2. Although we included parental stress as a potential covariate in the ANCOVA, it is imperative that interventions address additional aspects, including parental stress, to make a meaningful impact on daily life.

Discrepancies in the effectiveness of cognitive interventions in improving these outcomes highlight the need for further investigation in this field. Interventions to enhance QoL and participation of children with CP should include ecologically valid tasks, effectively target executive functions in daily life, and consider other additional factors.

5. Can cognitive interventions in children with cerebral palsy achieve "long-far" term effects?

Our results indicate that the **far transfer effects** on visual perception and memory were **not maintained** after a nine-month period. Additionally, no delayed effects on cognitive or non-cognitive functions were observed after the same timeframe. However, the near transfer effects of the ETCONNECT project demonstrated the maintenance of all core executive functions (García-Galant et al., 2023) and social cognition (García Galant et al., manuscript in preparation) even after nine months. It is important to note that, if there are few studies on the far transfer effect of cognitive interventions, the number of studies investigating the long-term effects is even more limited (Bombonato et al., 2023).

Study 1 of this thesis revealed a gap regarding the follow-up effects of cognitive interventions and, moreover, in general in interventions with an impact on cognitive functions in the CP population. Study 3 was the first to investigate the long-term effects of cognitive interventions on CP. These results are not in line with earlier findings (Grunewaldt et al., 2013, 2016; Løhaugen et al., 2011) in which far transfer effects on memory were maintained during follow-up assessment. One possible explanation for the differences in results between studies is the variation in the follow-up assessment periods. Løhaugen (2011) and Grunewaldt (2013, 2016) conducted follow-up assessments after 6 and 7 months, respectively, while our assessment was not performed until 9 months after the intervention (García-Galant et al., 2020). This longer period between the intervention and follow-up assessment may have contributed to the lack of maintained effects in our case. Long-term effects are essential for confirming the effectiveness of training (De Vries et al., 2015).

Various strategies can be employed to maintain these improvements. On the one hand, administer a booster dose one period after the intervention is completed. Given that previous studies have reported follow-up effects around six months after the intervention (Grunewaldt et al., 2013, 2016; Løhaugen et al., 2011), it would be interesting to investigate the follow-up effects on non-trained cognitive functions at three and six months after the intervention ended. This could help determine the moment at which the effect is lost and anticipate the administration of a booster dose. On the other hand, further research should explore the effects of executive function interventions that primarily focus on core and higher-order executive function tasks, while also incorporating visual perception and memory tasks in a minor way. This research could determine whether this approach leads to major optimisation of beneficial effects as well as its maintenance, thus implying less fatigue and required resources.

6. Is the future of home-based computerized executive function interventions promising?

The intervention was implemented using a computerized program at home. First, computer-based interventions have proven to be highly cost-effective compared to traditional individual-directed therapy sessions (Sandgreen et al., 2021). In today's digital era, there is increasing emphasis on the use of technology, supported by a growing body of literature demonstrating the effectiveness of computerized cognitive interventions in children with neurodevelopmental disabilities (Oldrati et al., 2020). These interventions are crucial for two main reasons: first, they effectively train specific skills with interactive feedback and facilitate their improvement, and second, they are present in an attractive way, enhancing motivation and maintaining engagement. To further enhance the potential of cognitive interventions, it is important to incorporate more immersive and attractive therapy environments such as virtual reality systems (Boato et al., 2022; Vacca et al., 2023). These types of interventions allow the remote treatment of cognitive function.

Second, our intervention was **home-based** and had several positive aspects. Home-based interventions in diseases, such as CP, eliminate barriers between the person and treatment. Additionally, the context in which treatment is applied is meaningful because the realization of intervention in natural environments, such as home or school, enhances engagement, and at the same time, research has evidenced the possibility of transferring to daily life aspects (Beckers et al., 2020; Novak et al., 2009). Although no far transfer effects were found in daily life, improvements can be made considering the aspects discussed earlier, Beckers et al. (2020) conducted a systematic review to assess the feasibility and effectiveness of home-based occupational and physiotherapy programs in children with CP. The results of the included studies indicate that home-based training programs are feasible. The key elements of the effectiveness of interventions were the intensity of the intervention and parents' implications (Beckers et al., 2020). Parents play an important role in home-based interventions and become active participants in their children's therapy (Boato et al., 2022). Otherwise, parents' responsibilities may hinder their participation in and follow-up with the therapy. Hence, effective coaching by therapists can help parents become more confident in carrying out the program and make it easier to implement in their daily routines (Beckers et al., 2020).

Combining the advantages of home-based interventions with computerized devices can provide a comprehensive treatment for CP. In summary, **home-based computer gaming** is a feasible, safe, cost-effective, and attractive executive function intervention with the active role of families. Further research is required to investigate the effects of immersive intervention in severe cases.

STRENGTHS, LIMITATIONS AND FURTHER RESEARCH

In addition to what has already been mentioned in the articles and in this discussion, here we highlight the most remarkable points of the present work. This thesis has some **strengths** to consider. This work represents a step forward in the current knowledge regarding optimising interventions to improve cognition in individuals with CP applicable to clinical, educational, and research settings. The application of different designs, including a systematic review, a cross-sectional study and an RCT, allows for a better understanding of the available interventions. The systematic review conducted in the field of interventions with an impact on cognitive functions provided an overview of the state-of-the-art. The use of international guidelines (such as PRISMA, Cochrane Collaboration's risk of bias, and CEBM guidelines) resulted in a rigorous search strategy and assessment of the quality of evidence. The use of cross-sectional and RCT designs enabled us to establish the relationship between cognitive variables and QoL while also exploring the causality of interventions on cognitive function improvement. In terms of assessment, we conducted an extensive neuropsychological assessment by a researcher who was blinded about group assignment during the project. Moreover, the tests were carefully selected to reduce any influence from motor severity or time constraints, ensuring minimization of possible biases by the non-cognitive aspects associated with CP. Furthermore, we employed condition specific QoL and participation questionnaires designed for populations with CP.

Interventions for CP can be challenging because of the high burden on the child and their family, along with motor restrictions that hinder visits to the health centre for treatment. A home-based intervention tailored to each participant's performance and including numerous games targeting specific executive functions helps professionals increase engagement, reduce costs, adapt to the routine, individualize treatment, and consequently achieve greater improvements. Following the Cochrane Collaboration's risk of bias tool, our RCT had a low risk of bias in the categories of random sequence generation, allocation concealment, blinding of outcome assessment, and selective reporting outcomes. The overall low of bias in our study represents an improvement in the methodology of cognitive interventions in CP compared to the previous one (Di Lieto et al. 2021) in which the overall risk of bias was unclear. The low risk of bias in our study represents an improvement in the methodology of cognitive interventions for CP and increases the validity and reliability of our study results.

The strengths mentioned are accompanied by some **limitations** that should be taken into account. One limitation was the characteristics of the participants. Most participants involved in the three studies had mild-to-moderate motor severity, with spastic CP being the most prevalent type. While the generalization across the CP spectrum is limited, including mild to moderate cases in Studies 2 and 3, it helped homogenize the sample characteristics and the effective time of the cognitive intervention among participants. Furthermore, in Study 1, only published literature was included, thus limiting the inclusion of interventions reported in grey literature that might be effective in improving cognition, which is not evidenced in the present thesis. The visual perceptual assessment in the cross-sectional and RCT studies (Studies 2 and 3) was also limited to specific domains of this cognitive function, hindering analysis of the possible relationship between other visual perceptual domains and QoL, or their improvement after the executive function intervention. Another limitation is that participants and their families were unblinded to their assignment to either intervention or waitlist control group. This was necessary because of difficulties in conducting a study involving suitable passive cognitive interventions. Passive cognitive interventions are challenging to implement without incorporating tasks that require a certain level of executive function.

In general, the findings obtained in the present thesis raise the need for **further research** to explore the far transfer effects of executive function interventions. Firstly, the effects of these interventions on other cognitive and non-cognitive functions, should be examined using the ICF framework. Understanding the impact of cognitive interventions on different aspects of individuals with CP is of special relevance to determining which intervention is the most effective in this population. Recent research (Duarte Machado et al., 2023) has investigated the effectiveness of interventions across ICF domains, and further research is needed in this field. From a neuropsychological approach, it would be of particular interest to explore the effects on other cognitive functions, such as general intellectual functioning or language. Additionally, the beneficial effects observed in mild-to-moderate CP research raises the need for future work to examine the far transfer effects on the most severe cases.

Future works should include tools that facilitate the assessment and intervention of severe cases. Nowadays, neuropsychological assessments in severe cases imply the need to conduct some adaptations to the tools, and in some cases these changes are not enough to evaluate the individual with CP (Stadskleiv et al., 2021). Consequently, further research should guide which test should be administered and may feasible the use of relatively new techniques such as eye-tracking. Severe cases of CP are associated with higher cognitive impairments and it is crucial to determine whether more pronounced benefits could be obtained. While some studies have considered the inclusion of an active control group as an advantage, others have viewed it as a disadvantage, leading to an ongoing debate on the subject. Beliefs and expectations play a significant role in the effectiveness of control groups in research studies (Au et al., 2015, 2020; Melby-Lervåg et al., 2016; Melby-Lervåg & Hulme, 2013; Tsai et al., 2018). To address this issue, further research is necessary to identify and quantify any non-specific effects of interventions that may exist, such as placebo effects, participants' characteristics, and other influences. Neuroplasticity is crucial for the rehabilitation process and can provide a better understanding of the impact of cognitive interventions on individuals with CP (Pereira et al., 2018). Consequently, further research should include neuroimaging studies to determine the changes in brain connectivity in children with CP after cognitive interventions. A major comprehension of far transfer effects is possible after investigating the brain changes underlying to intervention.

Finally, in line with obtaining greater optimisation of intervention in CP, further research should explore the inclusion of booster doses and more ecological interventions to investigate the possilibity of obtaining long-term far transfer effects on cognitive functions as well as their impact on well-being.

CONCLUSIONS

The main conclusions of the thesis can be summarized as follows:

I. Available evidence shows that the interventions proposed to assess their effects on cognitive functions in CP are mainly physical interventions. These physical interventions enhance general cognitive functioning and the inhibitory control domain of executive functions. Interventions that combine physical and computerized cognitive tasks (multi-modal interventions) improve other cognitive functions such as visual perception.

II. Among the scarce cognitive interventions available for CP, interventions targeting executive functions stand out due to obtaining near transfer effects on a major number of core executive functions in children with CP.

III. A home-based computerized executive function intervention of 12 weeks, with sessions lasting 30 minutes per day, 5 days per week, is effective in obtaining far transfer effects not only in visual perception but also in memory in children with CP.

IV. Applying the ICF framework, our results indicate that the determinants of QoL include body function and structure, activities, and environmental factors. In particular, executive functioning plays an important role in the QoL of children with CP, influencing both the overall and specific QoL domains. In addition to executive functions, gross motor functional status is a significant explanatory variable for the overall QoL of children with CP. Visual perception, ASD symptoms, and parental stress are explanatory variables for the specific QoL domains.

V. Until now, interventions targeting executive functions have not improved the well-being of children with CP (quality of life and participation in daily activities).

VI. A home-based computerized executive function intervention fails to produce long-term far transfer effects on cognitive functions and well-being in children with CP.

To sum up, the results of this thesis emphasize the importance of considering executive functions to optimise interventions in CP population. Among cognition, executive functions play the most relevant role in the QoL of children with CP. A home-based computerized executive function intervention produces far transfer effects on other cognitive functions. New insights should explore ways to maximize these far transfer effects over time and achieve impact on the well-being across the CP spectrum.

REFERENCES

Abd Elmagid, D. S., & Magdy, H. (2021). Evaluation of risk factors for cerebral palsy. The Egyptian Journal of Neurology, *Psychiatry and Neurosurgery, 57*(1), 13. https://doi.org/10.1186/s41983-020-00265-1

Abuin-Porras, V., Pedersini, P., Berjano, P., & Villafañe, J. H. (2019). The efficacy of physical therapy on the improvement of the motor components of visual attention in children with cerebral palsy: A case series study. *Journal of Exercise Rehabilitation, 15*(1), 103–108. https://doi.org/10.12965/jer.1836568.284

Acosta, V., Hernandez, S., & Ramirez, G. (2019). Effectiveness of a working memory intervention program in children with language disorders. *Applied Neuropsychology: Child, 8*(1), 15–23. https://doi.org/10.1080/21622965.2017.1374866

Ahn, B., Joung, Y.-S., Kwon, J.-Y., Lee, D. I., Oh, S., Kim, B.-U., Cha, J. Y., Kim, J.-H., Lee, J. Y., & Shin, H. Y. (2021). Effects of equine-assisted activities on attention and quality of life in children with cerebral palsy in a randomized trial: Examining the comorbidity with attention-deficit/hyperactivity disorder. *BMC Pediatrics, 21*(1), 1–9. https://doi.org/10.1186/s12887-021-02597-0

Alloway, T. P., Bibile, V., & Lau, G. (2013). Computerized working memory training: Can it lead to gains in cognitive skills in students? *Computers in Human Behavior, 29*(3), 632–638. https://doi.org/10.1016/j.chb.2012.10.023

Alloway, T. P., Gathercole, S. E., Willis, C., & Adams, A.-M. (2004). A structural analysis of working memory and related cognitive skills in young children. *Journal of Experimental Child Psychology, 87*(2), 85–106. https://doi.org/10.1016/j.jecp.2003.10.002

Almasri, N. A., & Alquaqzeh, F. A. (2023). Determinants of Quality of Life of Children and Adolescents with Cerebral Palsy: A Systematic Review. *Physical & Occupational Therapy In Pediatrics, 43*(4), 367–388. https://doi.org/10.1080/01942638.2022.2162358

Alriksson-Schmidt, A., & Hägglund, G. (2016). Pain in children and adolescents with cerebral palsy: A population-based registry study. *Acta Paediatrica, 105*(6), 665–670. https://doi.org/10.1111/apa.13368

Alwhaibi, R. M., Alsakhawi, R. S., & ElKholi, S. M. (2020). Augmented Biofeedback Training with Physical Therapy Improves Visual-Motor Integration, Visual Perception, and Motor Coordination in Children with Spastic Hemiplegic Cerebral Palsy: A Randomised Control Trial. *Physical and Occupational Therapy in Pediatrics, 40*(2), 134–151. https://doi.org/10.1080/01942638.2019.1646375

Amankwah, N., Oskoui, M., Garner, R., Bancej, C., Manuel, D. G., Wall, R., Finès, P., Bernier, J., Tu, K., & Reimer, K. (2020). Cerebral palsy in Canada, 2011–2031: Results of a microsimulation modelling study of epidemiological and cost impacts. *Health Promotion and Chronic Disease Prevention in Canada, 40*(2), 25–37. https://doi.org/10.24095/hpcdp.40.2.01

Amoah, D. K. (2022). Advances in the understanding and enhancement of the human cognitive functions of learning and memory. *Brain Science Advances, 8*(4), 276–297. https://doi.org/10.26599/BSA.2022.9050023

Andersen, G. L., Irgens, L. M., Haagaas, I., Skranes, J. S., Meberg, A. E., & Vik, T. (2008). Cerebral palsy in Norway: Prevalence, subtypes and severity. European Journal of Paediatric Neurology, 12(1), 4–13. https://doi.org/10.1016/j.ejpn.2007.05.001

Anderson, V., Jacobs, R., & Anderson, P. J. (2010). Executive functions and the frontal lobes: A lifespan perspective. Psychology Press.

Anttila, H., Autti-Rämö, I., Suoranta, J., Mäkelä, M., & Malmivaara, A. (2008). Effectiveness of physical therapy interventions for children with cerebral palsy: A systematic review. *BMC Pediatrics, 8*, 1–10. https://doi.org/10.1186/1471-2431-8-14

Aran, O. T., Şahin, S., Köse, B., Ağce, Z. B., & Kayihan, H. (2020). Effectiveness of the virtual reality on cognitive function of children with hemiplegic cerebral palsy: A single-blind randomized controlled trial. *International Journal of Rehabilitation Research, 43*(1), 12–19. https://doi.org/10.1097/MRR.0000000000000378

Ardoy, D. N., Fernández-Rodríguez, J. M., Jiménez-Pavón, D., Castillo, R., Ruiz, J. R., & Ortega, F. B. (2014). A physical education trial improves adolescents' cognitive performance and academic achievement: The EDUFIT study. *Scandinavian Journal of Medicine & Science in Sports, 24*(1), e52–e61. https://doi.org/10.1111/sms.12093

Arnaud, C., White-Koning, M., Michelsen, S. I., Parkes, J., Parkinson, K., Thyen, U., Beckung, E., Dickinson, H. O., Fauconnier, J., Marcelli, M., McManus, V., & Colver, A. (2008). Parent-Reported Quality of Life of Children With Cerebral Palsy in Europe. *Pediatrics, 121*(1), 54–64. https://doi.org/10.1542/peds.2007-0854

Astle, D. E., Barnes, J. J., Baker, K., Colclough, G. L., & Woolrich, M. W. (2015). Cognitive training enhances intrinsic brain connectivity in childhood. *Journal of Neuroscience, 35*(16), 6277–6283. https://doi.org/10.1523/JNEUROSCI.4517-14.2015

Au, J., Gibson, B. C., Bunarjo, K., Buschkuehl, M., & Jaeggi, S. M. (2020). Quantifying the Difference between Active and Passive Control Groups in Cognitive Interventions Using two Meta-Analytical Approaches. Journal of Cognitive Enhancement : *Towards the Integration of Theory and Practice, 4*(2), 192–210. https://doi.org/10.1007/s41465-020-00164-6

Au, J., Sheehan, E., Tsai, N., Duncan, G. J., Buschkuehl, M., & Jaeggi, S. M. (2015). Improving fluid intelligence with training on working memory: A meta-analysis. Psychonomic Bulletin & Review, 22(2), 366–377. https://doi.org/10.3758/s13423-014-0699-x

Baddeley, A. (1998). Working memory. Comptes Rendus de l'Académie Des Sciences-Series III-Sciences de La Vie, 321(2–3), 167–173. https://doi.org/10.1016/s0764-4469(97)89817-4

Baddeley, A. (2012). Working memory: Theories, models, and controversies. Annual Review of Psychology, 63, 1–29. https://doi.org/10.1146/annurev-psych-120710-100422

Baddeley, A., Jarrold, C., & Vargha-Khadem, F. (2011). Working memory and the hippocampus. *Journal of Cognitive Neuroscience, 23*(12), 3855–3861. https://doi.org/10.1162/jocn_a_00066

Baddeley, A., Kopelman, M. D., & Wilson, B. A. (2003). *The handbook of memory disorders*. John Wiley & Sons.

Badia, M., Orgaz, M. B., Gomez-Vela, M., Verdugo, M. A., Ullan, A. M., & Longo, E. (2016). Do environmental barriers affect the parent-reported quality of life of children and adolescents with cerebral palsy? *Research in Developmental Disabilities, 49*, 312–321. https://doi.org/10.1016/j.ridd.2015.12.011

Balf, C. L., & Ingram, T. T. S. (1955). Problems in the classification of cerebral palsy in childhood. *British Medical Journal, 2*(4932), 163. https://doi.org/10.1136/bmj.2.4932.163

Ballantyne, M., Liscumb, L., Brandon, E., Jaffar, J., Macdonald, A., & Beaune, L. (2019). Mothers' Perceived Barriers to and Recommendations for Health Care Appointment Keeping for Children Who Have Cerebral Palsy. *Global Qualitative Nursing Research, 6*. https://doi.org/10.1177/2333393619868979

Ballester-Plané, J., Laporta-Hoyos, O., Macaya, A., Póo, P., Meléndez-Plumed, M., Toro-Tamargo, E., Gimeno, F., Narberhaus, A., Segarra, D., & Pueyo, R. (2018). Cognitive functioning in dyskinetic cerebral palsy: Its relation to motor function, communication and epilepsy. *European Journal of Paediatric Neurology, 22*(1), 102–112. https://doi.org/10.1016/j.ejpn.2017.10.006

Ballester-Plané, J., Laporta-Hoyos, O., Macaya, A., Poo, P., Meléndez-Plumed, M., Vazquez, E., Delgado, I., Zubiaurre-Elorza, L., Narberhaus, A., & Toro-Tamargo, E. (2016). Measuring intellectual ability in cerebral palsy: The comparison of three tests and their neuroimaging correlates. *Research in Developmental Disabilities, 56*, 83–98. https://doi.org/10.1016/j.ridd.2016.04.009

Ballester-Plané, J., Schmidt, R., Laporta-Hoyos, O., Junqué, C., Vázquez, É., Delgado, I., Zubiaurre-Elorza, L., Macaya, A., Póo, P., Toro, E., de Reus, M. A., van den Heuvel, M. P., & Pueyo, R. (2017). Whole-brain structural connectivity in dyskinetic cerebral palsy and its association with motor and cognitive function. *Human Brain Mapping, 38*(9), 4594–4612. https://doi.org/10.1002/hbm.23686

Bangirana, P., Allebeck, P., Boivin, M. J., John, C. C., Page, C., Ehnvall, A., & Musisi, S. (2011). Cognition, behaviour and academic skills after cognitive rehabilitation in Ugandan children surviving severe malaria: A randomised trial. *BMC Neurology, 11*(1), 96. https://doi.org/10.1186/1471-2377-11-96

Bangirana, P., Giordani, B., John, C. C., Page, C., Opoka, R. O., & Boivin, M. J. (2009). Immediate neuropsychological and behavioral benefits of computerized cognitive rehabilitation in Ugandan pediatric cerebral malaria survivors. *Journal of Developmental and Behavioral Pediatrics: JDBP, 30*(4), 310–318. https://doi.org/10.1097/DBP.0b013e3181b0f01b

Barnett, S. M., & Ceci, S. J. (2002). When and where do we apply what we learn?: A taxonomy for far transfer. *Psychological Bulletin, 128*, 612–637. https://doi.org/10.1037/0033-2909.128.4.612

Bax, M. C. O. (1964). Terminology and classification of cerebral palsy. *Developmental Medicine & Child Neurology, 6*(3), 295–297. https://doi.org/10.1111/j.1469-8749.1964.tb10791.x

Beckers, L. W. M. E., Geijen, M. M. E., Kleijnen, J., Rameckers, E. A. A., Schnackers, M. L. A. P., Smeets, R. J. E. M., & Janssen-Potten, Y. J. M. (2020). Feasibility and effectiveness of home-based therapy programmes for children with cerebral palsy: A systematic review. *BMJ Open, 10*(10), e035454. https://doi.org/10.1136/bmjopen-2019-035454

Beckung, E., White-Koning, M., Marcelli, M., McManus, V., Michelsen, S., Parkes, J., Parkinson, K., Thyen, U., Arnaud, C., & Fauconnier, J. (2008). Health status of children with cerebral palsy living in Europe: A multi-centre study. *Child: Care, Health and Development,* 34(6), 806–814. https://doi.org/10.1111/j.1365-2214.2008.00877.x

Beery, K. E. (1997). *The Beery-Buktenica developmental test of visual-motor integration.* Administration Scoring and Teaching Manual. Pearson.

Belmonte-Darraz, S., Montoro, C. I., Andrade, N. C., Montoya, P., & Riquelme, I. (2021). Alteration of emotion knowledge and its relationship with emotion regulation and psychopathological behavior in children with cerebral palsy. *Journal of Autism and Developmental Disorders, 51*, 1238–1248. https://doi.org/10.1007/s10803-020-04605-1

Ben Itzhak, N., Franki, I., Jansen, B., Kostkova, K., Wagemans, J., & Ortibus, E. (2022). An individualized and adaptive game-based therapy for cerebral visual impairment: design, development, and evaluation. International *Journal of Child-Computer Interaction, 31*, 100437. https://doi.org/10.1016/j.ijcci.2021.100437

Ben Itzhak, N., Vancleef, K., Franki, I., Laenen, A., Wagemans, J., & Ortibus, E. (2021). Quantifying visuoperceptual profiles of children with cerebral visual impairment. *Child Neuropsychology, 27*(8), 995–1023. https://doi.org/10.1080/09297049.2021.1915265

Benton, A. L., Hamsher, K. D., Varney, N. R., & Spreen, O. (1994). *Contributions to neuropsychological assessment: A clinical manual (2nd ed.*). Oxford University Press.

Berry, J. O., & Jones, W. H. (1995). The Parental Stress Scale: Initial psychometric evidence. Journal of Social and Personal Relationships, 12(3), 463–472. https://doi.org/10.1177/0265407595123009

Bialik, G., & Givon, U. (2009). Cerebral palsy: Classification and etiology. *Acta Orthopaedica et Traumatologica Turcica, 43*(2), 77–80. https://doi.org/10.3944/AOTT.2009-.077

Bilde, P. E., Kliim-Due, M., Rasmussen, B., Petersen, L. Z., Petersen, T. H., & Nielsen, J. B. (2011). Individualized, home-based interactive training of cerebral palsy children delivered through the Internet. *BMC Neurology, 11*(1), 32. https://doi.org/10.1186/1471-237711-32

Blasco, M., García-Galant, M., Berenguer-González, A., Caldú, X., Arqué, M., Laporta-Hoyos, O., Ballester-Plané, J., Miralbell, J., Jurado, M. Á., & Pueyo, R. (2022). Interventions with an Impact on Cognitive Functions in Cerebral Palsy: A Systematic Review. *Neuropsychology Review,* 33 (2), 551-577. https://doi.org/10.1007/s11065-022-09550-7

Blasco, M., García-Galant, M., Laporta-Hoyos, O., Ballester-Plané, J., Jorba-Bertran, A., Caldú, X., Miralbell, J., Alonso, X., Meléndez-Plumed, M., & Toro-Tamargo, E. (2023). Factors Related to Quality of Life in Children With Cerebral Palsy. *Pediatric Neurology, 141*, 101–108. https://doi.org/10.1016/j.pediatrneurol.2023.01.006

Boato, E., Melo, G., Filho, M., Moresi, E., Lourenço, C., & Tristão, R. (2022). The Use of Virtual and Computational Technologies in the Psychomotor and Cognitive Development of Children with Down Syndrome: A Systematic Literature Review. *International Journal of Environmental Research and Public Health, 19*(5). https://doi.org/10.3390/ijerph19052955

Bodimeade, H. L., Whittingham, K., Lloyd, O., & Boyd, R. N. (2013). Executive function in children and adolescents with unilateral cerebral palsy. *Developmental Medicine and Child Neurology, 55*(10), 926–933. https://doi.org/10.1111/dmcn.12195

Böling, S., Varho, T., Kiviranta, T., & Haataja, L. (2016). Quality of life of Finnish children with cerebral palsy. *Disability and Rehabilitation, 38*(7), 683–688. https://doi.org/10.3109/09638288.2015.1061607

Bombonato, C., Del Lucchese, B., Ruffini, C., Di Lieto, M. C., Brovedani, P., Sgandurra, G., Cioni, G., & Pecini, C. (2023). Far Transfer Effects of Trainings on Executive Functions in Neurodevelopmental Disorders: A Systematic Review and Meta Analysis. *Neuropsychology Review*, 1–36. https://doi.org/10.1007/s11065-022-09574-z

Bottcher, L. (2010). Children with spastic cerebral palsy, their cognitive functioning, and social participation: A review. *Child Neuropsychology, 16*(3), 209–228. https://doi.org/10.1080/09297040903559630

Bottcher, L., Flachs, E. M., & Uldall, P. (2009). Attentional and executive impairments in children with spastic cerebral palsy. *Developmental Medicine and Child Neurology, 52*(2), e42-7. https://doi.org/10.1111/j.1469-8749.2009.03533.x

Brock, L. L., Murrah, W. M., Cottone, E. A., Mashburn, A. J., & Grissmer, D. W. (2018). An after-school intervention targeting executive function and visuospatial skills also improves classroom behavior. *International Journal of Behavioral Development, 42*(5), 474–484. https://doi.org/10.1177/0165025417738057

Brock, L. L., Rimm-Kaufman, S. E., Nathanson, L., & Grimm, K. J. (2009). The contributions of 'hot'and 'cool'executive function to children's academic achievement, learning-related behaviors, and engagement in kindergarten. *Early Childhood Research Quarterly, 24*(3), 337–349.

Brown, S. H., Lewis, C. A., McCarthy, J. M., Doyle, S. T., & Hurvitz, E. A. (2010). The effects of internet-based home training on upper limb function in adults with cerebral palsy. *Neurorehabilitation and Neural Repair, 24*(6), 575–583. https://doi.org/10.1177/1545968310361956

Burak, M., & Kavlak, E. (2019). Investigation of the relationship between quality of life, activity participation and environmental factors in adolescents with cerebral palsy. *NeuroRehabilitation, 45*(4), 555–565. https://doi.org/10.3233/NRE-191288

Buschkuehl, M., & Jaeggi, S. M. (2010). Improving intelligence: A literature review. *Swiss Medical Weekly, 140*(19–20), 266–272. https://doi.org/10.4414/smw.2010.12852

Caillies, S., Hody, A., & Calmus, A. (2012). Theory of mind and irony comprehension in children with cerebral palsy. *Research in Developmental Disabilities, 33*(5), 1380–1388. https://doi.org/10.1016/j.ridd.2012.03.012

Çalik, B., Kitis, A., Cavlak, U., & OOğuzhanoğlu, A. (2012). The impact of attention training on children with low vision: A randomized trial. *Turkish Journal of Medical Sciences, 42*(7), 1186–1193. https://doi.org/10.3906/sag-1112-26

Calley, A., Williams, S., Reid, S., Blair, E., Valentine, J., Girdler, S., & Elliott, C. (2012). A comparison of activity, participation and quality of life in children with and without spastic diplegia cerebral palsy. *Disability and Rehabilitation, 34*(15), 1306–1310. https://doi.org/10.3109/09638288.2011.641662

Cankurtaran, D., Tezel, N., Yildiz, S. Y., Celik, G., & Unlu Akyuz, E. (2021). Evaluation of the effects of the COVID-19 pandemic on children with cerebral palsy, caregivers' quality of life, and caregivers' fear of COVID-19 with telemedicine. *Irish Journal of Medical Science, 190*, 1473–1480. https://doi.org/10.1007/s11845-021-02622-2

Cans, C. (2000). Surveillance of cerebral palsy in Europe: A collaboration of cerebral palsy surveys and registers. *Developmental Medicine & Child Neurology, 42*(12), 816–824. https://doi.org/10.1017/s0012162200001511

Cans, C., Dolk, H., Platt, M. J., & Colver, A. (2007). Recommendations from the SCPE collaborative group for defining and classifying cerebral palsy. *Developmental Medicine and Child Neurology, 49*, 35. https://doi.org/10.1111/j.1469-8749.2007.tb12626.x

Carson, V., Hunter, S., Kuzik, N., Wiebe, S. A., Spence, J. C., Friedman, A., Tremblay, M. S., Slater, L., & Hinkley, T. (2016). Systematic review of physical activity and cognitive development in early childhood. *Journal of Science and Medicine in Sport, 19*(7), 573–578. https://doi.org/10.1016/j.jsams.2015.07.011

Chen, K.-L., Tseng, M.-H., Shieh, J.-Y., Lu, L., & Huang, C.-Y. (2014). Determinants of quality of life in children with cerebral palsy: A comprehensive biopsychosocial approach. *Research in Developmental Disabilities, 35*(2), 520–528. https://doi.org/10.1016/j.ridd.2013.12.002

Chen, M.-D., Tsai, H.-Y., Wang, C.-C., & Wuang, Y.-P. (2015). The effectiveness of racket-sport intervention on visual perception and executive functions in children with mild intellectual disabilities and borderline intellectual functioning. *Neuropsychiatric Disease and Treatment, 11*, 2287–2297. https://doi.org/10.2147/NDT.S89083

Chen, N., Cai, P., Zhou, T., Thompson, B., & Fang, F. (2016). Perceptual learning modifies the functional specializations of visual cortical areas. *Proceedings of the National Academy of Sciences, 113*(20), 5724–5729. https://doi.org/10.1073/pnas.1524160113

Chen, Y.-N., Lin, C.-K., Wei, T.-S., Liu, C.-H., & Wuang, Y.-P. (2013). The effectiveness of multimedia visual perceptual training groups for the preschool children with developmental delay. *Research in Developmental Disabilities, 34*(12), 4447–4454. https://doi.org/10.1016/j.ridd.2013.09.023

Cherriere, C., Martel, M., Sarrasin, A., Ballaz, L., Tallet, J., & Lemay, M. (2020). Benefits of a dance intervention on balance in adolescents with cerebral palsy. Physical & Occupational Therapy in Pediatrics, 40(5), 518–533. https://doi.org/10.1080/01942638.2020.1720053

Cherriere, C., Robert, M., Fung, K., Tremblay Racine, F., Tallet, J., & Lemay, M. (2020). Is there evidence of benefits associated with dancing in children and adults with cerebral palsy? A scoping review. *Disability and Rehabilitation, 42(*23), 3395–3402. https://doi.org/10.1080/09638288.2019.1590866

Cho, M., Kim, D., & Yang, Y. (2015). Effects of visual perceptual intervention on visual-motor integration and activities of daily living performance of children with cerebral palsy. *Journal of Physical Therapy Science, 27*(2), 411–413. https://doi.org/10.1589/jpts.27.411

Chounti, A., Hägglund, G., Wagner, P., & Westbom, L. (2013). Sex differences in cerebral palsy incidence and functional ability: A total population study. *Acta Paediatrica, 102*(7), 712–717. https://doi.org/10.1111/apa.12240

Christensen, M. S., Jensen, T., Voigt, C. B., Nielsen, J. B., & Lorentzen, J. (2017). To be active through indoor-climbing: An exploratory feasibility study in a group of children with cerebral palsy and typically developing children. *BMC Neurology, 17*(1), 1–20. https://doi.org/10.1186/s12883-017-0889-z

Cloutman, L. L. (2013). Interaction between dorsal and ventral processing streams: Where, when and how? *Brain and Language, 127*(2), 251–263. https://doi.org/10.1016/j.bandl.2012.08.003

Coceski, M., Hocking, D. R., Reid, S. M., Abu-Rayya, H. M., Reddihough, D. S., Wrennall, J., & Stargatt, R. (2022). Assessing IQ in adolescents with mild to moderate cerebral palsy using the WISC-V. *The Clinical Neuropsychologist, 36(*7), 1767–1786. https://doi.org/10.1080/13854046.2021.1928290

Cohen, J. (1988). *Statistical Power Analysis for the Behavioral Sciences (2nd ed.).* In Statistical power analysis for the behavioural sciences (Issue 363). Academic Press.

Cohen, J. (1992). A power primer. *Psychological Bulletin, 112*(1), 155–159. https://doi.org/10.1037//0033-2909.112.1.155

Colver, A. (2006). Study protocol: SPARCLE–a multi-centre European study of the relationship of environment to participation and quality of life in children with cerebral palsy. *BMC Public Health, 6*(1), 1–10. https://doi.org/10.1186/1471-2458-6-105

Colver, A. (2009). Quality of life and participation. *Developmental Medicine & Child Neurology, 51*(8), 656–659. https://doi.org/10.1111/j.1469-8749.2009.03321.x

Colver, A. (2012). Outcomes for people with cerebral palsy: Life expectancy and quality of life. *Paediatrics and Child Health, 22*(9), 384–387. https://doi.org/10.1016/j.paed.2012.03.003

Colver, A., Fairhurst, C., & Pharoah, P. O. D. (2014). Cerebral palsy. *The Lancet, 383*(9924), 1240–1249. https://doi.org/10.1016/S0140-6736(13)61835-8

Colver, A., Rapp, M., Eisemann, N., Ehlinger, V., Thyen, U., Dickinson, H. O., Parkes, J., Parkinson, K., Nystrand, M., & Fauconnier, J. (2015). Self-reported quality of life of adolescents with cerebral palsy: A cross-sectional and longitudinal analysis. *The Lancet, 385*(9969), 705–716. https://doi.org/10.1016/S0140-6736(14)61229-0

Coster, W., Bedell, G., Law, M., Khetani, M. A., Teplicky, R., Liljenquist, K., Gleason, K., & Kao, Y. (2011). Psychometric evaluation of the Participation and Environment Measure for Children and Youth. *Developmental Medicine & Child Neurology, 53(*11), 1030–1037. https://doi.org/10.1111/j.1469-8749.2011.04094.x

Cotton, K., & Ricker, T. J. (2022). Examining the relationship between working memory consolidation and long-term consolidation. *Psychonomic Bulletin & Review, 29*(5), 1625–1648. https://doi.org/10.3758/s13423-022-02084-2

Cowan, N. (2008). What are the differences between long-term, short-term, and working memory? *Progress in Brain Research, 169*, 323–338. https://doi.org/10.1016/S0079-6123(07)00020-9

Cristofori, I., Cohen-Zimerman, S., & Grafman, J. (2019). Chapter 11—Executive functions. In M. D'Esposito & J. H. Grafman (Eds.), Handbook of Clinical Neurology, 163, 197-219. https://doi.org/10.1016/B978-0-12-804281-6.00011-2

Critten, V., Campbell, E., Farran, E., & Messer, D. (2018). Visual perception, visual-spatial cognition and mathematics: Associations and predictions in children with cerebral palsy. *Research in Developmental Disabilities, 80*, 180–191. https://doi.org/10.1016/j.ridd.2018.06.007

Critten, V., Messer, D., & Sheehy, K. (2019). Delays in the reading and spelling of children with cerebral palsy: Associations with phonological and visual processes. *Research in Developmental Disabilities, 85*, 131–142. https://doi.org/10.1016/j.ridd.2018.12.001

Dang, V. M., Colver, A., Dickinson, H. O., Marcelli, M., Michelsen, S. I., Parkes, J., Parkinson, K., Rapp, M., Arnaud, C., Nystrand, M., & Fauconnier, J. (2015). Predictors of participation of adolescents with cerebral palsy: A European multi-centre longitudinal study. Research in Developmental Disabilities, 36, 551–564. https://doi.org/10.1016/j.ridd.2014.10.043

Das, S., Aggarwal, A., Roy, S., & Kumar, P. (2017). Quality of life in Indian children with cerebral palsy using cerebral palsy-quality of life questionnaire. *Journal of Pediatric Neurosciences, 12*(3), 251. https://doi.org/10.4103/jpn.JPN_127_16

De Gaetano, K., Saviola, D., Brunetti, D., & De Tanti, A. (2022). The importance of assessing parent stress in families with children with severe neuromotor and intellectual disability – a pilot study. *Applied Neuropsychology: Child, 11*(4), 804–810. https://doi.org/10.1080/21622965.2021.1971525

De Lisi, R., & Wolford, J. L. (2002). Improving Children's Mental Rotation Accuracy With Computer Game Playing. *The Journal of Genetic Psychology, 163*(3), 272–282. https://doi.org/10.1080/00221320209598683

De Vries, M., & Geurts, H. (2015). Influence of autism traits and executive functioning on quality of life in children with an autism spectrum disorder. *Journal of Autism and Developmental Disorders, 45*, 2734–2743. https://doi.org/10.1007/s10803-015-2438-1

De Vries, M., Prins, P. J. M., Schmand, B. A., & Geurts, H. M. (2015). Working memory and cognitive flexibility-training for children with an autism spectrum disorder: A randomized controlled trial. *Journal of Child Psychology and Psychiatry, 56*(5), 566–576. https://doi.org/10.1111/jcpp.12324

Delacy, M. J., & Reid, S. M. (2016). Profile of associated impairments at age 5 years in Australia by cerebral palsy subtype and Gross Motor Function Classification System level for birth years 1996 to 2005. *Developmental Medicine & Child Neurology, 58*(S2), 50–56. https://doi.org/10.1111/dmcn.13012

Delis, D. C., Kaplan, E., & Kramer, J. H. (2001). *Manual for the Delis-Kaplan Executive Function System (D-KEFS)*. Psychological Corp.

Desai, T., Chow, K., Mumford, L., Hotze, F., & Chau, T. (2014). Implementing an iPad-based alternative communication device for a student with cerebral palsy and autism in the classroom via an access technology delivery protocol. *Computers & Education, 79*, 148–158. https://doi.org/10.1016/j.compedu.2014.07.009

Dewar, R., Love, S., & Johnston, L. M. (2015). Exercise interventions improve postural control in children with cerebral palsy: A systematic review. *Developmental Medicine and Child Neurology, 57*(6), 504–520. https://doi.org/10.1111/dmcn.12660

Dhir, S., Teo, W.-P., Chamberlain, S. R., Tyler, K., Yücel, M., & Segrave, R. A. (2021). The effects of combined physical and cognitive training on inhibitory control: A systematic review and meta-analysis. *Neuroscience & Biobehavioral Reviews, 128*, 735–748. https://doi.org/10.1016/j.neubiorev.2021.07.008

Di Lieto, M. C., Brovedani, P., Pecini, C., Chilosi, A. M., Belmonti, V., Fabbro, F., Urgesi, C., Fiori, S., Guzzetta, A., & Perazza, S. (2017). Spastic diplegia in preterm-born children: Executive function impairment and neuroanatomical correlates. *Research in Developmental Disabilities, 61*, 116–126. https://doi.org/10.1016/j.ridd.2016.12.006

Di Lieto, M. C., Pecini, C., Brovedani, P., Sgandurra, G., Dell'Omo, M., Chilosi, A. M., Guzzetta, A., Perazza, S., Sicola, E., & Cioni, G. (2021). Adaptive Working Memory Training Can Improve Executive Functioning and Visuo-Spatial Skills in Children With Pre-term Spastic Diplegia. *Frontiers in Neurology, 11*, 601148. https://doi.org/10.3389/fneur.2020.601148

Diamond, A. (2013). Executive functions. *Annual Review of Psychology, 64*, 135–168. https://doi.org/10.1146/annurev-psych-113011-143750

Diamond, A. (2020). *Executive functions*. In Handbook of clinical neurology (Vol. 173, pp. 225–240). Elsevier.

Dickinson, H. O., Parkinson, K. N., Ravens-Sieberer, U., Schirripa, G., Thyen, U., Arnaud, C., Beckung, E., Fauconnier, J., McManus, V., & Michelsen, S. I. (2007). Self-reported quality of life of 8–12-year-old children with cerebral palsy: A cross-sectional European study. *The Lancet, 369*(9580), 2171–2178. https://doi.org/10.1016/S0140-6736(07)61013-7

Dodd, K. J., Taylor, N. F., & Damiano, D. L. (2002). A systematic review of the effectiveness of strength-training programs for people with cerebral palsy. *Archives of Physical Medicine and Rehabilitation, 83*(8), 1157–1164. https://doi.org/10.1053/apmr.2002.34286

Dong, V. A. Q., Tung, I. H. H., Siu, H. W. Y., & Fong, K. N. K. (2013). Studies comparing the efficacy of constraint-induced movement therapy and bimanual training in children with unilateral cerebral palsy: A systematic review. *Developmental Neurorehabilitation, 16*(2), 133–143. https://doi.org/10.3109/17518423.2012.702136

Dovis, S., Van der Oord, S., Wiers, R. W., & Prins, P. J. M. (2015). Improving executive functioning in children with ADHD: training multiple executive functions within the context of a computer game. A randomized double-blind placebo controlled trial. *PloS One, 10*(4), e0121651. https://doi.org/10.1371/journal.pone.0121651

Downs, J., Blackmore, A. M., Epstein, A., Skoss, R., Langdon, K., Jacoby, P., Whitehouse, A. J. O., Leonard, H., Rowe, P. W., & Glasson, E. J. (2018). The prevalence of mental health disorders and symptoms in children and adolescents with cerebral palsy: A systematic review and meta-analysis. *Developmental Medicine & Child Neurology, 60*(1), 30–38. https://doi.org/10.1111/dmcn.13555

Duarte Machado, E., Cole, M. H., Miller, L., McGuckian, T. B., & Wilson, P. H. (2023). The efficacy of dance interventions for the activity and participation of individuals with cerebral palsy–a systematic review and meta-analysis. *Disability and Rehabilitation*, 1–17. https://doi.org/10.1080/09638288.2023.2200259

Dufresne, D., Dagenais, L., Shevell, M. I., & Consortium, R. (2014). Spectrum of visual disorders in a population-based cerebral palsy cohort. *Pediatric Neurology, 50*(4), 324–328. https://doi.org/10.1016/j.pediatrneurol.2013.11.022

Dutton, G. N. (2013). The spectrum of cerebral visual impairment as a sequel to premature birth: An overview. *Documenta Ophthalmologica, 127*, 69–78. https://doi.org/10.1007/s10633-013-9382-1

Ego, A., Lidzba, K., Brovedani, P., Belmonti, V., Gonzalez-Monge, S., Boudia, B., Ritz, A., & Cans, C. (2015). Visual–perceptual impairment in children with cerebral palsy: A systematic review. *Developmental Medicine & Child Neurology, 57*, 46–51. https://doi.org/10.1111/dmcn.12687

Ehlers, S., Gillberg, C., & Wing, L. (1999). A screening questionnaire for Asperger syndrome and other high-functioning autism spectrum disorders in school age children. *Journal of Autism and Developmental Disorders, 29*(2), 129–141. https://doi.org/10.1023/A:1023040610384

Elema, A., Zalmstra, T. A. L., Boonstra, A. M., Narayanan, U. G., Reinders-Messelink, H. A., & vd Putten, A. A. J. (2016). Pain and hospital admissions are important factors associated with quality of life in nonambulatory children. *Acta Paediatrica, 105*(9), e419–e425. https://doi.org/10.1111/apa.13493

Eliasson, A.-C., Krumlinde-Sundholm, L., Rösblad, B., Beckung, E., Arner, M., Öhrvall, A.-M., & Rosenbaum, P. (2006). The Manual Ability Classification System (MACS) for children with cerebral palsy: Scale development and evidence of validity and reliability. *Developmental Medicine and Child Neurology, 48*(7), 549–554. https://doi.org/10.1017/S0012162206001162

Ellenberg, J. H., & Nelson, K. B. (2013). The association of cerebral palsy with birth asphyxia: A definitional quagmire. *Developmental Medicine and Child Neurology, 55*(3), 210–216. https://doi.org/10.1111/dmcn.12016

Elvrum, A.-K. G., Andersen, G. L., Himmelmann, K., Beckung, E., Öhrvall, A.-M., Lydersen, S., & Vik, T. (2016). Bimanual fine motor function (BFMF) classification in children with cerebral palsy: Aspects of construct and content validity. *Physical & Occupational Therapy in Pediatrics, 36*(1), 1–16. https://doi.org/10.3109/01942638.2014.975314

Erickson, K. I., Hillman, C., Stillman, C. M., Ballard, R. M., Bloodgood, B., Conroy, D. E., Macko, R., Marquez, D. X., Petruzzello, S. J., & Powell, K. E. (2019). Physical activity, cognition, and brain outcomes: A review of the 2018 physical activity guidelines. *Medicine and Science in Sports and Exercise, 51*(6), 1242. https://doi.org/10.1249/MSS.0000000000001936

Eriksson, E., Hägglund, G., & Alriksson-Schmidt, A. I. (2020). Pain in children and adolescents with cerebral palsy–a cross-sectional register study of 3545 individuals. *BMC Neurology, 20*, 1–9. https://doi.org/10.1186/s12883-019-1597-7

Esteban-Cornejo, I., Tejero-Gonzalez, C. M., Sallis, J. F., & Veiga, O. L. (2015). Physical activity and cognition in adolescents: A systematic review. *Journal of Science and Medicine in Sport, 18*(5), 534–539. https://doi.org/10.1016/j.jsams.2014.07.007

Fahey, M. C., Maclennan, A. H., Kretzschmar, D., Gecz, J., & Kruer, M. C. (2017). The genetic basis of cerebral palsy. *Developmental Medicine & Child Neurology, 59*(5), 462–469. https://doi.org/10.1111/dmcn.13363

Fandim, J. V., Saragiotto, B. T., Porfírio, G. J. M., & Santana, R. F. (2021). Effectiveness of virtual reality in children and young adults with cerebral palsy: A systematic review of randomized controlled trial. *Brazilian Journal of Physical Therapy, 25*(4), 369–386. https://doi.org/10.1016/j.bjpt.2020.11.003

Fauconnier, J., Dickinson, H. O., Beckung, E., Marcelli, M., McManus, V., Michelsen, S. I., Parkes, J., Parkinson, K. N., Thyen, U., & Arnaud, C. (2009). Participation in life situations of 8-12 year old children with cerebral palsy: Cross sectional European study. *Bmj, 338*. https://doi.org/10.1136/bmj.b1458

Fazzi, E., Bova, S. M., Uggetti, C., Signorini, S. G., Bianchi, P. E., Maraucci, I., Zoppello, M., & Lanzi, G. (2004). Visual–perceptual impairment in children with periventricular leukomalacia. *Brain and Development, 26*(8), 506–512. https://doi.org/10.1016/j.braindev.2004.02.002

Fazzi, E., Maraucci, I., Torrielli, S., Motta, F., & Lanzi, G. (2005). Factors predicting the efficacy of botulinum toxin-A treatment of the lower limb in children with cerebral palsy. *Journal of Child Neurology, 20*(8), 661–666. https://doi.org/10.1177/08830738050200080501

Fazzi, E., Signorini, S. G., Bova, S. M., La Piana, R., Ondei, P., Bertone, C., Misefari, W., & Bianchi, P. E. (2007). Spectrum of visual disorders in children with cerebral visual impairment. *Journal of Child Neurology, 22*(3), 294–301. https://doi.org/10.1177/08830738070220030801

Findlay, B., Switzer, L., Narayanan, U., Chen, S., & Fehlings, D. (2016). Investigating the impact of pain, age, Gross Motor Function Classification System, and sex on health-related quality of life in children with cerebral palsy. *Developmental Medicine & Child Neurology, 58*(3), 292–297. https://doi.org/10.1111/dmcn.12936

Fisher, R. S., Acevedo, C., Arzimanoglou, A., Bogacz, A., Cross, J. H., Elger, C. E., Engel, J., Forsgren, L., French, J. A., Glynn, M., Hesdorffer, D. C., Lee, B. I. I., Mathern, G. W., Moshé, S. L., Perucca, E., Scheffer, I. E., Tomson, T., Watanabe, M., & Wiebe, S. (2014). ILAE Official Report: A practical clinical definition of epilepsy. *Epilepsia, 55*(4), 475–482. https://doi.org/10.1111/epi.12550

Fluss, J., & Lidzba, K. (2020). Cognitive and academic profiles in children with cerebral palsy: A narrative review. *Annals of Physical and Rehabilitation Medicine, 63*(5), 447–456. https://doi.org/10.1016/j.rehab.2020.01.005

Freire, T. C., & Osório, A. A. C. (2020). Executive functions and drawing in young children with cerebral palsy: Comparisons with typical development. *Child Neuropsychology, 26*(5), 635–648. https://doi.org/10.1080/09297049.2019.1694648

Freud, S. (1968). *Infantile cerebral paralysis*. University of Texas Press.

Gabis, L. V., Tsubary, N. M., Leon, O., Ashkenasi, A., & Shefer, S. (2015). Assessment of abilities and comorbidities in children with cerebral palsy. *Journal of Child Neurology, 30*(12), 1640–1645. https://doi.org/10.1177/0883073815576792

Gagliardi, C., Tavano, A., Turconi, A. C., Pozzoli, U., & Borgatti, R. (2011). Sequence learning in cerebral palsy. Pediatric Neurology, 44(3), 207–213. https://doi.org/10.1016/j.pediatrneurol.2010.10.004

Galetto, V., & Sacco, K. (2017). Neuroplastic Changes Induced by Cognitive Rehabilitation in Traumatic Brain Injury: A Review. *Neurorehabilitation and Neural Repair, 31*(9), 800–813. https://doi.org/10.1177/1545968317723748

García-Galant, M., Blasco, M., Laporta-Hoyos, O., Berenguer-González, A., Moral-Salicrú, P., Ballester-Plané, J., Caldú, X., Miralbell, J., Alonso, X., Medina-Cantillo, J., Povedano-Bulló, E., Leiva, D., Boyd, R. N., & Pueyo, R. (2023). A randomized controlled trial of a home-based computerized executive function intervention for children with cerebral palsy. *European Journal of Pediatrics*. https://doi.org/10.1007/s00431-023-05072-3

García-Galant, M., Blasco, M., Reid, L., Pannek, K., Leiva, D., Laporta-Hoyos, O., Ballester-Plané, J., Miralbell, J., Caldú, X., Alonso, X., Toro-Tamargo, E., Meléndez-Plumed, M., Gimeno, F., Coronas, M., Soro-Camats, E., Boyd, R., & Pueyo, R. (2020). Study protocol of a randomized controlled trial of home-based computerized executive function training for children with cerebral palsy. *BMC Pediatrics, 20*(1), 1–9. https://doi.org/10.1186/s12887-019-1904-x

García-Galant, M., Blasco, M., Moral-Salicrú, Soldevilla, J., Pueyo R., (*manuscript in preparation*). Social cognition in children with cerebral palsy: association with executive functions and improvements after intervention.

Garne, E., Dolk, H., Krägeloh-Mann, I., Ravn, S. H., Cans, C., & Group, S. C. (2008). Cerebral palsy and congenital malformations. *European Journal of Paediatric Neurology, 12*(2), 82–88. https://doi.org/10.1016/j.ejpn.2007.07.001

Gathercole, S. E., Pickering, S. J., Knight, C., & Stegmann, Z. (2004). Working memory skills and educational attainment: Evidence from national curriculum assessments at 7 and 14 years of age. *Applied Cognitive Psychology: The Official Journal of the Society for Applied Research in Memory and Cognition, 18*(1), 1–16. https://doi.org/10.1002/acp.934

Genolini, C., écochard, R., & Jacqmin-Gadda, H. (2013). Copy Mean: A New Method to Impute Intermittent Missing Values in Longitudinal Studies. *Open Journal of Statistics, 03*(04), 26–40. https://doi.org/10.4236/OJS.2013.34A004

Genolini, C., Lacombe, A., Écochard, R., & Subtil, F. (2016). CopyMean: A new method to predict monotone missing values in longitudinal studies. *Computer Methods and Programs in Biomedicine, 132*, 29–44. https://doi.org/10.1016/J.CMPB.2016.04.010

Gilson, K.-M., Davis, E., Reddihough, D., Graham, K., & Waters, E. (2014). Quality of life in children with cerebral palsy: Implications for practice. *Journal of Child Neurology, 29*(8), 1134–1140. https://doi.org/10.1177/0883073814535502

Gioia, G. A., Isquith, P. K., & Guy, S. C. (2001). Assessment of executive functions in children with neurological impairment. In *Psychological and developmental assessment: Children with disabilities and chronic conditions*. (pp. 317–356). The Guilford Press.

Gioia, G. A., Isquith, P. K., Guy, S. C., & Kenworthy, L. (2000). Test Review Behavior Rating Inventory of Executive Function. *Child Neuropsychology, 6*(3), 235–238. https://doi.org/10.1076/chin.6.3.235.3152

Giray, E., Şimşek, H. İ., Aydoğduoğlu, M., Kangal, A. Ç., Çelik, A., Kurt, C., & Saygı, E. K. (2018). Pain evaluation in a sample of Turkish children with cerebral palsy and its association with dependency level, verbal abilities, and the quality of life of patients and sociodemographic status, depression, and quality of life of their caregivers. *Turkish Journal of Physical Medicine & Rehabilitation, 64*(3), 222–229. https://doi.org/10.5606/tftrd.2018.1871

Goldsmith, S., McIntyre, S., Blair, E., Smithers-Sheedy, H., Badawi, N., & Hansen, M. (2023). Cerebral Palsy: Epidemiology. In *Neurodevelopmental Pediatrics: Genetic and Environmental Influences* (pp. 479–495). Springer.

Goldsmith, S., McIntyre, S., Hansen, M., & Badawi, N. (2019). Congenital anomalies in children with cerebral palsy: A systematic review. *Journal of Child Neurology, 34*(12), 720–727. https://doi.org/10.1177/0883073819854595

Goodman, R. (1997). The strengths and difficulties questionnaire: A research note. *Journal of Child Psychology and Psychiatry and Allied Disciplines, 38*(5), 581–586. https://doi.org/10.1111/j.1469-7610.1997.tb01545.x

Gosling, A. S. (2017). Recent advances in the neuroimaging and neuropsychology of cerebral palsy. *Applied Neuropsychology: Child, 6*(1), 55–63. https://doi.org/10.1080/21622965.2015.1074914

Gough, M., Shafafy, R., & Shortland, A. (2008). Does sex influence outcome in ambulant children with bilateral spastic cerebral palsy? *Developmental Medicine & Child Neurology, 50*(9), 702–705. https://doi.org/10.1111/j.1469-8749.2008.03038.x

Graham, H. K., Rosenbaum, P., Paneth, N., Dan, B., Lin, J. P., Damiano, D. L., Becher, J. G., Gaebler-Spira, D., Colver, A., Reddihough, D. S., Crompton, K. E., & Lieber, R. L. (2016). Cerebral palsy. *Nature reviews. Disease primers, 2*, 15082. https://doi.org/10.1038/nrdp.2015.82

Grassmann, V., Alves, M. V., Santos-Galduróz, R. F., & Galduróz, J. C. F. (2017). Possible cognitive benefits of acute physical exercise in children with ADHD: a systematic review. *Journal of Attention Disorders, 21*(5), 367–371. https://doi.org/10.1177/1087054714526041

Grunewaldt, K. H., Løhaugen, G. C. C., Austeng, D., Brubakk, A.-M., & Skranes, J. (2013). Working memory training improves cognitive function in VLBW preschoolers. *Pediatrics, 131*(3), e747–e754. https://doi.org/10.1542/peds.2012-1965

Grunewaldt, K. H., Skranes, J., Brubakk, A., & Lähaugen, G. C. C. (2016). Computerized working memory training has positive long-term effect in very low birthweight preschool children. *Developmental Medicine & Child Neurology, 58*(2), 195–201. https://doi.org/10.1111/dmcn.12841

Guindos-Sanchez, L. D., Lucena-Anton, D., Moral-Munoz, J. A., Salazar, A., & Carmona-Barrientos, I. (2020). The Effectiveness of Hippotherapy to Recover Gross Motor Function in Children with Cerebral Palsy: A Systematic Review and Meta-Analysis. *Children, 7*(9), 106. https://doi.org/10.3390/children7090106

Guo, W., Zang, M., Klich, S., Kawczyński, A., Smoter, M., & Wang, B. (2020). Effect of combined physical and cognitive interventions on executive functions in older adults: A meta-analysis of outcomes. *International Journal of Environmental Research and Public Health, 17*(17), 6166. https://doi.org/10.3390/ijerph17176166

Guyard, A., Fauconnier, J., Mermet, M. A., & Cans, C. (2010). Impact on parents of cerebral palsy in children: A literature review. *Archives de Pediatrie: Organe Officiel de La Societe Francaise de Pediatrie, 18*(2), 204–214. https://doi.org/10.1016/j.arcped.2010.11.008

Hahn-Markowitz, J., Berger, I., Manor, I., & Maeir, A. (2020). Efficacy of Cognitive-Functional (Cog-Fun) Occupational Therapy Intervention Among Children With ADHD: An RCT. *Journal of Attention Disorders, 24*(5), 655–666. https://doi.org/10.1177/1087054716666955

Harris, A. (2021). Quality of life in children with cerebral palsy: Don't forget to ask the child. *Developmental Medicine and Child Neurology, 63*(1), 9. https://doi.org/10.1111/dmcn.14727

Heathcock, J. C., Baranet, K., Ferrante, R., & Hendershot, S. (2015). Daily intervention for young children with cerebral palsy in GMFCS level V: a case series. *Pediatric Physical Therapy, 27*(3), 285–292. https://doi.org/10.1097/PEP.0000000000000149

Heydarian, S., Abbasabadi, M. M., Khabazkhoob, M., Hoseini-Yazdi, H., & Gharib, M. (2022). Vision Abnormalities in Children and Young Adults with Cerebral Palsy; A Systematic Review. *Seminars in Ophthalmology, 37*(4), 471–479. https://doi.org/10.1080/08820538.2021.2021248

Hidecker, M. J. C., Paneth, N., Rosenbaum, P. L., Kent, R. D., Lillie, J., Eulenberg, J. B., Chester, K., Johnson, B., Michalsen, L., Evatt, M., & Taylor, K. (2011). Developing and validating the Communication Function Classification System for individuals with cerebral palsy. *Developmental Medicine and Child Neurology, 53*(8), 704–710. https://doi.org/10.1111/j.1469-8749.2011.03996.x

Higgins, J., & Green, S. (2012). Manual Cochrane de Revisiones Sistemáticas de Intervenciones, versión 5.1. 0. *Manual Cochrane de Revisiones Sistemáticas de Intervenciones, Versión 5.1.0, 7*(3), 1–639.

Himmelmann, K., Ahlin, K., Jacobsson, B. O., Cans, C., & Thorsen, P. (2011). Risk factors for cerebral palsy in children born at term. *Acta Obstetricia et Gynecologica Scandinavica, 90*(10), 1070–1081. https://doi.org/10.1111/j.1600-0412.2011.01217.x

Himmelmann, K., Horber, V., De La Cruz, J., Horridge, K., Mejaski-Bosnjak, V., Hollody, K., Krägeloh-Mann, I., Group, S. W., Cans, C., & Bakel, V. (2017). MRI classification system (MRICS) for children with cerebral palsy: Development, reliability, and recommendations. *Developmental Medicine & Child Neurology, 59*(1), 57–64. https://doi.org/10.1111/dmcn.13166

Himmelmann, K., Horber, V., Sellier, E., De la Cruz, J., Papavasiliou, A., & Krägeloh-Mann, I. (2021). Neuroimaging patterns and function in cerebral palsy—Application of an MRI classification. *Frontiers in Neurology*, 1889. https://doi.org/10.3389/fneur.2020.617740

Himmelmann, K., & Sundh, V. (2015). Survival with cerebral palsy over five decades in western Sweden. *Developmental Medicine & Child Neurology, 57*(8), 762–767. https://doi.org/10.1111/dmcn.12718

Himmelmann, K., & Uvebrant, P. (2014). The panorama of cerebral palsy in Sweden. XI. Changing patterns in the birth-year period 2003–2006. *Acta Paediatrica, 103*(6), 618–624. https://doi.org/10.1111/apa.12614

Hoare, B., Imms, C., Carey, L., & Wasiak, J. (2007). Constraint-induced movement therapy in the treatment of the upper limb in children with hemiplegic cerebral palsy: A Cochrane systematic review. *Clinical Rehabilitation, 21*(8), 675–685. https://doi.org/10.1177/0269215507080783

Hoffman, L., Marquis, J., Poston, D., Summers, J. A., & Turnbull, A. (2006). Assessing family outcomes: Psychometric evaluation of the beach center family quality of life scale. *Journal of Marriage and Family, 68*(4), 1069–1083. https://doi.org/10.1111/j.1741-3737.2006.00314.x

Horber, V., Sellier, E., Horridge, K., Rackauskaite, G., Andersen, G. L., Virella, D., Ortibus, E., Dakovic, I., Hensey, O., Radsel, A., Papavasiliou, A., Cruz De la, J., Arnaud, C., Krägeloh-Mann, I., & Himmelmann,

K. (2020). The Origin of the Cerebral Palsies: Contribution of Population-Based Neuroimaging Data. *Neuropediatrics, 51*(2), 113–119. https://doi.org/10.1055/s-0039-3402007

Hrabok, M., Sherman, E. M. S., Bello-Espinosa, L., & Hader, W. (2013). Memory and health-related quality of life in severe pediatric epilepsy. *Pediatrics, 131*(2), e525–e532. https://doi.org/10.1542/peds.2012-1428

Hsieh, Y., Yang, C., Sun, S., Chan, S., Wang, T., & Luo, H. (2017). Effects of hippotherapy on body functions, activities and participation in children with cerebral palsy based on ICF-CY assessments. *Disability and Rehabilitation,* 39(17), 1703–1713. https://doi.org/10.1080/09638288.2016.1207108

Hutton, J. L., & Pharoah, P. O. D. (2002). Effects of cognitive, motor, and sensory disabilities on survival in cerebral palsy. *Archives of Disease in Childhood, 86*(2), 84–89. https://doi.org/10.1136/adc.86.2.84

Jacobs, N. P. T., Pouwels, P. J. W., van Der Krogt, M. M., Meyns, P., Zhu, K., Nelissen, L., Schoonmade, L. J., Buizer, A. I., & van de Pol, L. A. (2023). Brain structural and functional connectivity and network organization in cerebral palsy: A scoping review. *Developmental Medicine & Child Neurology*. https://doi.org/10.1111/dmcn.15516

Jacobsson, B., & Hagberg, G. (2004). Antenatal risk factors for cerebral palsy. *Best Practice & Research Clinical Obstetrics & Gynaecology, 18*(3), 425–436. https://doi.org/10.1016/j.bpobgyn.2004.02.011

Jahan, I., Muhit, M., Hardianto, D., Laryea, F., Chhetri, A. B., Smithers-Sheedy, H., McIntyre, S., Badawi, N., & Khandaker, G. (2021). Epidemiology of cerebral palsy in low-and middle-income countries: Preliminary findings from an international multi-centre cerebral palsy register. *Developmental Medicine & Child Neurology, 63*(11), 1327–1336. https://doi.org/10.1111/dmcn.14926

James, S., Ziviani, J., Ware, R. S., & Boyd, R. N. (2015a). Relationships between activities of daily living, upper limb function, and visual perception in children and adolescents with unilateral cerebral palsy. *Developmental Medicine & Child Neurology, 57*(9), 852–857. https://doi.org/10.1111/DMCN.12715

James, S., Ziviani, J., Ware, R. S., & Boyd, R. N. (2015b). Randomized controlled trial of web-based multimodal therapy for unilateral cerebral palsy to improve occupational performance. *Developmental Medicine & Child Neurology, 57*(6), 530–538. https://doi.org/10.1111/dmcn.12705

Jiang, B., Walstab, J., Reid, S. M., Davis, E., & Reddihough, D. (2016). Quality of life in young adults with cerebral palsy. *Disability and Health Journal,* 9(4), 673–681. https://doi.org/10.1016/j.dhjo.2016.04.006

Jonsson, U., Eek, M. N., Sunnerhagen, K. S., & Himmelmann, K. (2019). Cerebral palsy prevalence, subtypes, and associated impairments: A population-based comparison study of adults and children. *Developmental Medicine & Child Neurology, 61*(10), 1162–1167. https://doi.org/10.1111/dmcn.14229

Kakooza-Mwesige, A., Andrews, C., Peterson, S., Mangen, F. W., Eliasson, A. C., & Forssberg, H. (2017). Prevalence of cerebral palsy in Uganda: A population-based study. *The Lancet Global Health, 5*(12), e1275–e1282. https://doi.org/10.1016/S2214-109X(17)30374-1

Kassai, R., Futo, J., Demetrovics, Z., & Takacs, Z. K. (2019). A meta-analysis of the experimental evidence on the near- and far-transfer effects among children's executive function skills. *Psychological Bulletin, 145*(2), 165–188. https://doi.org/10.1037/bul0000180

Khandaker, G., Muhit, M., Karim, T., Smithers-Sheedy, H., Novak, I., Jones, C., & Badawi, N. (2019). Epidemiology of cerebral palsy in Bangladesh: A population-based surveillance study. Developmental Medicine & Child Neurology, 61(5), 601–609. https://doi.org/10.1111/dmcn.14013

Kim, H. S., Steinbok, P., & Wickenheiser, D. (2006). Predictors of poor outcome after selective dorsal rhizotomy in treatment of spastic cerebral palsy. *Child's Nervous System, 22*, 60–66. https://doi.org/10.1007/s00381-005-1160-2

Kim, S., Nordling, J. K., Yoon, J. E., Boldt, L. J., & Kochanska, G. (2013). Effortful control in "hot" and "cool" tasks differentially *predicts children's behavior problems and academic performance. Journal* of Abnormal Child Psychology, 41, 43–56. https://doi.org/10.1007/s10802-012-9661-4

Klawonn, M. A., Klamar, K., & Turk, M. A. (2020). Trends in publications about cerebral palsy 1990 to 2020. *Journal of Pediatric Rehabilitation Medicine, 13*(2), 107–117. https://doi.org/10.3233/PRM-200697

Klingberg, T., Forssberg, H., & Westerberg, H. (2002). Training of working memory in children with ADHD. *Journal of Clinical and Experimental Neuropsychology, 24*(6), 781–791. https://doi.org/10.1076/jcen.24.6.781.8395

Korkman, M., Kirk, U., & Kemp, S. (2014). *NEPSY-II*. Pearson.

Korzeniewski, S. J., Slaughter, J., Lenski, M., Haak, P., & Paneth, N. (2018). The complex aetiology of cerebral palsy. *Nature Reviews Neurology, 14*(9), 528–543. https://doi.org/10.1038/s41582-018-0043-6

Koščak Tivadar, B. (2017). Physical activity improves cognition: Possible explanations. *Biogerontology, 18*(4), 477–483. https://doi.org/10.1007/s10522-017-9708-

Krigger, K. W. (2006). Cerebral palsy: An overview. *American Family Physician, 73*(1), 91–100.

Krivitzky, L., Bosenbark, D. D., Ichord, R., Jastrzab, L., & Billinghurst, L. (2019). Brief report: Relationship between performance testing and parent report of attention and executive functioning profiles in children following perinatal arterial ischemic stroke. *Child Neuropsychology, 25*(8), 1116–1124. https://doi.org/10.1080/09297049.2019.1588957

Lakes, K. D., Sharp, K., Grant-Beuttler, M., Neville, R., Haddad, F., Sunico, R., Ho, D., Schneider, M., Sawitz, S., Paulsen, J., Caputo, K., Lu, K. D., Aminian, A., López-Ortiz, C., & Radom-Aizik, S. (2019). A six week therapeutic ballet intervention improved gait and inhibitory control in children with cerebral palsy-A pilot study. *Frontiers in Public Health, 7*, 137. https://doi.org/10.3389/fpubh.2019.00137

Landgraf, J. M. (2020). Child health questionnaire (CHQ). In *Encyclopedia of quality of life and well-being research (pp. 1–6)*. Springer.

Laporta-Hoyos, O., Ballester-Plané, J., Leiva, D., Ribas, T., Miralbell, J., Torroja-Nualart, C., Russi, M. E., Toro-Tamargo, E., Meléndez-Plumed, M., Gimeno, F., Macaya, A., & Pueyo, R. (2019). Executive function and general intellectual functioning in dyskinetic cerebral palsy: Comparison with spastic cerebral palsy and typically developing controls. *European Journal of Paediatric Neurology, 23*(4), 546–559. https://doi.org/10.1016/j.ejpn.2019.05.010

Laporta-Hoyos, O., Ballester-Plané, J., Póo, P., Macaya, A., Meléndez-Plumed, M., Vázquez, E., Delgado, I., Zubiaurre-Elorza, L., Botellero, V. L., Narberhaus, A., Toro-Tamargo, E., Segarra, D., & Pueyo, R. (2017). Proxy-reported quality of life in adolescents and adults with dyskinetic cerebral palsy is associated with executive functions and cortical thickness. *Quality of Life Research, 26*(5), 1209–1222. https://doi.org/10.1007/s11136-016-1433-0

Larsen, M. L., Rackauskaite, G., Greisen, G., Laursen, B., Uldall, P., Krebs, L., & Hoei-Hansen, C. E. (2022). Declining prevalence of cerebral palsy in children born at term in Denmark. *Developmental Medicine & Child Neurology, 64*(6), 715–722. https://doi.org/10.1111/dmcn.15136

Law, M. (2002). Participation in the occupations of everyday life. *The American Journal of Occupational Therapy, 56*(6), 640–649. https://doi.org/10.5014/ajot.56.6.640

Lee, J. K., Ekstrom, A. D., & Ghetti, S. (2014). Volume of hippocampal subfields and episodic memory in childhood and adolescence. *NeuroImage, 94*, 162–171. https://doi.org/10.1016/j.neuroimage.2014.03.019

Lélis, A. L. P. A., Cardoso, M. V. L. M., & Hall, W. A. (2016). Sleep disorders in children with cerebral palsy: An integrative review. *Sleep Medicine Reviews, 30*, 63–71. https://doi.org/10.1016/j.smrv.2015.11.008

Lezak, M. D., Howieson, D. B., Loring, D. W., & Fischer, J. S. (2004). *Neuropsychological assessment*. Oxford University Press, USA.

Li, X., Wang, K., Wu, J., Hong, Y., Zhao, J., Feng, X., Xu, M., Wang, M., Ndasauka, Y., & Zhang, X. (2014). The link between impaired theory of mind and executive function in children with cerebral palsy. *Research in Developmental Disabilities, 35*(7), 1686–1693. https://doi.org/10.1016/j.ridd.2014.03.017

Liang, X., Li, R., Wong, S. H. S., Sum, R. K. W., & Sit, C. H. P. (2021). The impact of exercise interventions concerning executive functions of children and adolescents with attention-deficit/hyperactive disorder: A systematic review and meta-analysis. *International Journal of Behavioral Nutrition and Physical Activity, 18*(1), 68. https://doi.org/10.1186/s12966-021-01135-6

Liang, X., Li, R., Wong, S. H. S., Sum, R. K. W., Wang, P., Yang, B., & Sit, C. H. P. (2022). The effects of exercise interventions on executive functions in children and adolescents with autism spectrum disorder: A systematic review and meta-analysis. Sports Medicine, 52(1), 75–88. https://doi.org/10.1007/s40279-021-01545-3

Lins, A. A., de Oliveira, J. M., Rodrigues, J. J., & de Albuquerque, V. H. C. (2019). Robot-assisted therapy for rehabilitation of children with cerebral palsy-a complementary and alternative approach. Computers in Human Behavior, 100, 152–167. https://doi.org/10.1016/j.chb.2018.05.012

Little W.J. Courses of lectures on the "Deformities of the Human Frame." Lancet.1843–44;1:5–7;38–44;70–74;209–12;230–33;257–60;290–93;318–20;346–9;350–54

Liu, W.-Y., Hou, Y.-J., Wong, A. M. K., Lin, P.-S., Lin, Y.-H., & Chen, C.-L. (2009). Relationships between gross motor functions and health-related quality of life of Taiwanese children with cerebral palsy. American Journal of Physical Medicine & Rehabilitation, 88(6), 473–483. https://doi.org/10.1097/PHM.0b013e3181a0de3a

Llamas-Ramos, R., Sánchez-González, J. L., & Llamas-Ramos, I. (2022). Robotic Systems for the Physiotherapy Treatment of Children with Cerebral Palsy: A Systematic Review. International Journal of Environmental Research and Public Health, 19(9), 5116. https://doi.org/10.3390/ijerph19095116

Løhaugen, G. C. C., Antonsen, I., Håberg, A., Gramstad, A., Vik, T., Brubakk, A.-M., & Skranes, J. (2011). Computerized working memory training improves function in adolescents born at extremely low birth weight. The Journal of Pediatrics, 158(4), 555–561. https://doi.org/10.1016/j.jpeds.2010.09.060

López-Ortiz, C., Gaebler-Spira, D. J., Mckeeman, S. N., Mcnish, R. N., & Green, D. (2019). Dance and rehabilitation in cerebral palsy: A systematic search and review. Developmental Medicine & Child Neurology, 61(4), 393–398. https://doi.org/10.1111/dmcn.14064

Love, C. E., Webbe, F., Kim, G., Lee, K. H., Westerveld, M., & Salinas, C. M. (2016). The role of executive functioning in quality of life in pediatric intractable epilepsy. Epilepsy & Behavior, 64, 37–43. https://doi.org/10.1016/j.yebeh.2016.08.018

Luis-Ruiz, S., Caldu, X., Sanchez-Castaneda, C., Pueyo, R., Garolera, M., & Jurado, M. Á. (2020). Is cognitive training an effective tool for improving cognitive function and real-life behaviour in healthy children and adolescents? A systematic review. Neuroscience & Biobehavioral Reviews, 116, 268–282. https://doi.org/10.1016/j.neubiorev.2020.06.019

Macintyre-Beon, C., Young, D., Calvert, J., Ibrahim, H., Dutton, G. N., & Bowman, R. (2012). Reliability of a question inventory for structured history taking in children with cerebral visual impairment. Eye, 26(10), 1393. https://doi.org/10.1038/eye.2012.154

MacLennan, A. H., Thompson, S. C., & Gecz, J. (2015). Cerebral palsy: Causes, pathways, and the role of genetic variants. American Journal of Obstetrics and Gynecology, 213(6), 779–788. https://doi.org/10.1016/j.ajog.2015.05.034

Majnemer, A., & Mazer, B. (2004). New directions in the outcome evaluation of children with cerebral palsy. Seminars in Pediatric Neurology, 11(1), 11–17. https://doi.org/10.1016/j.spen.2004.01.003

Majnemer, A., Shevell, M., Rosenbaum, P., Law, M., & Poulin, C. (2007). Determinants of life quality in school-age children with cerebral palsy. The Journal of Pediatrics, 151(5), 470–475. https://doi.org/10.1016/j.jpeds.2007.04.014

Mak, C., Whittingham, K., Cunnington, R., & Boyd, R. N. (2018). Effect of mindfulness yoga programme MiYoga on attention, behaviour, and physical outcomes in cerebral palsy: A randomized controlled trial. *Developmental Medicine and Child Neurology, 60*(9), 922–932. https://doi.org/10.1111/dmcn.13923

Mak, C., Whittingham, K., Cunnington, R., Chatfield, M., & Boyd, R. N. (2020). Six-month follow-up of a mindfulness yoga program, MiYoga, on attention, executive function, behaviour and physical outcomes in cerebral palsy. *Disability and Rehabilitation*, *44*(6), 966-972. https://doi.org/10.1080/09638288.2020.1783582

Makris, T., Dorstyn, D., & Crettenden, A. (2021). Quality of life in children and adolescents with cerebral palsy: A systematic review with meta-analysis. *Disability and Rehabilitation, 43*(3), 299–308. https://doi.org/10.1080/09638288.2019.1623852

Martin, N. A., & Gardner, M. F. (2006). *Test of visual perceptual skills*. Academic Therapy Publications Novato, CA.

Martiny, K. M., & Aggerholm, K. (2016). Embodying cognition: Working with self-control in cerebral palsy. The Cognitive Behaviour Therapist, 9, e33. https://doi.org/10.1017/S1754470X16000192

McManus, V., Corcoran, P., & Perry, I. J. (2008). Participation in everyday activities and quality of life in pre-teenage children living with cerebral palsy in South West Ireland. BMC Pediatrics, 8, 1–10. https://doi.org/10.1186/1471-2431-8-50

McGinley, J. L., Dobson, F., Ganeshalingam, R., Shore, B. J., Rutz, E., & Graham, H. K. (2012). Single-event multilevel surgery for children with cerebral palsy: A systematic review. Developmental Medicine & Child Neurology, 54(2), 117–128. https://doi.org/10.1111/j.1469-8749.2011.04143.x

McIntyre, S., Goldsmith, S., Webb, A., Ehlinger, V., Hollung, S. J., McConnell, K., Arnaud, C., Smithers-Sheedy, H., Oskoui, M., & Khandaker, G. (2022). Global prevalence of cerebral palsy: A systematic analysis. Developmental Medicine & Child Neurology, 64(12), 1494–1506. https://doi.org/10.1111/dmcn.15346

McIntyre, S., Taitz, D., Keogh, J., Goldsmith, S., Badawi, N., & Blair, E. V. E. (2013). A systematic review of risk factors for cerebral palsy in children born at term in developed countries. Developmental Medicine & Child Neurology, 55(6), 499–508. https://doi.org/10.1111/dmcn.12017

McKillop, E., Bennett, D., McDaid, G., Holland, B., Smith, G., Spowart, K., & Dutton, G. (2006). Problems experienced by children with cognitive visual dysfunction due to cerebral visual impairment – and the approaches which parents have adopted to deal with these problems. British Journal of Visual Impairment, 24(3), 121–127. https://doi.org/10.1177/0264619606066186

Medios EG. de Asociación para la Investigacion de Medios de Comunicacion. http://www.aimc.es/egm/audiencia-internet-egm/.

Mei, C., Reilly, S., Bickerton, M., Mensah, F., Turner, S., Kumaranayagam, D., Pennington, L., Reddihough, D., & Morgan, A. T. (2020). Speech in children with cerebral palsy. *Developmental Medicine & Child Neurology, 62*(12), 1374–1382. https://doi.org/10.1111/dmcn.14592

Mei, C., Reilly, S., Reddihough, D., Mensah, F., Pennington, L., & Morgan, A. (2016). Language outcomes of children with cerebral palsy aged 5 years and 6 years: A population-based study. *Developmental Medicine & Child Neurology, 58*(6), 605–611. https://doi.org/10.1111/dmcn.12957

Melby-Lervåg, M., & Hulme, C. (2013). Is working memory training effective? A meta-analytic review. Developmental Psychology, 49(2), 270–291. https://doi.org/10.1037/a0028228

Melby-Lervåg, M., Redick, T. S., & Hulme, C. (2016). Working Memory Training Does Not Improve Performance on Measures of Intelligence or Other Measures of 'Far Transfer': Evidence From a Meta-Analytic Review. Perspectives on Psychological Science: *A Journal of the Association for Psychological Science, 11*(4), 512–534. https://doi.org/10.1177/1745691616635612

Michael-Asalu, A., Taylor, G., Campbell, H., Lelea, L.-L., & Kirby, R. S. (2019). Cerebral palsy: Diagnosis, epidemiology, genetics, and clinical update. *Advances in Pediatrics, 66*, 189–208. https://doi.org/10.1016/j.yapd.2019.04.002

Mitry, D., Williams, C., Northstone, K., Akter, A., Jewel, J., Khan, N., Muhit, M., Gilbert, C. E., & Bowman, R. (2016). Perceptual visual dysfunction, physical impairment and quality of life in Bangladeshi children with cerebral palsy. *British Journal of Ophthalmology, 100*(9), 1245–1250. https://doi.org/10.1136/bjophthalmol-2015-307296

Modi, A. C., Mara, C. A., Schmidt, M., Smith, A. W., Turnier, L., & Wade, S. L. (2021). Pilot Executive Functioning Intervention in Epilepsy: Behavioral and Quality of Life Outcomes. *Journal of Pediatric Psychology, 46*(4), 363–374. https://doi.org/10.1093/jpepsy/jsaa119

Moher, D., Schulz, K. F., & Altman, D. G. (2001). The CONSORT statement: Revised recommendations for improving the quality of reports of parallel-group randomised trials. *The Lancet, 357*(9263), 1191–1194.

Moher, D., Shamseer, L., Clarke, M., Ghersi, D., Liberati, A., Petticrew, M., Shekelle, P., Stewart, L. A., Estarli, M., Barrera, E. S. A., Martínez-Rodríguez, R., Baladia, E., Agüero, S. D., Camacho, S., Buhring, K., Herrero-López, A., Gil-González, D. M., Altman, D. G., Booth, A., … Whitlock, E. (2015). Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews, 4*(1). https://doi.org/10.1186/2046-4053-4-1

Montoro-Cárdenas, D., Cortés-Pérez, I., Zagalaz-Anula, N., Osuna-Pérez, M. C., Obrero-Gaitán, E., & Lomas-Vega, R. (2021). Nintendo Wii Balance Board therapy for postural control in children with cerebral palsy: A systematic review and meta-analysis. *Developmental Medicine & Child Neurology, 63*(11), 1262–1275. https://doi.org/10.1111/dmcn.14947

Mora-Gonzalez, J., Esteban-Cornejo, I., Cadenas-Sanchez, C., Migueles, J. H., Molina-Garcia, P., Rodriguez-Ayllon, M., Henriksson, P., Pontifex, M. B., Catena, A., & Ortega, F. B. (2019). Physical fitness, physical activity, and the executive function in children with overweight and obesity. *The Journal of Pediatrics, 208*, 50–56. https://doi.org/10.1016/j.jpeds.2018.12.028

Morgan, C., Darrah, J., Gordon, A. M., Harbourne, R., Spittle, A., Johnson, R., & Fetters, L. (2016a). Effectiveness of motor interventions in infants with cerebral palsy: A systematic review. *Developmental Medicine & Child Neurology, 58*(9), 900–909. https://doi.org/10.1111/dmcn.13105

Morgan, C., Novak, I., Dale, R. C., Guzzetta, A., & Badawi, N. (2016b). Single blind randomised controlled trial of GAME (Goals—Activity—Motor Enrichment) in infants at high risk of cerebral palsy. *Research in Developmental Disabilities, 55*, 256–267. https://doi.org/10.1016/j.ridd.2016.04.005

Morris, S. B. (2008). Estimating effect sizes from pretest-posttest-control group designs. *Organizational Research Methods, 11*(2), 364–386. https://doi.org/10.1177/1094428106291059

Morris, S. B., & DeShon, R. P. (2002). Combining effect size estimates in meta-analysis with repeated measures and independent-groups designs. *Psychological Methods, 7*(1), 105. https://doi.org/10.1037/1082-989x.7.1.105

Murias, K., Brooks, B., Kirton, A., & Iaria, G. (2014). A review of cognitive outcomes in children following perinatal stroke. *Developmental Neuropsychology, 39*(2), 131–157. https://doi.org/10.1080/87565641.2013.870178

Muriel, V., García-Molina, A., Aparicio-López, C., Enseñat, A., & Roig-Rovira, T. (2014). Estimulación cognitiva en niños con parálisis cerebral. *Rev. Neurol. (Ed. Impr.), 59*(10), 443–448. PMID: 25354506

Myrhaug, H., Østensjø, S., Larun, L., Odgaard-Jensen, J., & Jahnsen, R. (2015). Intensive training of motor function and functional skills among young children with cerebral palsy: A systematic review and meta-analysis. *BMC Pediatrics,* 1–19. https://doi.org/10.1186/s12887-014-0292-5

Noreau, L., Desrosiers, J., Robichaud, L., Fougeyrollas, P., Rochette, A., & Viscogliosi, C. (2004). Measuring social participation: Reliability of the LIFE-H in older adults with disabilities. *Disability and Rehabilitation, 26*(6), 346–352. https://doi.org/10.1080/09638280410001658649

Noten, S., Selb, M., Troenosemito, L. A. A., Thorpe, D. E., Rodby-Bousquet, E., van der Slot, W. M. A., Roebroeck, M. E., & ICF Core Set for Adults with CP Consensus Group (2022). ICF Core Sets for the assessment of functioning of adults with cerebral palsy. *Developmental medicine and child neurology, 64*(5), 569–577. https://doi.org/10.1111/dmcn.15104

Novak, I., Cusick, A., & Lannin, N. (2009). Occupational Therapy Home Programs for Cerebral Palsy: Double-Blind, Randomized, Controlled Trial. *Pediatrics, 124*(4), e606–e614. https://doi.org/10.1542/peds.2009-0288

Novak, I., Hines, M., Goldsmith, S., & Barclay, R. (2012). Clinical prognostic messages from a systematic review on cerebral palsy. *Pediatrics, 130*(5), e1285–e1312. https://doi.org/10.1542/peds.2012-0924

Novak, I., Mcintyre, S., Morgan, C., Campbell, L., Dark, L., Morton, N., Stumbles, E., Wilson, S. A., & Goldsmith, S. (2013). A systematic review of interventions for children with cerebral palsy: State of the evidence. *Developmental Medicine and Child Neurology, 55*(10), 885–910. https://doi.org/10.1111/dmcn.12246

Novak, I., Morgan, C., Fahey, M., Finch-Edmondson, M., Galea, C., Hines, A., Langdon, K., Namara, M. M., Paton, M. C. B., & Popat, H. (2020). State of the evidence traffic lights 2019: Systematic review of interventions for preventing and treating children with cerebral palsy. *Current Neurology and Neuroscience Reports, 20(*2), 1–21. https://doi.org/10.1007/s11910-020-1022-z

OCEBM Levels of Evidence Working Group. (2011). The Oxford 2011 Levels of Evidence.

O'Connell, N. E., Smith, K. J., Peterson, M. D., Ryan, N., Liverani, S., Anokye, N., Victor, C., & Ryan, J. M. (2019). Incidence of osteoarthritis, osteoporosis and inflammatory musculoskeletal diseases in adults with cerebral palsy: A population-based cohort study. *Bone, 125*, 30–35. https://doi.org/10.1016/j.bone.2019.05.007

Odding, E., Roebroeck, M. E., & Stam, H. J. (2006). The epidemiology of cerebral palsy: Incidence, impairments and risk factors. *Disability and Rehabilitation, 28*(4), 183–191. https://doi.org/10.1080/09638280500158422

Ofen, N. (2012). The development of neural correlates for memory formation. *Neuroscience & Biobehavioral Reviews, 36*(7), 1708–1717. https://doi.org/10.1016/j.neubiorev.2012.02.016

Oldrati, V., Corti, C., Poggi, G., Borgatti, R., Urgesi, C., & Bardoni, A. (2020). Effectiveness of Computerized Cognitive Training Programs (CCTP) with game-like features in children with or without neuropsychological disorders: A meta-analytic investigation. *Neuropsychology Review, 30*(1), 126–141. https://doi.org/10.1007/s11065-020-09429-5

Omura, J., Fuentes, M., & Bjornson, K. (2018). Participation in Daily Life: Influence on Quality of Life in Ambulatory Children with Cerebral Palsy. *PM and R, 10*(11), 1185–1191. https://doi.org/10.1016/j.pmrj.2018.05.010

Ortibus, E., Fazzi, E., & Dale, N. (2019). Cerebral Visual Impairment and Clinical Assessment: The European Perspective. Seminars in Pediatric Neurology, 31, 15–24. https://doi.org/10.1016/j.spen.2019.05.004

Oskoui, M., Coutinho, F., Dykeman, J., Jette, N., & Pringsheim, T. (2013). An update on the prevalence of cerebral palsy: A systematic review and meta-analysis. *Developmental Medicine & Child Neurology, 55*(6), 509–519. https://doi.org/10.1111/dmcn.12080

Osler, W. (1889a) *Cerebral palsies of children*. Mac Keith Presss.

Osler, W. (1889b). *The cerebral palsies of children: A clinical study from the infirmary for nervous diseases*, Philadelphia.

Østensjø, S., Carlberg, E. B., & Vøllestad, N. K. (2003). Everyday functioning in young children with cerebral palsy: Functional skills, caregiver assistance, and modifications of the environment. *Developmental Medicine and Child Neurology, 45*(9), 603–612. https://doi.org/10.1017/S0012162203001105

Ozkan, Y. (2018). Child's quality of life and mother's burden in spastic cerebral palsy: A topographical classification perspective. *Journal of International Medical Research, 46*(8), 3131–3137. https://doi.org/10.1177/0300060518772758

Pagliano, E., Fedrizzi, E., Erbetta, A., Bulgheroni, S., Solari, A., Bono, R., Fazzi, E., Andreucci, E., & Riva, D. (2007). Cognitive profiles and visuoperceptual abilities in preterm and term spastic diplegic children with periventricular leukomalacia. *Journal of Child Neurology, 22*(3), 282–288. https://doi.org/10.1177/0883073807300529

Påhlman, M., Gillberg, C., & Himmelmann, K. (2019). One-third of school-aged children with cerebral palsy have neuropsychiatric impairments in a population-based study. *Acta Paediatrica, 108*(11), 2048–2055. https://doi.org/10.1111/apa.14844

Påhlman, M., Gillberg, C., & Himmelmann, K. (2021). Autism and attention-deficit/hyperactivity disorder in children with cerebral palsy: High prevalence rates in a population-based study. *Developmental Medicine & Child Neurology, 63*(3), 320–327. https://doi.org/10.1111/dmcn.14736

Palisano, R. J., Rosenbaum, P., Bartlett, D., & Livingston, M. H. (2008). Content validity of the expanded and revised Gross Motor Function Classification System. *Developmental Medicine & Child Neurology, 50*(10), 744–750. https://doi.org/10.1111/j.1469-8749.2008.03089.x

Paneth, N., & Yeargin-Allsopp, M. (2022). Thinking about differences in the worldwide prevalence of cerebral palsy. *Developmental Medicine and Child Neurology, 64*(12), 436. https://doi.org/10.1111/dmcn.15361

Panteliadis, C., Panteliadis, P., & Vassilyadi, F. (2013). Hallmarks in the history of cerebral palsy: From antiquity to mid-20th century. *Brain and Development, 35*(4), 285–292. https://doi.org/10.1016/j.braindev.2012.05.003

Park, E. Y. (2017). Relationship between activity limitation and health-related quality of life in school-aged children with cerebral palsy: A cross-sectional study. *Health and Quality of Life Outcomes, 15*(1), 1–7. https://doi.org/10.1186/s12955-017-0650-8

Park, J.-H., & Park, J.-H. (2015). A randomized controlled trial of the computer-based cognitive rehabilitation program for children (CoTras-C) to examine cognitive function and visual perception in children with developmental disabilities. *Journal of Physical Therapy Science, 27*(12), 3623–3626. https://doi.org/10.1589/jpts.27.3623

Parkes, J., White-Koning, M., Dickinson, H. O., Thyen, U., Arnaud, C., Beckung, E., Fauconnier, J., Marcelli, M., McManus, V., & Michelsen, S. I. (2008). Psychological problems in children with cerebral palsy: A cross-sectional European study. *Journal of Child Psychology and Psychiatry, 49*(4), 405–413. https://doi.org/10.1111/j.1469-7610.2007.01845.x

Pasqualotto, A., Mazzoni, N., Bentenuto, A., Mulè, A., Benso, F., & Venuti, P. (2021). Effects of cognitive training programs on executive function in children and adolescents with autism spectrum disorder: A systematic review. *Brain Sciences, 11*(10), 1280. https://doi.org/10.3390/brainsci11101280

Paul, B., Appelbaum, M., Carapetian, S., Hesselink, J., Nass, R., Trauner, D., & Stiles, J. (2014). Face and location processing in children with early unilateral brain injury. *Brain and Cognition, 88*, 6–13. https://doi.org/10.1016/j.bandc.2014.03.003

Paul, S., Nahar, A., Bhagawati, M., & Kunwar, A. J. (2022). A Review on Recent Advances of Cerebral Palsy. *Oxidative Medicine and Cellular Longevity*. https://doi.org/10.1155/2022/2622310

Pavone, P., Gulizia, C., Le Pira, A., Greco, F., Parisi, P., Di Cara, G., Falsaperla, R., Lubrano, R., Minardi, C., & Spalice, A. (2020). Cerebral palsy and epilepsy in children: Clinical perspectives on a common comorbidity. *Children, 8*(1), 16 https://doi.org/10.3390/children8010016

Pennington, L., Virella, D., Mjøen, T., da Graça Andrada, M., Murray, J., Colver, A., Himmelmann, K., Rackauskaite, G., Greitane, A., Prasauskiene, A., Andersen, G., & de la Cruz, J. (2013). Development of The Viking Speech Scale to classify the speech of children with cerebral palsy. *Research in Developmental Disabilities, 34*(10), 3202–3210. https://doi.org/10.1016/j.ridd.2013.06.035

Peny-Dahlstrand, M., Bergqvist, L., Hofgren, C., Himmelmann, K., & Öhrvall, A. M. (2018). Potential benefits of the cognitive orientation to daily occupational performance approach in young adults with spina bifida or cerebral palsy: A feasibility study. *Disability and Rehabilitation, 42*(2), 228–239. https://doi.org/10.1080/09638288.2018.1496152

Pereira, A., Lopes, S., Magalhães, P., Sampaio, A., Chaleta, E., & Rosário, P. (2018). How Executive Functions Are Evaluated in Children and Adolescents with Cerebral Palsy? A Systematic Review. *Frontiers in Psychology, 9*, 21. https://doi.org/10.3389/fpsyg.2018.00021

Pereira, A., Rosário, P., Lopes, S., Moreira, T., Magalhães, P., Núñez, J. C., Vallejo, G., & Sampaio, A. (2019). Promoting school engagement in children with cerebral palsy: A narrative based program. *International Journal of Environmental Research and Public Health, 16*(19). https://doi.org/10.3390/ijerph16193634

Phelps, W. M. (1941). The management of the cerebral palsies. *Journal of the American Medical Association, 117*(19), 1621–1625. https://doi.org/10.1001/jama.1941.72820450003012

Philip, S. S., & Dutton, G. N. (2014). Identifying and characterising cerebral visual impairment in children: A review. *Clinical and Experimental Optometry, 97*(3), 196–208. https://doi.org/10.1111/cxo.12155

Pino Muñoz, M., & Arán Filippetti, V. (2021). Confirmatory Factor Analysis of the BRIEF-2 Parent and Teacher Form: Relationship to Performance-Based Measures of Executive Functions and Academic Achievement. *Applied Neuropsychology: Child, 10*(3), 219–233. https://doi.org/10.1080/21622965.2019.1660984

Piovesana, A. M., Ross, S., Lloyd, O., Whittingham, K., Ziviani, J., Ware, R. S., & Boyd, R. N. (2017). Randomized controlled trial of a web-based multi-modal therapy program for executive functioning in children and adolescents with unilateral cerebral palsy. *Disability & Rehabilitation, 39*(21), 2021–2028. https://doi.org/10.1080/09638288.2016.1213899

Piovesana, A. M., Ross, S., Whittingham, K., Ware, R. S., & Boyd, R. N. (2015). Stability of executive functioning measures in 8–17-year-old children with unilateral cerebral palsy. *The Clinical Neuropsychologist, 29*(1), 133–149. https://doi.org/10.1080/13854046.2014.999125

Pirila, S., van der Meere, J. J., Rantanen, K., Jokiluoma, M., & Eriksson, K. (2011). Executive functions in youth with spastic cerebral palsy. Journal of Child Neurology, 26(7), 817–821. https://doi.org/10.1177/0883073810392584

Pirila, S., Van der Meere, J., Korhonen, P., Ruusu-Niemi, P., Kyntaja, M., Nieminen, P., & Korpela, R. (2004). A retrospective neurocognitive study in children with spastic diplegia. *Developmental Neuropsychology, 26*(3), 679–690. https://doi.org/10.1207/s15326942dn2603_2

Pirila, S., van der Meere, J., Pentikainen, T., Ruusu-Niemi, P., Korpela, R., Kilpinen, J., & Nieminen, P. (2007). Language and motor speech skills in children with cerebral palsy. *Journal of Communication Disorders, 40*(2), 116–128. https://doi.org/10.1016/j.jcomdis.2006.06.002

Poon, K. W., Li-Tsang, C. W. P., Weiss, T. P. L., & Rosenblum, S. (2010). The effect of a computerized visual perception and visual-motor integration training program on improving Chinese handwriting of children with handwriting difficulties. *Research in Developmental Disabilities, 31*(6), 1552–1560. https://doi.org/10.1016/j.ridd.2010.06.001

Powell, K. B., & Voeller, K. K. S. (2004). Prefrontal executive function syndromes in children. *Journal of Child Neurology, 19*(10), 785–797. https://doi.org/10.1177/08830738040190100801

Power, R., Galea, C., Muhit, M., Heanoy, E., Karim, T., Badawi, N., & Khandaker, G. (2020). What predicts the proxy-reported health-related quality of life of adolescents with cerebral palsy in Bangladesh? *BMC Public Health, 20*(1), 18. https://doi.org/10.1186/s12889-019-8130-1

Pueyo, R., Junqué, C., Vendrell, P., Narberhaus, A., & Segarra, D. (2008). Raven's Coloured Progressive Matrices as a measure of cognitive functioning in Cerebral Palsy. *Journal of Intellectual Disability Research, 52*(5), 437–445. https://doi.org/10.1111/jir.2008.52.issue-5

Pueyo, R., Junqué, C., Vendrell, P., Narberhaus, A., & Segarra, D. (2009). Neuropsychologic impairment in bilateral cerebral palsy. *Pediatric Neurology, 40*(1), 19–26. https://doi.org/10.1016/j.pediatrneurol.2008.08.003

Pugin, F., Metz, A. J., Stauffer, M., Wolf, M., Jenni, O. G., & Huber, R. (2014). Working memory training shows immediate and long-term effects on cognitive performance in children. *F1000Research, 3,* 82. https://doi.org/10.12688/f1000research.3665.2

Qin, Y., Sun, B., Zhang, H., Li, Y., Zhang, T., Luo, C., Sun, C., & Yao, D. (2019). Aberrant interhemispheric functional organization in children with dyskinetic cerebral palsy. *BioMed Research International.* https://doi.org/10.1155/2019/4362539

Radsel, A., Osredkar, D., & Neubauer, D. (2017). Health-related quality of life in children and adolescents with cerebral palsy. *Slovenian Journal of Public Health, 56*(1), 1-10. https://doi.org/10.1515/sjph-2017-0001

Raju, T. N. (2006). Historical perspectives on the etiology of cerebral palsy. *Clinics in Perinatology, 33*(2), 233–250. https://doi.org/10.1016/j.clp.2006.03.006

Ramkumar, S., & Gupta, A. (2016). A study on effect of occupational therapy intervention program using cognitive-perceptual and perceptual-motor activities on visual perceptual skills in children with cerebral palsy. *Indian Journal of Physiotherapy and Occupational Therapy, 10*(3), 60. https://doi.org/10.5958/0973-5674.2016.00083.6

Rapp, M., Eisemann, N., Arnaud, C., Ehlinger, V., Fauconnier, J., Marcelli, M., Michelsen, S. I., Nystrand, M., Colver, A., & Thyen, U. (2017). Predictors of parent-reported quality of life of adolescents with cerebral palsy: A longitudinal study. *Research in Developmental Disabilities, 62*, 259–270. https://doi.org/10.1016/j.ridd.2016.12.005

Raven, J. C., Court, J. J., & Raven, J. (2011). *Raven matrices progresivas: CPM color, SPM general*. TEA Ediciones.

Ravi, D. K., Kumar, N., & Singhi, P. (2017). Effectiveness of virtual reality rehabilitation for children and adolescents with cerebral palsy: An updated evidence-based systematic review. *Physiotherapy, 103*(3), 245–258. https://doi.org/10.1016/j.physio.2016.08.004

Reid, L. B., Rose, S. E., & Boyd, R. N. (2015). Rehabilitation and neuroplasticity in children with unilateral cerebral palsy. Nature Reviews. *Neurology, 11*(7), 390–400. https://doi.org/10.1038/nrneurol.2015.97

Reynolds, C. R. (1998). Reliability of performance on the test of memory and learning (TOMAL) by an adolescent learning disability sample. *Educational and Psychological Measurement, 58*(5), 832–835.

Rieker, J. A., Reales, J. M., Muiños, M., & Ballesteros, S. (2022). The effects of combined cognitive-physical interventions on cognitive functioning in healthy older adults: A systematic review and multilevel meta-analysis. *Frontiers in Human Neuroscience, 16*, 112. https://doi.org/10.3389/fnhum.2022.838968

Riva, D., Franceschetti, S., Erbetta, A., Baranello, G., Esposito, S., & Bulgheroni, S. (2013). Congenital brain damage: Cognitive development correlates with lesion and electroencephalographic features. *Journal of Child Neurology, 28*(4), 446–454. https://doi.org/10.1177/0883073812447684

Robledo-Castro, C., Castillo-Ossa, L. F., & Corchado, J. M. (2023). Artificial Cognitive Systems Applied in Executive Function Stimulation and Rehabilitation Programs: A Systematic Review. *Arabian Journal for Science and Engineering, 48*(2), 2399–2427. https://doi.org/10.1007/s13369-022-07292-5

Romeo, D. M., Sini, F., Brogna, C., Albamonte, E., Ricci, D., & Mercuri, E. (2016). Sex differences in cerebral palsy on neuromotor outcome: A critical review. *Developmental Medicine & Child Neurology, 58*(8), 809–813. https://doi.org/10.1111/dmcn.13137

Romeo, D. M., Venezia, I., Pede, E., & Brogna, C. (2023). Cerebral palsy and sex differences in children: A narrative review of the literature. *Journal of Neuroscience Research, 101*(5), 783–795. https://doi.org/10.1002/jnr.25020

Roostaei, M., Baharlouei, H., Azadi, H., & Fragala-Pinkham, M. A. (2017). Effects of Aquatic Intervention on Gross Motor Skills in Children with Cerebral Palsy: a Systematic Review. *Physical and Occupational Therapy in Pediatrics, 37*(5), 496–515. https://doi.org/10.1080/01942638.2016.1247938

Rosenbaum, P., Paneth, N., Leviton, A., Goldstein, M., Bax, M., Damiano, D., Dan, B., & Jacobsson, B. (2007). A report: The definition and classification of cerebral palsy April 2006. *Developmental Medicine & Child Neurology, 49*(suppl.109), 8–14. https://doi.org/10.1111/j.1469-8749.2007.tb12610.x

Roy, A., Roulin, J.-L., Gras-Le Guen, C., Corbat, M.-L., & Barbarot, S. (2021). Executive functions and quality of life in children with neurofibromatosis type 1. *Orphanet Journal of Rare Diseases, 16*, 1–9. https://doi.org/10.1186/s13023-021-02051-5

Rzezak, P., Valente, K. D., & Duchowny, M. S. (2014). Temporal lobe epilepsy in children: Executive and mnestic impairments. *Epilepsy and Behavior, 31*, 117–122. https://doi.org/10.1016/j.yebeh.2013.12.005

Sadowska, M., Sarecka-Hujar, B., & Kopyta, I. (2020). Cerebral palsy: Current opinions on definition, epidemiology, risk factors, classification and treatment options. *Neuropsychiatric Disease and Treatment*, 1505–1518. https://doi.org/10.2147/NDT.S235165

Sajan, J. E., John, J. A., Grace, P., Sabu, S. S., & Tharion, G. (2017). Wii-based interactive video games as a supplement to conventional therapy for rehabilitation of children with cerebral palsy: A pilot, randomized controlled trial. *Developmental Neurorehabilitation, 20*(6), 361–367. https://doi.org/10.1080/17518423.2016.1252970

Sakki, H. E. A., Dale, N. J., Sargent, J., Perez-Roche, T., & Bowman, R. (2018). Is there consensus in defining childhood cerebral visual impairment? A systematic review of terminology and definitions. *British Journal of Ophthalmology, 102*(4), 424–432. https://doi.org/10.1136/bjophthalmol-2017-310694

Sala, G., Aksayli, N. D., Tatlidil, K. S., Tatsumi, T., Gondo, Y., & Gobet, F. (2019). Near and far transfer in cognitive training: A second-order meta-analysis. *Collabra: Psychology,* 5(1). https://doi.org/10.1525/collabra.203

Sandgreen, H., Frederiksen, L. H., & Bilenberg, N. (2021). Digital Interventions for Autism Spectrum Disorder: A Meta-analysis. *Journal of Autism and Developmental Disorders, 51*(9), 3138–3152. https://doi.org/10.1007/s10803-020-04778-9

Sanz, J. H., Wang, J., Berl, M. M., Armour, A. C., Cheng, Y. I., & Donofrio, M. T. (2018). Executive Function and Psychosocial Quality of Life in School Age Children with Congenital Heart Disease. *The Journal of Pediatrics, 202*, 63–69. https://doi.org/10.1016/j.jpeds.2018.07.018

Schaffer, Y., & Geva, R. (2016). Memory outcomes following cognitive interventions in children with neurological deficits: A review with a focus on under-studied populations. *Neuropsychological Rehabilitation, 26*(2), 286–317. https://doi.org/10.1080/09602011.2015.1016537

Scheck, S. M., Boyd, R. N., & Rose, S. E. (2012). New insights into the pathology of white matter tracts in cerebral palsy from diffusion magnetic resonance imaging: A systematic review. *Developmental Medicine & Child Neurology, 54*(8), 684–696. https://doi.org/10.1111/j.1469-8749.2012.04332.x

Schenker, R., Coster, W. J., & Parush, S. (2005). Neuroimpairments, activity performance, and participation in children with cerebral palsy mainstreamed in elementary schools. *Developmental Medicine and Child Neurology, 47*(12), 808–814. https://doi.org/10.1017/S0012162205001714

Schiariti, V., Selb, M., Cieza, A., & O'Donnell, M. (2015). International Classification of Functioning, Disability and Health Core Sets for children and youth with cerebral palsy: A consensus meeting. *Developmental Medicine & Child Neurology, 57*(2), 149–158. https://doi.org/10.1111/dmcn.12551

Schifrin, B. S., & Longo, L. D. (2000). William John Little and cerebral palsy: A reappraisal. European *Journal of Obstetrics & Gynecology and Reproductive Biology, 90*(2), 139–144. https://doi.org/10.1016/s0301-2115(00)00261-x

Schmidt, M., Mavilidi, M. F., Singh, A., & Englert, C. (2020). Combining physical and cognitive training to improve kindergarten children's executive functions: A cluster randomized controlled trial. *Contemporary Educational Psychology, 63*, 101908. https://doi.org/10.1016/j.cedpsych.2020.101908

Schneck, C. M. (2013). *Visual perception. Occupational Therapy for Children*. Sixth Ed. Mosby Inc, 373–403.

Schneider, R. E., Ng, P., Zhang, X., Andersen, J., Buckley, D., Fehlings, D., Kirton, A., Wood, E., van Rensburg, E., & Shevell, M. I. (2018). The association between maternal age and cerebral palsy risk factors. *Pediatric Neurology, 82*, 25–28. https://doi.org/10.1016/j.pediatrneurol.2018.01.005

Schraegle, W. A., & Titus, J. B. (2016). Executive function and health-related quality of life in pediatric epilepsy. *Epilepsy & Behavior, 62*, 20–26. https://doi.org/10.1016/j.yebeh.2016.06.006

Scionti, N., Cavallero, M., Zogmaister, C., & Marzocchi, G. M. (2020). Is cognitive training effective for improving executive functions in preschoolers? A systematic review and meta-analysis. *Frontiers in Psychology, 10*, 2812. https://doi.org/10.3389/fpsyg.2019.02812

Sellier, E., McIntyre, S., Smithers-Sheedy, H., & Platt, M. J. (2020). European and Australian cerebral palsy surveillance networks working together for collaborative research. *Neuropediatrics, 51*(02), 105–112. https://doi.org/10.1055/s-0039-3402003

Sellier, E., Platt, M. J., Andersen, G. L., Krägeloh-Mann, I., De La Cruz, J., Cans, C., & Network, S. of C. P. (2016). Decreasing prevalence in cerebral palsy: A multi-site European population-based study, 1980 to 2003. *Developmental Medicine & Child Neurology, 58*(1), 85–92. https://doi.org/10.1111/dmcn.12865

Sentenac, M., Rapp, M., Ehlinger, V., Colver, A., Thyen, U., & Arnaud, C. (2021). Disparity of child/parent-reported quality of life in cerebral palsy persists into adolescence. *Developmental Medicine and Child Neurology, 63*(1), 68–74. https://doi.org/10.1111/dmcn.14638

Shaunak, M., & Kelly, V. B. (2018). Cerebral palsy in under 25 s: Assessment and management (NICE Guideline NG62). *Archives of Disease in Childhood-Education and Practice, 103*(4), 189–193. https://doi.org/10.1136/archdischild-2017-312970

Shepard, E., Sweeney, C., Thompson, L., Jacobs, S., Grimm, J., & Weyandt, L. L. (2022). Effectiveness of executive functioning training among heterogeneous adolescent samples: A systematic review. *Applied Neuropsychology: Child*, 1–17. https://doi.org/10.1080/21622965.2022.2106436

Sherman, E. M. S., Slick, D. J., & Eyrl, K. L. (2006). Executive dysfunction is a significant predictor of poor quality of life in children with epilepsy. *Epilepsia, 47*(11), 1936–1942. https://doi.org/10.1111/j.1528-1167.2006.00816.x

Shevell, M. (2019). Cerebral palsy to cerebral palsy spectrum disorder: Time for a name change? *Neurology, 92*(5), 233–235. https://doi.org/10.1212/WNL.0000000000006747

Shin, J. W., & Song, G. Bin. (2016). The effects of neck and trunk stabilization exercises on upper limb and visuoperceptual function in children with cerebral palsy. *Journal of Physical Therapy Science, 28*(11), 3232–3235. https://doi.org/10.1589/jpts.28.3232

Sigurdardottir, S., Eiriksdottir, A., Gunnarsdottir, E., Meintema, M., Arnadottir, U., & Vik, T. (2008). Cognitive profile in young Icelandic children with cerebral palsy. *Developmental Medicine & Child Neurology, 50*(5), 357–362. https://doi.org/10.1111/j.1469-8749.2008.02046.x

Smith, M. L. (2009). ' I can't remember': Memory deficits in children with epilepsy. *The Canadian Journal of Neurological Sciences/Le Journal Canadien Des Sciences Neurologiques*.

Smithers-Sheedy, H., McIntyre, S., Gibson, C., Meehan, E., Scott, H., Goldsmith, S., Watson, L., Badawi, N., Walker, K., & Novak, I. (2016). A special supplement: Findings from the Australian Cerebral Palsy Register, birth years 1993 to 2006. *Developmental Medicine & Child Neurology, 58*, 5–10. https://doi.org/10.1111/dmcn.13026

Sørensen, K., Liverød, J. R., Lerdal, B., Vestrheim, I. E., & Skranes, J. (2016). Executive functions in preschool children with cerebral palsy—Assessment and early intervention—A pilot study. *Developmental Neurorehabilitation, 19*(2), 111–116. https://doi.org/10.3109/17518423.2014.916761

Soto, G., & Clarke, M. T. (2018). Conversation-based intervention for adolescents using augmentative and alternative communication. AAC: Augmentative & Alternative Communication, 34(3), 180–193. https://doi.org/10.1080/07434618.2018.1490926

Stadskleiv, K. (2020). Cognitive functioning in children with cerebral palsy. *Developmental Medicine & Child Neurology, 62*(3), 283–289. https://doi.org/10.1111/dmcn.14463

Stiers, P., & Vandenbussche, E. (2004). The dissociation of perception and cognition in children with early brain damage. *Brain and Development, 26*(2), 81–92. https://doi.org/10.1016/j.braindev.2003.09.005

Stiers, P., Vanderkelen, R., Vanneste, G., Coene, S., De Rammelaere, M., & Vandenbussche, E. (2002). Visual–perceptual impairment in a random sample of children with cerebral palsy. *Developmental Medicine and Child Neurology, 44*(6), 370–382. https://doi.org/10.1017/s0012162201002249

Straub, K., & Obrzut, J. E. (2009). Effects of cerebral palsy on neuropsychological function. *Journal of Developmental and Physical Disabilities, 21*(2), 153–167. https://doi.org/10.1007/s10882-009-9130-3

Strobach, T., & Huestegge, L. (2017). Evaluating the effectiveness of commercial brain game training with working-memory tasks. *Journal of Cognitive Enhancement, 1*, 539–558. https://doi.org/10.1007/s41465-017-0053-0

Studer-Luethi, B., Bauer, C., & Perrig, W. J. (2016). Working memory training in children: Effectiveness depends on temperament. *Memory & Cognition, 44*(2), 171–186. https://doi.org/10.3758/s13421-015-0548-9

Surveillance of Cerebral Palsy in Europe (SCPE). (2000). Surveillance of cerebral palsy in Europe: A collaboration of cerebral palsy surveys and registers. *Developmental Medicine & Child Neurology, 42*(12), 816–824. https://doi.org/10.1111/j.1469-8749.2000.tb00695.x

Szpindel, A., Myers, K. A., Ng, P., Dorais, M., Koclas, L., Pigeon, N., Shevell, M., & Oskoui, M. (2022). Epilepsy in children with cerebral palsy: A data linkage study. *Developmental Medicine & Child Neurology, 64*(2), 259–265. https://doi.org/10.1111/dmcn.15028

Tan, B. W. Z., Pooley, J. A., & Speelman, C. P. (2016). A meta-analytic review of the efficacy of physical exercise interventions on cognition in individuals with autism spectrum disorder and ADHD. *Journal of Autism and Developmental Disorders, 46*, 3126–3143. https://doi.org/10.1007/s10803-016-2854-x

Tang, L., Shafer, A. T., & Ofen, N. (2018). Prefrontal Cortex Contributions to the Development of Memory Formation. *Cerebral Cortex, 28*(9), 3295–3308. https://doi.org/10.1093/cercor/bhx200

Teixeira-Machado, L., Azevedo-Santos, I., & DeSantana, J. M. (2017). Dance Improves Functionality and Psychosocial Adjustment in Cerebral Palsy. *American Journal of Physical Medicine & Rehabilitation, 96*(6), 424–429. https://doi.org/10.1097/phm.0000000000000646

THE WHOQOL GROUP. (1995). The World Health Organization quality of life assessment (WHOQOL): Position paper from the World Health Organization. Social Science and Medicine, 41(10), 1403–1409. https://doi.org/10.1016/0277-9536(95)00112-K

Thorell, L. B., Lindqvist, S., Bergman Nutley, S., Bohlin, G., & Klingberg, T. (2009). Training and transfer effects of executive functions in preschool children. *Developmental Science, 12*(1), 106–113. https://doi.org/10.1111/j.1467-7687.2008.00745.x

Tomporowski, P. D., Davis, C. L., Miller, P. H., & Naglieri, J. A. (2008). Exercise and Children's Intelligence, Cognition, and Academic Achievement. *Educational Psychology Review, 20*(2), 111–131. https://doi.org/10.1007/s10648-007-9057-0

Toomela, A. (2012). Short-term memory in young adults with spastic diplegic cerebral palsy. *Developmental Neuropsychology, 37*(4), 317–332. https://doi.org/10.1080/87565641.2011.632461

Toronto, A. S. (1973). *Screening test of Spanish grammar*. Evenston, IL: Northwestern University Press.

Tsai, N., Buschkuehl, M., Kamarsu, S., Shah, P., Jonides, J., & Jaeggi, S. M. (2018). (un)great expectations: The role of placebo effects in cognitive training. *Journal of Applied Research in Memory and Cognition, 7*(4), 564–573. https://doi.org/10.1037/h0101826

Tsirka, A., Liasis, A., Kuczynski, A., Vargha-Khadem, F., Kukadia, R., Dutton, G., & Bowman, R. (2020). Clinical use of the Insight Inventory in cerebral visual impairment and the effectiveness of tailored habilitational strategies. *Developmental Medicine & Child Neurology, 62*(11), 1324–1330. https://doi.org/10.1111/dmcn.14650

Tsoi, W. S. E., Zhang, L. A., Wang, W. Y., Tsang, K. L., & Lo, S. K. (2012). Improving quality of life of children with cerebral palsy: A systematic review of clinical trials. *Child: Care, Health and Development, 38*(1), 21–31. https://doi.org/10.1111/j.1365-2214.2011.01255.x

Türkoğlu, G., Türkoğlu, S., Çelik, C., & Halil, U. (2017). Intelligence, functioning, and related factors in children with cerebral palsy. *Archives of Neuropsychiatry, 54*(1), 33. https://doi.org/10.5152/npa.2015.12676

Türkoğlu, S., Bilgic, A., Türkoğlu, G., & Yilmaz, S. (2016). Impact of symptoms of maternal anxiety and depression on quality of life of children with cerebral palsy. *Nöro Psikiyatri Arşivi, 53*(1), 49. https://doi.org/10.5152/npa.2015.10132

Umegaki, H., Sakurai, T., & Arai, H. (2021). Active life for brain health: A narrative review of the mechanism underlying the protective effects of physical activity on the brain. *Frontiers in Aging Neuroscience, 13*, 761674. https://doi.org/10.3389/fnagi.2021.761674

Vacca, R. A., Augello, A., Gallo, L., Caggianese, G., Malizia, V., La Grutta, S., Murero, M., Valenti, D., Tullo, A., & Balech, B. (2023). Serious Games in the new era of digital-health interventions: A narrative review of their therapeutic applications to manage neurobehavior in neurodevelopmental disorders. *Neuroscience & Biobehavioral Reviews*, 105156. https://doi.org/10.1016/j.neubiorev.2023.105156

Van Der Slot, W. M., Nieuwenhuijsen, C., Van Den Berg-Emons, R. J., Bergen, M. P., Hilberink, S. R., Stam, H. J., & Roebroeck, M. E. (2012). Chronic pain, fatigue, and depressive symptoms in adults with spastic bilateral cerebral palsy. *Developmental medicine and child neurology, 54*(9), 836–842. https://doi.org/10.1111/j.1469-8749.2012.04371.x

Van der Zee, Y., Stiers, P. L., Lagae, L., Pel, J., & Evenhuis, H. (2019). Chronological age versus developmental age in evaluating patients' performances on motion perception tests. Neuropsychol. *Trends, 25*, 73–94. https://doi.org/10.7358/neur-2019-025-vand

Vander Linden, C., Verhelst, H., Verleysen, G., Caeyenberghs, K., Deblaere, K., & Vingerhoets, G. (2019). Prefrontal and temporal cortical thickness in adolescents with traumatic brain injury. *Developmental Medicine & Child Neurology, 61*(6), 672–679. https://doi.org/10.1111/dmcn.14100

van't Hooft, I., Andersson, K., Bergman, B., Sejersen, T., von Wendt, L., & Bartfai, A. (2005). Beneficial effect from a cognitive training programme on children with acquired brain injuries demonstrated in a controlled study. *Brain Injury, 19*(7), 511–518. https://doi.org/10.1080/02699050400025224

van't Hooft, I., & Norberg, A. L. (2010). SMART cognitive training combined with a parental coaching programme for three children treated for medulloblastoma. *NeuroRehabilitation, 26*(2), 105–113. https://doi.org/10.3233/NRE-2010-0541

Verschuren, O., Ketelaar, M., Takken, T., Helders, P. J. M., & Gorter, J. W. (2008). Exercise programs for children with cerebral palsy: A systematic review of the literature. *American Journal of Physical Medicine and Rehabilitation, 87*(5), 404–417. https://doi.org/10.1097/PHM.0b013e31815b2675

Virella, D., Pennington, L., Andersen, G. L., Andrada, M. da G., Greitane, A., Himmelmann, K., Prasauskiene, A., Rackauskaite, G., De La Cruz, J., & Colver, A. (2016). Classification systems of communication for use in epidemiological surveillance of children with cerebral palsy. *Developmental Medicine & Child Neurology, 58*(3), 285–291. https://doi.org/10.1111/dmcn.12866

Vitrikas, K., Dalton, H., & Breish, D. (2020). Cerebral palsy: An overview. *American Family Physician, 101*(4), 213–220.

Voorman, J. M., Dallmeijer, A. J., Van Eck, M., Schuengel, C., & Becher, J. G. (2010). Social functioning and communication in children with cerebral palsy: Association with disease characteristics and personal and environmental factors. *Developmental Medicine & Child Neurology, 52*(5), 441–447. https://doi.org/10.1111/j.1469-8749.2009.03399.x

Ward, N., Paul, E., Watson, P., Cooke, G. E., Hillman, C. H., Cohen, N. J., Kramer, A. F., & Barbey, A. K. (2017). Enhanced learning through multimodal training: Evidence from a comprehensive cognitive, physical fitness, and neuroscience intervention. *Scientific Reports, 7*(1), 5808. https://doi.org/10.1038/s41598-017-06237-5

Waters, E., Davis, E., Mackinnon, A., Boyd, R., Graham, H. K., Kai Lo, S., Wolfe, R., Stevenson, R., Bjornson, K., Blair, E., Hoare, P., Ravens-Sieberer, U., & Reddihough, D. (2007). Psychometric properties of the quality of life questionnaire for children with CP. *Developmental Medicine and Child Neurology, 49*(1), 49–55. https://doi.org/10.1111/j.1469-8749.2007.0126a.x

Weber, P., Bolli, P., Heimgartner, N., Merlo, P., Zehnder, T., & Kätterer, C. (2016). Behavioral and emotional problems in children and adults with cerebral palsy. *European Journal of Paediatric Neurology, 20*(2), 270–274. https://doi.org/10.1016/j.ejpn.2015.12.003

Wechsler, D., & Naglieri, J. A. (2006). *Wechsler Nonverbal Scale of Ability (WNV)*. Pearson.

Wechsler, D., Raiford, S. E., & Holdnack, J. A. (2015). WISC-V: Escala de inteligencia de Wechsler para niños-V. Madrid: Pearson.

Weierink, L., Vermeulen, R. J., & Boyd, R. N. (2013). Brain structure and executive functions in children with cerebral palsy: A systematic review. Research in Developmental Disabilities, 34(5), 1678–1688. https://doi.org/10.1016/j.ridd.2013.01.035

Weir, F. W., Hatch, J. L., McRackan, T. R., Wallace, S. A., & Meyer, T. A. (2018). Hearing Loss in Pediatric Patients With Cerebral Palsy. Otology & neurotology : official publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology, 39(1), 59–64. https://doi.org/10.1097/MAO.0000000000001610

Whalen, C. N., & Case-Smith, J. (2012). Therapeutic effects of horseback riding therapy on gross motor function in children with cerebral palsy: A systematic review. Physical and Occupational Therapy in Pediatrics, 32(3), 229–242. https://doi.org/10.3109/01942638.2011.619251

White-Koning, M., Grandjean, H., Colver, A., & Arnaud, C. (2008). Parent and professional reports of the quality of life of children with cerebral palsy and associated intellectual impairment. Developmental Medicine and Child Neurology, 50(8), 618–624. https://doi.org/10.1111/j.1469-8749.2008.03026.x

Whitney, D. G., Warschausky, S. A., & Peterson, M. D. (2019). Mental health disorders and physical risk factors in children with cerebral palsy: A cross-sectional study. Developmental Medicine & Child Neurology, 61(5), 579–585. https://doi.org/10.1111/dmcn.14083

Williams, C., Gilchrist, I. D., Fraser, S., McCarthy, H., Parker, J., Warnes, P., Young, J., & Hyvarinen, L. (2015). Normative data for three tests of visuocognitive function in primary school children: Cross-sectional study. British Journal of Ophthalmology, 99(6), 752–756. https://doi.org/10.1136/bjophthalmol-2014-305868

Williams, C., Northstone, K., Sabates, R., Feinstein, L., Emond, A., & Dutton, G. N. (2011). Visual perceptual difficulties and under-achievement at school in a large community-based sample of children. PLoS One, 6(3), e14772. https://doi.org/10.1371/journal.pone.0014772

Willis, S. L., Tennstedt, S. L., Marsiske, M., Ball, K., Elias, J., Koepke, K. M., Morris, J. N., Rebok, G. W., Unverzagt, F. W., & Stoddard, A. M. (2006). Long-term effects of cognitive training on everyday functional outcomes in older adults. Jama, 296(23), 2805–2814. https://doi.org/10.1001/jama.296.23.2805

World Health Organization. (2001) International Classification of Functioning Disability and Health. Geneva, WHO .

World Health Organization. (2007). International Classification of Functioning, Disability, and Health: Children & Youth Version: ICF-CY. World Health Organization.

World Health Organization. (2019). Risk Reduction Of Cognitive Decline And Dementia: WHO guidelines.

Wu, W.-L., Huang, Y.-L., Liang, J.-M., Chen, C.-H., Wang, C.-C., & Ho, W.-H. (2022). Interactive Digital Game for Improving Visual–Perceptual Defects in Children With a Developmental Disability: Randomized Controlled Trial. JMIR Serious Games, 10(2), e34756. https://doi.org/10.2196/34756

Yildirim, Y., Budak, M., Tarakci, D., & Algun, Z. C. (2021). The effect of video-based games on hand functions and cognitive functions in cerebral palsy. Games for Health Journal, 10(3), 180–189. https://doi.org/10.1089/g4h.2020.0182

Zanon, M. A., Pacheco, R. L., Latorraca, C. de O. C., Martimbianco, A. L. C., Pachito, D. V., & Riera, R. (2019). Neurodevelopmental Treatment (Bobath) for Children With Cerebral Palsy: A Systematic Review. Journal of Child Neurology, 34(11), 679–686. https://doi.org/10.1177/0883073819852237

Zehnder, F., Martin, M., Altgassen, M., & Clare, L. (2009). Memory training effects in old age as markers of plasticity: A meta-analysis. Restorative Neurology and Neuroscience, 27(5), 507–520. https://doi.org/10.3233/RNN-2009-0491

Zelazo, P. D., & Carlson, S. M. (2012). Hot and cool executive function in childhood and adolescence: Development and plasticity. Child Development Perspectives, 6(4), 354–360. https://doi.org/10.1111/j.1750-8606.2012.00246.x

ANNEX

Table 1. Participants with cognitive impairments in intervention and waitlist control groups.

Cognitive function	Measure	Baseline		Post		Follow-up		Baseline		Post		Follow-up	
		n	%	n	%	n	%	n	%	n	%	n	%
Memory													
Immediate memory, verbal	Digit Span Forward – WISC-V	3	10	3	10	3	10	6	20	8	28	9	30
Immediate memory, visual	Spatial Span Forward – WNV	8	27	6	20	7	23	10	33	10	33	10	33
Learning, verbal	Word Selective Reminding – TOMAL	6	20	4	13	4	13	16	53	10	33	9	31
Learning, visual	Memory for Designs – NEPSY-II	11	38	7	24	5	17	18	60	17	57	11	41
Long-term memory, verbal	Word Selective Reminding Delayed – TOMAL	2	6.7	1	3	2	7	7	23	8	27	5	17
Lonong-term memory, visual	Memory for Designs Delayed – NEPSY-II	11	39	8	28	6	21	17	57	16	53	10	38
Visual perception													
Object recognition	Facial Recognition Test	2	6.7	4	13	1	3	4	13	5	17	2	7
Visual spatial perception	Arrows – NEPSY-II	8	27	7	23	9	30	16	53	15	50	13	46

Notes. Impairment was determined by considering a Z-score < -1.5.

Abbreviations. NEPSY-Second Edition, A Developmental NEuroPSYchological Assessment-II; TOMAL, Test of Memory and Learning; WISC-V, Wechsler Intelligence Scale for Children-Fifth Edition; WNV, Wechsler Non-Verbal Scale of Ability.