Int J Adv Life Sci Res. Volume 7(4) 46-63
https://doi.org/10.31632/ijalsr.2024.v07i04.005

International Journal of Advancement in Life Sciences Research

Online ISSN: 2581-4877

Journal homepage http://ijalsr.org

Review Article

Application of Smart Electronics in the Prevention of Neurodevelopmental Disorders in Children

Ankit Ghosh, Debolina Samanta, Shirsa Ray, Anuradha Roy, Tamalika Chakraborty*

Department of Microbiology, Guru Nanak Institute of Pharmaceutical Science and Technology 157/F Nilgunj Road, Sodepur, Panihati, Kolkata 700114, India

**Correspondence E-mail:tamalika.chakraborty@gnipst.ac.in*

Abstract

The most common cause of impairment is neurological or brain disorders throughout the world, as well as in developed market economies, where they also rank first in terms of disease burden. Some brain diseases, like stroke and suicide, can also lead to death. However, it is their devastating impact on communities and economies that is mainly caused by their being severely debilitating. But mainly, they are so crippling because they affect thinking, feeling, and behavior—the mind itself; therefore, mental health problems not only bring distress and suffering to individuals and families but interfere with children's learning at school or adults' ability to work, which may even lead to the total inability of self-care when severe occurs. Negative behavioral difficulties are common after the start of neurodevelopmental disorders and have a long-term influence on the affected children, particularly their social development level. Children's social development behavior has been found to mature spontaneously throughout time because of cognitive therapy interventions. This study conducted a meta-analysis to offer a statistical summary of the existing information on social development and behavioral changes following cognitive treatment in children with neurodevelopmental problems.

Keywords: *Assistive technology, Neurodevelopmental disorders, Rehabilitation, VR*

Introduction

The clinical condition of people with neurodevelopmental disorders (NDD) is severe to significant, and numerous disabilities (for example., cognitive, motor, and communication impairments) create problems in their daily life situations (e.g., medical, breath, postural abnormalities, lack of speech, challenging behaviors, isolation, and passivity), which is a serious concern not only for parents but also for teachers or caregivers who work with them (Edwards *et al*., 2021). Mood and anxiety disorders, together with developmental neuropsychiatric illnesses such as autism and schizophrenia, are common, occur in childhood or adolescence, and can have a chronic or recurrent course. As the proportion of individuals aged 60 years and above is rising worldwide, it is anticipated that there will be a dramatic increase in individuals affected by severely disabling neurodegenerative diseases like Parkinson's disease (PD), Alzheimer's disease (AD), and other dementias over the next few decades; this will result in huge financial burdens not only due to healthcare but also because caregivers may need to leave their jobs (Pessoa, 2017).

Kids and teens with NDDs often face difficulties in their cognitive, social, emotional, and communication abilities. This includes conditions such as attention deficit hyperactivity disorder

Received on :6th May 2024; Revised version received on :18thAugust 2024; Accepted: 8th September 2024

(ADHD), autism spectrum disorder (ASD), and cerebral palsy (CP). These individuals may also experience learning difficulties and academic challenges (Rey-Casserly *et al*., 2019). Additionally, their ongoing medical conditions can be burdensome for both caregivers and families, impacting their overall well-being and resulting in significant healthcare expenses (Hickie *et al*., 2019). The COVID-19 outbreak has quickly and unexpectedly deteriorated their precarious health states, due to a lack of medical services or rehabilitative help, as well as measures to avoid it such as quarantine and social isolation. Their way of life may be seriously impacted, and the burden on those who care for them may significantly increase (Masi *et al*., 2021).

One strategy for encouraging liberty, active participation, and positive engagement in kids and teens with NDD is to apply assistive technology (AT)-based treatment in conjunction with motivational strategies and learning concepts (Manta *et al*., 2020). New technologies (such as virtual reality, augmented reality, mobile technologies, and wearable technologies) have just emerged and are rapidly developing in the field of AT (Bailey *et al*., 2022; Valentine *et al*., 2020). Technology-assisted choices allow for the autonomous administration and self-regulation of beneficial therapies for both assessment and rehabilitation (Rahman *et al*., 2020). In addition to assistive technology-based programs, virtual reality (VR) and/or wearable technologies (WT) might be used.VR provides several advantages, such as ecological reliability, control over experiments, and psychological reaction monitoring (Stasolla & Bottiroli, 2020). Wearable gadgets may be easily transported and provide a realistic method of tracking and restoring adaptive responses (Gorman *et al*., 2003). Although the ADHD & Autism groups are intensively addressed, cerebral palsy and unusual hereditary disorders were further investigated (Valentine *et al*., 2020). Furthermore, verbal, psychological, social, and postural skills were evaluated. In contrast, aggressive actions, beneficial activities (e.g., ask and selection capacities), and recreational activities are mostly ignored (Berenguer *et al*., 2020). Over the past ten years, scientific studies on the use of electronic devices to strengthen adaptive capabilities and opportunities for interaction among persons with neurological developmental diseases have increased dramatically (Lussier-Desrochers *et al*., 2020).

During the COVID-19 epidemic, prospective remedies included a revolutionary at-home cognitive therapy program recently developed for individuals with neurological conditions and a reality-based set in a technologically aided method (Bernini *et al*., 2021; Stasolla & Bottiroli, 2020). Therefore, isolation and quarantine preventative therapies confined kids and teens suffering from NDD to their residences. Experts and doctors can virtually supervise to assess their patients utilizing remote rehabilitation treatments, which are electronic in computerized surroundings and increase online interactions in ways analogous to real life (Caprì *et al*., 2021; Varela-Aldás *et al*., 2021). Augmented reality, as a component of VR, allows for engagement in an actual environment, as opposed to the fake background offered by VR. For example, VR often requires wearing headgear, which could make it less comfortable for those with NDD. In contrast, AR may be deemed to be easy as it applies to cell phones, tablets, and I-PADs, which can be adaptive for the actual world (Akin & Gokturk, 2019; Liu *et al*., 2017; Mesa-Gresa *et al*., 2018).

Neurodevelopmental Disorders

DSM-III added "developmental disorders" for the first time, with one group containing autistic disorders (Fischer, 2012). "Neurodevelopmental disorders" (NDDs) have been added as an umbrella disorder group in DSM-5 (American Psychiatric Association. & American Psychiatric Association, DSM-5 Task Force., n.d.). This new part replaces the old chapter titled "Disorders usually first diagnosed in infancy, childhood, or adolescence." In the WHO's most recent edition of the International Classification of Diseases, NDDs were given even greater attention by being an essential part of the title of the psychiatry chapter: "Mental, behavioral, or neurodevelopmental disorders (Fischer, 2012)."

Neuro-Developmental Disorders are characterized as a group of disorders that begin during the developmental period and cause deficiencies that hinder functioning. NDDs include intellectual impairment (ID), communication difficulties, autism spectrum disorder (ASD), attention-

deficit/hyperactivity disorder (ADHD), specific learning disorders (SLD), and neurodevelopmental motor disorders, such as tic disorders (Sokolova *et al*., 2017) (Figure 1).

Children with neurodevelopmental abnormalities may have difficulties with speech and language development, motor abilities, habits, recollection of memories, and gaining knowledge, among other additional functions of brain processes. Such challenges are typically accompanied by comorbidities, including sensorimotor, sleep, and gastrointestinal issues (Gillberg, 2010). The manifestations of neurological developmental conditions frequently change and can get better as a child grows more mature, but a lot of them may be permanent. These diseases are difficult to diagnose and treat; treatment frequently consists of a combination of therapy, medicines, and home- or school-based activities. The origins of the beginnings of neurodevelopmental problems are becoming more understood as research in neurobiology and genetics advances (Gillberg, 2010; Pessoa, 2017).

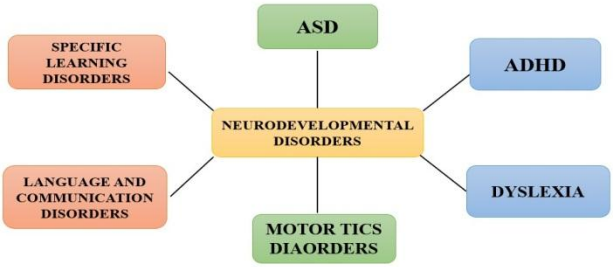

Figure 1: Neurodevelopmental Disorders

History

Neurodevelopmental disorders include intellectual difficulties, communication issues, ASD, ADHD, SLD, and mobility disorders. Many neurodevelopmental diseases were significantly reclassified all through the early 1900s, yet it was not before the twenty-first century that there was a large increase in research, a rapidly-developing literature, and widespread news coverage. Some neurological illnesses, like anorexia, are new syndromes that emerged as rare occurrences in the past, but others, like schizophrenia, have been associated with people for over a thousand years (Jackson & Mackillop, 2016).

SLD and ADHD are well-known phenomena today, yet they are relatively new in the history of humanity.

The first reports of SLD date to the late nineteenth century, when an ophthalmologist discovered that certain non-brain-damaged youngsters had trouble comprehending sequences of words, which was dubbed "word blindness" (Snowling, 1996). Kirk coined the phrase "learning difficulty," which was later expanded to encompass other educational issues observed surprisingly among kids lacking cognitive disability or behavioral problems, in the year 1962 (Kirk & Bateman, 1962).

Over the last 25 years, multidisciplinary research has explored the association between education, cognitive ability, and related comorbidities, providing the foundation for successful rehabilitation therapy. A Cochrane evaluation of the effectiveness of linguistic rehabilitation therapies was undertaken, and the results showed that they are effective in improving some parts of reading abilities (Mcarthur *et al*., 2018). Many additional studies used therapies or instructions based on various cognitive processes, such as memory, focus, and visual-motor ability (Yuzaidey *et al*., 2018; Franceschini *et al*., 2017). Modern technology has facilitated research into the neurobiology and genetics of SLD. As a result, advances in scientific knowledge of SLD have had far-reaching consequences for both evaluation and intervention, as well as the delivery of education structures. Simultaneously, institutions may have benefited from the significance of SLD, considering the prominence that education has gained in the past few decades (Griffiths & Stuart, 2013).

Similar to SLD, there has been no precise definition of ADHD in past research. A few rare allusions to analogous diseases may be found in European literature between the end of the seventeenth century

and the start of the 1900s and in the United States beginning in the first decade of the nineteenth century (Barkley & Peters, 2012). In the early nineteenth century, the phrase became regularly related to intellectual retardation, or "toddler brain damage syndrome," and scientists started employing it for exactly those youngsters who were subsequently labeled ADHD. That description eventually evolved into the more common phrases "minimal brain damage" or "minimal brain dysfunction," which were merely left in the early 1980s, about when the modern nomenclature was first applied inside the DSM-3-R, with the 3 signs and symptoms nonetheless identified these days as critical criteria: inattention, hyperactivity, and impulsivity.

Neurodevelopmental diseases have received more attention since their occurrence appears to be gradually increasing. The origins of this growth are still being debated, but increased attention to symptoms and improved diagnostic process organization have undoubtedly played major roles. Globally diagnoses of SLD have increased dramatically. According to National Center for Education Statistics data from 2015–16, a total of around 6.7 million children (13 percent of the total number of public school students) got special learning services. The proportion of kids with SLD rose from 21.5 percent of all disorders in 1976–77 to 34.8 percent in 2014–15, showing a steady increase throughout the 1980s. The ADHD ailment is also thought to have grown in recent years (Drechsler *et al*., 2020).

Premature onset of Neurodevelopmental Disorders

Early or premature-onset neurodevelopmental illnesses include fetal alcoholism, attention-deficit/hyperactivity disorder, intellectual disabilities, and autism spectrum disorders. Over ten percent of all children suffer from early-onset neurodevelopmental problems, which can have long-term ramifications for them and their families (Gillberg, 2010; Pessoa, 2017). His category is diverse regarding both seriousness and abnormalities: fetal alcoholism, attention-deficit/hyperactivity disorder (ADHD), intellectual disability (ID), tic disorder, developmental coordination problems, dyslexia, particular linguistic impairments, and autism spectrum disorders (Bishop, 2010). Muscular diseases, such as Becker or Duchenne neuromuscular dystrophies, may be classified as neurodevelopmental conditions since they impair cognition within certain groups of patients; nevertheless, due to their prominent symptoms, such illnesses are frequently regarded as a different cluster (Gilissen *et al*., 2014).

Most neurodevelopmental disorders appear to be more common in boys than in girls, implying specific gender vulnerability and protection factors. The quantity of financing and study allocated to a condition is frequently connected with its frequency and seriousness (Gilissen *et al*., 2014). Early-onset neurodevelopmental disorders are caused by a variety of factors, including extreme poverty, hereditary threats, metabolic illnesses, immunological abnormalities, viral illnesses, nutritional issues, physical trauma, and chemical and environmental exposures. Among them, the understanding of genetic risk factors is growing, prompting new neuroscience studies (Pessoa, 2017).

There are hundreds of genes associated with early or premature-onset developmental disorders. This inherent complication is exacerbated by the reality that every person may have a unique combination of alleles with major and minor effects, that emerge de novo or are inherited (Pessoa, 2017).

De-Novo Mutations

De-novo mutations include single base substitutions; trinucleotide repeat expansions; changes in copy number (CNVs); large chromosomal rearrangements and translocations; as well as aneuploidies, the latter distinguishing syndromic neurodevelopmental conditions such as Down syndrome and other trisomies like Klinefelter or Turner syndromes (Hoischen *et al*., 2014). Larger-scale events like chromosomal reorganizations within certain regions of the genome can occur recurrently too: chromosome 22q11.2 deletions giving rise to velocardiofacial syndrome are one example where this happens frequently enough that it has been recognized as being associated with different phenotypes depending on whether there is also a deletion at another nearby locus called DiGeorge critical region gene 8 (DGCR8). Similarly, it’s worth noting here about 15q11–13 duplications involving imprinting center(s) causing Angelman/Prader). However, usually, copy number

variations that affect one to several hundred genes are unique to everyone (Kong *et al*., 2012; O'Roak *et al*., 2011; Sanders *et al*., 2011).

Extremely permeable de-novo mutations are responsible for a significant fraction (15–50%) of serious symptoms that appear as developmental defects (Campbell & Eichler, 2013; Kong *et al*., 2012; Neale *et al*., 2012). The potential factors that contribute to the incidence of de-novo mutations, multiplications, deletions, and duplications are well understood (Toro *et al*., 2010). Huge segmental duplications, such as those on chromosomes 15 and 16p, increase the risk of illicit recombination causing deletion or duplication of human genome regions. Increased fatherhood age has been linked to de novo single base pair changes (Campbell & Eichler, 2013; Kong *et al*., 2012; Neale *et al*., 2012; O'Roak *et al*., 2011; Sanders *et al*., 2011).

In ASD and ID, patients have more de novo chromosomal modifications and CNVs than normal. In contrast, individuals and controls often have identical numbers of de-novo base-specific changes (about 60–70 de novo mutations across a genome of three billion base pairs, along with one per exome of sixty million base pairs). Nonetheless, as compared to controls, patients have a significantly higher rate of harmful (e.g., loss-of-function) changes in evolutionarily limited genes found in the brain (Campbell & Eichler, 2013; Frank, 2014; Kong *et al*., 2012; Sanders *et al*., 2011).

Most mutations described by individuals were discovered using DNA obtained from their blood or sputum. Thus, de novo cellular changes in certain cerebral cell lines were ignored. Deep genomic sequencing and postmortem brain tissue analysis are necessary to determine if somatic changes in brain cells contribute to the early start of NDDs (Poduri *et al*., 2013; Zhu *et al*., 2014).

Inherited Monogenic and Polygenic Forms

Inherited monogenic forms may account for a sizable proportion of people with early-onset developmental abnormalities (Morrow *et al*., 2008). It is estimated that 3–6% of ASD patients have two mutations that cause loss of function in the same gene, making them "homozygous knockout" carriers. Recessive mutations are expected to have a greater impact in nations with higher consanguinity rates (Girirajan *et al*., 2012).

Several hits in diverse sections within the genome may potentially increase vulnerability to an early-onset neurodevelopmental disease. Several investigations have found that such individuals carry more than one harmful mutation (Girirajan*et al*., 2010; Kieling *et al*., 2011; Leblond *et al*., 2012). In a large-scale study of 2,312 adolescents known for carrying a CNV linked to ID and congenital malformations, 10% had a secondary big CNV on top of the main genetic lesion (Girirajan *et al*., 2010). Adolescents with two major CNVs of unclear clinical relevance had an eightfold increased risk of developmental delay compared to controls. Among the afflicted kids, inherited CNVs were commonly linked to a significant second-site CNV. There was no familial tendency identified at the main de-novo or inherited location; nevertheless, 72 percent of second-site CNVs originated from their mother (Girirajan *et al*., 2010).

Further research has validated a multiple-hits paradigm in individuals who share a common "first hit." Among 42 carriers who had a 16p11.2 microdeletion, ten had an extra big CNV, which is a much greater proportion than in controls, conditional on a huge initial hit. Patients who had two mutations had unique as well as more serious clinical characteristics compared to those with a single concurrent mutation (Leblond *et al*., 2012). Another investigation found that 3 ASD individuals with a de-novo SHANK2 mutation also had a second CNV located in the 15q11 gene. Another kid with a neurodevelopmental condition having a SHANK2 translocation and a CHRNA7 duplication was identified (Kieling *et al*., 2011).

Mental disorders

According to the DSM-V, mental illnesses that get going in the adolescent years are classified as neurological developmental disorders (NDDs), which include intellectual disability; specific learning difficulties, such as dyslexia, attention-deficient hyperactivity disorder (ADHD), and autism spectrum

disorders (ASDs); and mental health disorders (MHDs), such as depressive, anxiety, stress-related, conduct, and psychotic disorders (Jeste, 2015). Childhood-onset mental problems are becoming more common all over the world, with rates ranging from 10 to 20% (Renemane *et al*., 2021). NDDs are increasingly recognized as the main cause of death in kids, having a significant effect not just on the individual kid, but also on the culture as a whole (Nepon *et al*., 2010). Suicidal thoughts may occur in depressive, anxiety-related, stress-related, behavioral, and psychotic illnesses (Oerbeck *et al*., 2017).

For example, between thirty percent and fifty percent of youngsters with ADHD are believed to have a concurrent MHD, like depressive symptoms, whereas over seventy percent of youngsters with ASD are thought to have a comorbidity MHD, the most prevalent of those with anxiety (40%) and ADHD (30–40%) (Hansen *et al*., 2018; Yerys *et al*., 2009). The intricate system of comorbidities between neurological disorders and mental health disorders can exacerbate the degree of learning difficulties in individual children's learning challenges and lower their quality of life. This complicated comorbidity has been linked to a lower long-term prognosis, which has consequences for treating individual children (Sheehan, 2017).

Both genetic and environmental variables influence the growth of Mental Disorders in adolescents. A kid's brain function and state of mind are impacted by the family's financial status, with poverty or poor earnings for the family having an adverse impact on the child's education, health, and self-esteem, influencing their advancement, development, and social engagement. Also, a parent's health troubles, psychological disorders, isolation from society, or lack of housing might impair their capacity to successfully parent the kid by creating an encouraging atmosphere for development and growth, which is required for avoiding mental health problems. (American Psychiatric Association. & American Psychiatric Association, DSM-5 Task Force., 2013)

Intellectual disability (Intellectual developmental disorder)

The DSM-5 defines intellectual disabilities (IDs), often known as intellectual developmental disorders, as "deficits in general mental abilities." They influence a person's capacity to absorb information, learn or remember knowledge, think critically or abstractly, and solve issues. They eventually limit a person's ability to adapt to their circumstances, to the point that they may fail to fulfill milestones of independent functioning or social responsibility in one or more activities of everyday life (Danielson *et al*., 2018).

ADHD (Attention Deficit Hyperactive Disorder)

NDD ADHD, which has a prevalence ranging from 9% to 40%, has numerous aetiologies, with environmental and genetic factors contributing to the etiology and different symptoms (Linnet *et al*., 2003). Non-genetic risks include brain damage, preterm birth, maternal use of tobacco and alcohol during pregnancy, and exposure to certain environmental chemicals while pregnant or at younger ages (Sridhar *et al*., 2017).

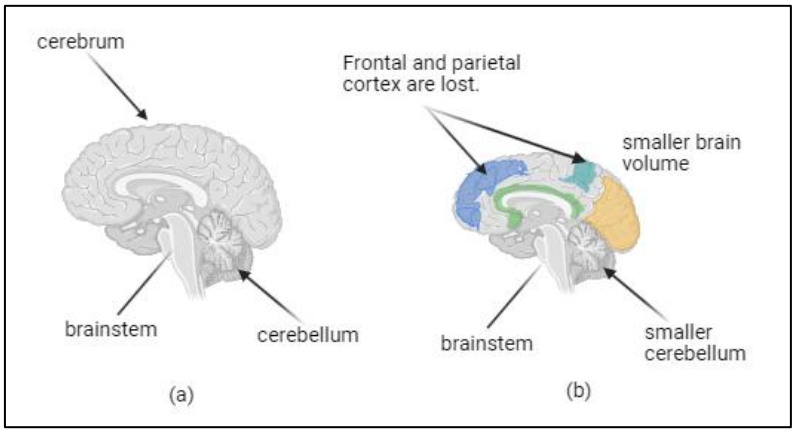

Figure 2: (a) normal brain (b) ADHD brain with smaller volume(Tsampalas *et al*., 2018)

Children who meet the diagnostic requirements for ADHD might also have additional conditions such as oppositional defiant behavioral disorders (ODD and CDs), depressive and anxiety disorders, and particular learning problems. Children with ADHD have difficulty sustaining continuous attention, are hyperactive, fidget, and struggle to take turns. Preliminary data suggests considerable changes in brain sizes in kids who have ADHD when compared to neurotypical kids, especially impacting both anterior and posterior cortices. (Tsampalas *et al*., 2018) (Figure 2)

Dyslexia

NDD dyslexia is a frequent kind of academic disorder that affects 3–15 percent of kids in school. People with dyslexia exhibit unique delays in their acquisition of competent comprehension abilities. Dyslexia is defined by issues with proper &/or fluent recognition of words, as well as poor spelling and reading abilities (Perrachione *et al*., 2016). Persons with dyslexia are demonstrated to exhibit changes in brain function when compared to non-dyslexic people, including impaired neural adaptation to recurrent stimuli. Adolescents with dyslexia may also have educational deficiencies, poor self-worth, stress, depressive disorder, low self-esteem, anxiety, and depression (Schmidt, 2003).

ASD (Autistic Spectrum Disorders)

Autism spectrum disorders (ASDs), which have a documented frequency of roughly 2% in developed nations, usually appear during the first few years of childhood. ASDs are distinguished by difficulties in interacting with others, delays in communication, a fear of gaze, an inability to adapt to environmental alterations, the display of routine actions, and anomalies in learning patterns (Schmidt, 2003). Anxiety and sadness are common among children and adults with ASD. Research into the pathophysiology of ASDs has shown neurological abnormalities between children with and without ASDs (‘neurotypical’ youngsters). Highlights the extrasynaptic link between neurons in an infant with an ASD brain relative to a neurologically normal individual (Sharif & Khan, 2022) (Figure 3).

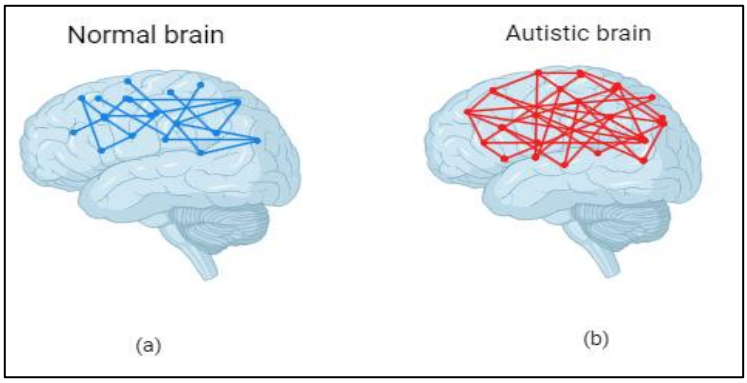

Figure 3: (a) neurotypical brain (b) ASD brains have more dense neural connections (Schmidt, 2003).

Such excess connections are hypothesized to result from inadequate ‘pruning’ of faulty connections between neurons during the development of the brain. This neuropathological variation is expected to produce aberrant neuronal patterns throughout the neural network and disruption in mental coordination between distinct brain regions. Thus, early-onset MDs overall and neurological disorders have a profound impact on people, their families, and the community, necessitating a thorough understanding of how to identify and treat these disorders. This methodical examination has two objectives. First, a review of the way artificial intelligence (AI) tools have been successfully utilized to help kids with frequent and significant NDDs, which include ASD, dyslexia, and ADHD, Secondly, to emphasize the drawbacks of current artificial intelligence instruments and give recommendations for future AI research routes, allowing for even more tailored teaching for these kids (Sharif & Khan, 2022).

Methodology

Many clinical and scientific efforts have lately focused on the important elements (e.g., assessment and rehabilitation). In terms of the appraisal, two major points of view may emerge. First, the existing research focuses on identifying the person's level of functioning. It is vital to determine whether individuals are in a state of unconsciousness or if a more favorable diagnosis of a vegetative condition may be established (Kim *et al*., 2012). Second, the differentiation between the two clinical circumstances (such as a dormant or minimally aware state) is crucially examined, and a special necessity for defining the borderline distinction between those two states necessitates the implementation of more direct measures. Various techniques for rehabilitation may be accepted. For example, one may envision environmental stimulation. Alternatively, deep brain stimulation may be used (Lancioni *et al*., 2017). Additionally, brain-computer interface techniques may be utilized. Those tactics are based on various theoretical frameworks, which may have clinical and practical consequences for the function of the evaluation and the patient. Before the intervention, it is critical to determine whether the individual is in a dormant or barely conscious state, and the intervention setup should be carefully tailored to ensure the participant's success with the learning process (Kayabinar *et al*., 2021).

The latest technologies for people's neurological disorders can be employed for two purposes: (a) assessment, and (b) rehabilitation. To assess the clinical severity of NDD, a VR setup might be used. A technology-based program may be designed to improve both cognitive and motor abilities (Sgandurra *et al*., 2018). A more complete evaluation tool for recording the biopsychosocial characteristics of young individuals with mental health problems was necessary. A comprehensive measure comprising a total of five areas (social and professional functioning, self-harming behaviors, suicidal ideas and actions, physical well-being, and illness kind, stage, and trajectory) was proposed (Hickie *et al*., 2019).

A new rehabilitative procedure, including a study called a randomized controlled trial (RCT), was described thoroughly, with the goal of comparing the performance of the RCT program in a group of children at a higher risk for cerebral palsy (CP) compared to the infant message (IM) intervention. Infants were assigned to either an 8-week trial or IM therapy. Dependent measurements included the infant's sensorimotor profile as well as footage of parent-infant interaction. Finally, guardians completed a questionnaire (the Bayley Emotional-Social and Parental Stress Index). A total of three points of inspection were examined. Data were gathered around the start of the experiment (T0), the finish of the 8-week course (T1), then after two months (T2), and ultimately at the age of eighteen months (T3) (Stasolla & Bottiroli, 2020).

In general, cognitive, and mental abilities, interpersonal abilities, emotional competence, improvement in posture, movement patterns, and motor motions were properly addressed in people with ASD and ADHD. Individuals with CP and uncommon genetic illnesses (e.g., Cornelia de Lange, Angelman, Down, fragile X, and/or Rett Williams syndrome) were not investigated, nor were demand and choice opportunities, leisure alternatives, or difficult behaviors considered main or secondary outcomes. Given, the present narrative overview has temporarily evaluated some studies on the application of VR, MT, WT, and AR to develop the ability to adapt and improve mental, linguistic, and motor skills in people with NDD (Ponsford *et al*., 2014) (Figure 4),

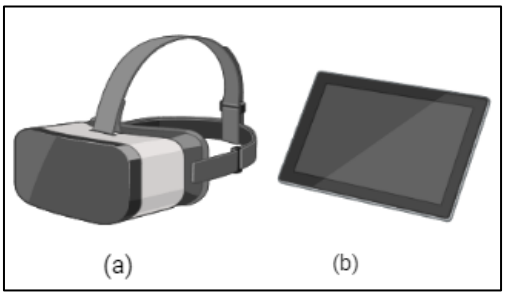

Figure 4: Smart Devices (a) VR headset (b) tablets.

Assessment Strategies

Basic diagnostic approaches for determining with certainty if an individual is in a dormant state or minimally aware state generally include psychological or behavioral parameters, cognitive examination, brain-imaging procedures, and behavioral information based on studies (Pistoia *et al*., 2013). Frequently, many tools and/or strategies are utilized in the evaluation. Behavioral scales are arguably the most used strategy. Frequently, many tools and/or strategies are utilized in the evaluation. Behavioral scales are arguably the most used strategy. Procedural difficulties may arise when a person loses head or hand power over their behavioral range that is compatible with the scale's standards or fails to grasp spoken directions. (Ricchi *et al*., 2022)

The patient's response is also assessed using neuropsychological factors such as potentials associated with events (P300) and/or mismatched negativity. Neuroimaging methods (for example, functional magnetic resonance imaging, or fMRI) may be a useful tool for identifying prospective talents or skills, even when the response is weak or missing. Nonetheless, their utilization remains complex, and their implementation may present major methodological issues in a wide range of healthcare or rehabilitation contexts owing to stimulus evaluation and/or comprehension of spoken instruction (Kayabinar *et al*., 2021).

Behavioral data derived from learning principles may indicate two distinct techniques. On one hand, the traditional model considers the patient's ability to favorably associate pairs of stimuli (Stasolla *et al*., 2015). On the other hand, the operational paradigm requires the patient's ability to appropriately match a behavioral response with an environmental result. Empirical evidence of learning in both ways, such as accurate associations or good outcomes, may indicate a non-reflective reaction and a minimally aware state. These tactics are therapeutically significant for individuals with limited behavioral repertoire, like eyelash or lip actions, who might have trouble with the JFK Coma Recovery Scale. (Stasolla & Bottiroli, 2020)

Rehabilitative Strategies

Environmental entertainment, deep stimulation of the brain, magnetic stimulation of the skull, brain computing interfaces, and learning-based courses or technologically assisted options are some of the therapeutic tactics accessible to persons suffering from consciousness problems. Choices are some of the intervention strategies available to those suffering from consciousness problems (Kayabinar *et al*., 2021; Lancioni *et al*., 2017; Lee *et al*., 2021).

A natural activation program is often administered by the client's therapist. In its simplest sense, it is the transmission of regular stimulation activities like familiar tunes or spoken inputs at the specified period. Essentially, it involves presenting daily stimuli, such as familiar sounds or verbal input, at preset periods. At a more advanced version, it may include regular sessions with intense multi-sensory treatment, as well as vocal and physical guidance for significant events offered by professionals. Brain digital interfaces are devices designed to monitor the brain’s activity and transform it into generated outputs that repair, replace, augment, or supplement the Central Nervous System's natural outputs. Thus, such an approach is likely to change the continuous connections between the CNS and its internal or external surroundings. Various approaches can be used to assess neural activity at interfaces between humans and computers (Kayabinar *et al*., 2021).

This paradigm includes conventional techniques like transcranial magnet therapy and deep brain stimulation, which do not require patient participation. Although there is evidence-based support for this strategy, studies recommend against using it due to its varied effects on patient awareness and consciousness, with varying amplitude and clinical importance (Selander *et al*., 2021).

Brain interfaces for computers are devices designed to monitor brain activity and transform it into artificial outputs that repair, replace, augment, or supplement the Central Nervous System's natural outputs. Thus, such a method is likely to affect the Central Nervous System's ongoing interactions

with its internal or external environment. Brain activity may be assessed using a variety of methods for brain-computer interfaces. The most common way is to detect electrical impulses using electrodes that are invasively or non-invasively attached to the cortical or scalp area. Furthermore, a metabolic metric may be captured using fMRI (Kayabinar *et al*., 2021).

Learning-based techniques were quite distinct from specific tactics. Such a method stresses the active participation of the participant, as well as constructive interaction and relationships facilitated by technology. The COVID-19 epidemic has recently highlighted the advancement of emerging technologies, with a concentration on VR installations and remote rehabilitation tactics to remotely oversee patients (Wiguna *et al*., 2020).

Virtual Reality

Virtual reality, especially augmented reality (AR), has lately been recognized as an important way of successful and appropriate intervention in several areas of health care sectors, including (a) evaluation, (b) determination, (c) recuperation (i.e., rehabilitation), and wellness or a better life. In terms of rehabilitation programs, virtual reality is being extensively used to effectively tackle NDDs, including ADHD and autism spectrum disorder. Virtual Reality provides persons with NDD with sensations that are electronic means of communication in artificial surroundings, boosting virtual experiences like those in real life. Augmented Reality, as part of Virtual Reality, allows for interaction in an actual environment, as opposed to the fake context offered by VR. For example, VR often requires the wearing of headgear, which might not be comfortable for those with NDD. In contrast, AR may be deemed easier because it pertains to tablets, cell phones, and mobile devices, which may be more adaptive to the actual environment (Akin & Gokturk, 2019; Liu *et al*., 2017; Mesa-Gresa *et al*., 2018).

Behavioral monitoring, ecological reliability, and control over experiments are widely recognized as major benefits of VR. A virtual driving test (SDT) and 2 neuropsychological assessments (the Useful Field of View (UFV) and the Test of Variable Attention (TOVA)) were evaluated to assess driving fitness in 51 young volunteers with ADHD, 33 individuals who had ASD, and 38 adolescents who did not have an NDD diagnosis. Participants with ADHD and ASD performed worse in the SDT and TOVA, with more variability overall. Data revealed increased effort and sensitivity to motivational difficulties, as well as a loss of sustained attention across many assessments. Finally, the SDT demonstrated strong sensitivity and validity on the face. TOVA was responsive to the neuropsychiatric aspects of secure driving. It was believed that the SDT and TOVA were complementary to one another, and differences in test results needed special attention. Among children with ASD, the study underlined the usefulness of AR-based programs in promoting and supporting wellness, health, and quality of life in people with ASD. A working prototype of an artificially intelligent application for a digital game assessment tool for ADHD has been developed for kids (Dellazizzo *et al*., 2020).

Wiguna *et al*., (2020) developed a four-step mixed-method study strategy that incorporated qualitative and quantitative tactics to avoid bias and capture crucial information while using a VR-based setup and machine learning technologies such as deep learning applications. The creation of a prospective ADHD-VR digital game assessment tool for children based on a framework for a deep learning model was presented. It was a very promising evaluation tool for people with ADHD, as well as an ideal option because it was intended to increase the fullness and clarity of diagnostic tool accuracy study findings. Apart from a quick evaluation of the prototype ADHD-VR game diagnostic device utilizing a deep learning framework, the study suggested a new four-step method for its development in ADHD kids.

Dellazizzo *et al*., (2020) Conducted a systematic review and evaluated the present state of evidence on virtual reality-based therapy for mental diseases, examining the feasibility and appropriateness of the evidence provided by the study. The results found that the evidence's quality ranged from low to moderate. Inadequate data was attributed to a small number of randomized controlled studies, a deficiency of monitoring and control teams, variability, and bias in publication.

Clark *et al*., (2021) conducted protocol research to examine self-management capacity in children aged 6 to 11 years with NDD (particularly, ADHD and ASD participants were targeted). A randomized controlled study was done utilizing a non-immersive virtual reality system in which children could manipulate virtual items naturally with their own hands. An experimental group and a control group were suggested. A ten-week curriculum was devised. The dependent metrics were self-management and technological acceptability.

Gualniera *et al*., (2021) Developed and investigated the LEAP Motion concept. The LEAP Motion controller was a cheaper USB device capable of tracking and capturing natural interactions with digital information using a virtual reality-based system and optical tracking of hand and finger gestures. NDD and neurodegenerative illnesses (including ADHD, ASD, moderate cognitive deficits, and dementia) were addressed.

VR has been widely embraced in rehabilitation programs to help patients overcome neurological impairments such as neurodevelopmental disorders and neurodegenerative illnesses. VR provides sensory experiences to people with neurological impairments in computer-mediated artificial settings, increasing virtual interactions in ways that are akin to real life. Augmented Reality (AR), as part of Virtual Reality (VR), emphasizes physical interaction, as opposed to VR's artificial setting. That is, VR often necessitates the use of headgear, which may not be comfortably used by those with neurological diseases. AR, on the other hand, may be perceived as more user-friendly because it pertains to I-PADs, tablets, and mobile devices or smartphones, all of which are more appropriate for the real world. For evaluation and rehabilitation reasons, even if it may be considered ethically controversial and controversial, this idea should be scientifically confirmed and finally integrated with an assistive technology device (Billeci *et al*., 2018)

Wearable Technologies

WT includes fundamental options and plays an important part in both daily living and the healthcare business. WT can assist, protect, and help both medical professionals and consumers. Numerous steps to collaboration with remote partners, real-time remote observation, warning of symptoms, appraisal, and accomplishment of recovery objectives can be made and implemented as main purposes (Di Palma *et al*., 2017).

Gualniera *et al*., (2021) did behavioral, clinical, and emotional evaluations in patients who have been diagnosed with Rett syndrome by using web-based technologies. Use of a non-invasive wearable sensor technology was used to evaluate autonomic function through electrodermal activity and heart rate variability. This researcher also recruited ten people who had been diagnosed with RTT and then used emotional, behavioral, and autonomic dys-virtual regulation as their outcome measure. These participants were also prescribed extra-pharmacological therapy. Results showed that three people improved EBAD and normalized EDA. One person had a slight improvement. Two people, on the other hand, showed they were performing poorly. Some of the conclusions from this study were that EDA normalization was associated with symptomatic improvement in Rett syndrome. Very high levels of EDA were hypothesized to be biomarkers of underlying significant physical illness in people with RTT.

Billeci *et al*., (2018) justified that using wireless technology would make it possible to access the possibility of monitoring and recording autonomic activity in children with ASD when presenting joint attention cues. Twenty males with ASD infants and twenty normal-developing infants were recruited and monitored at baseline and during the Joint Attention Task. Worcestershire, or the task was monitored using a chest strap that was comfortable for ECG. The research result proved the possibility and usefulness of applying WT to assess autonomic activity in WI.

Sgandurra *et al*., (2018) developed the unique medical-related equipment. It enabled the parents of newborn babies with congenital brain injuries to institute a home-based, early, intensive, and targeted intervention while overseen virtually by medical professionals. We proposed a new feasible trial process using a sample of high-risk newborns A randomized controlled trial was conducted for a

broader comparison of the technology system versus a rubbing intervention. a high likelihood of cerebral palsy. A randomized controlled trial was conducted for a broader comparison of the technology system versus a rubbing intervention. All 42 newborns were mitigated. An 8-week program incorporated three data collection points followed by a baseline assessment at the end of the intervention, and two follow-ups after 18 months.

Di Palma *et al*., (2017) conducted a WT-based investigation to obtain the signals obtained during therapeutic sessions involving IVA-SGs and the link between autonomic action and child engagement in socio-cognitive assignments in a pediatric population suffering from ASD. The purpose was to quantify the influence of the intervention and tailor therapy. The study engaged five, six- to eight-year-old children with ASD-high functioning. A portable chest ECG tool was used. The observations lasted for six months. The data showed that the device was feasible and clinically applicable.

Airaksinen *et al*., (2020) revealed how they used an infant WT to monitor the posture and movements of 22 seven-month-old infants at risk of ASD and cerebral palsy. The technology responded to the newborns' movements and attitudes.

Mobile Technologies (MTs)

MTs are commonly utilized for wireless communication. MT has changed considerably in recent years. Standard MT has lately evolved beyond simply being a two-way sheet to consist of a mobile phone, satellite navigation system, in-built web browser, and portable game console. MT has several meanings in different contexts, but it is mostly used in the field of information technology and is based on wireless communication for handheld devices. Laptop computers, phones, tablets, and hardware with technological integration are frequently employed (Zamin *et al*.2019).

For example, Davidson *et al.,* (2019) *conducted* a pilot study on a tablet-based application to improve staff service standards for children receiving treatment for mental health issues. The application was designed for use in the delivery and quality improvement of trauma-focused cognitive-behavioral therapy (TF-CBT). In four community mental health care organizations, a blocked randomized control trial was conducted to explore the feasibility of deploying tablet-assisted TF-CBT versus traditional TF-CBT. A total of 13 therapists and 27 families took part in the trial. Faithfulness by a provider to the model of treatment and the child's involvement in therapy were observed using session audio recording. Structured interviews and mixed-method analysis were employed to determine how parents and children experienced the tablet application. Providers used the tablet-based TF-CBT to upgrade their therapeutic activities. Both providers and parents gave high approval of how this approach was done. Satisfied with the service they received, people and their caretakers reported good relationships with mental health professionals who were delivering either method. The tablet-based program was effective and could easily be added to the repertoire of mental health workers with no training. Research was needed to establish to what extent technology-based applications can increase their psycho-social support components to help disadvantaged families improve the long-term life chances of children suffering from mental health herbs.

Zhang *et al., (*2020) gathered medical experts' comments regarding the limits of the existing task and investigated if elements of gamification components may be integrated to improve the standard intervention. A plan of study was given, using a qualitative approach to study techniques and focus group discussions with psychological specialists. In the focus group, members were asked to remark on the limits of current psychological prejudice therapies. They were subsequently prompted to offer ways to improve the treatment and to share their opinions on how gamification may be used to enhance it. The research was scheduled to be completed in 12 months.

Zamin *et al*. (2019) evaluated that a 9-year-old girl who had a cerebral palsy case and was born with auditory, speech problem, and motor problem which made her unable to move like the rest of the people. Her senses and brain failed to communicate properly, hence failing to understand what they said. In this case, her parents also found it difficult to understand her. The main objective of the

program was to help the involved students have the most important communication tools without using any communication signs.

An alternative and augmentative tool, through mobile technology, was developed that allowed people with CP to communicate gradually with other people. The application was not only for people with CP but for all other people. It was thought to be beneficial for anyone with communication issues. It was created in two languages (the English language and Malay), with bespoke content. The results showed that the participant successfully handled the application, and her adaptive responses were meaningful (Fabio *et al*., 2020).

Discussion

Reviewed research on both technical concerns (such as., VR, MT, and WT) demonstrated the cost, efficacy, and compatibility of the chosen technologies in ensuring kids and teens with NDD have adaptive abilities (Airaksinen *et al*., 2020; Colombini *et al*., 2021; Iannizzotto *et al*., 2020). Some research did not explain NDD features or participant ages. Both evaluation and rehabilitation aims were successfully pursued (Clark *et al*., 2021; Colombini *et al*., 2021). Individuals with ADHD and ASD were given extensive attention in terms of cognition and executive functions, communication and emotional ability, stance, and physical motions. Individuals with intellectual disabilities and unusual inheritable illnesses (e.g., Rett syndrome) remained unstudied, as they requested choice possibilities, leisure alternatives, and difficult behavior as an initial or subsequent effect (Matamala-Gomez *et al*., 2021).

To promote cognitive empowerment, a new virtual reality-based approach was created to remotely test and recover cognitive performance in persons with neurodegenerative disorders. Patients with neurological problems were given internet access and recreational options. (Matamala-Gomez *et al*., 2021)

Furthermore, HomeCoRe (Homepage Cognition Rehabilitation software) has been used as a unique and viable solution for house-based cognitive therapy in neurological conditions in hospitals, particularly effective during the COVID-19 epidemic (Bernini *et al*., 2021).

Smart Aging is a premium gaming system that creates a 3D VR world in which players may complete a series of tests that are ultimately determined by a comprehensive and global cognitive assessment. An appropriate extension may be offered for kids and teens with NDD. For example, one could envision a modified version to assess requests, choices, leisure options, and the internet. Similarly, difficult behaviors and enthusiastic participation might be considered initial and subsequent outcomes. Alternatively, tele-rehabilitative procedures can be used or combined to remotely oversee and recover people with NDD (Gillberg, 2010).

While promising, there are several restrictions to consider. The present opinion article relied on just 10 contributions, which included empirical research, reviews of literature, and protocol studies. Second, just VR and WT possibilities were analyzed. Furthermore, only kids and teens were targeted. Fourth, just the previous 5 years' interval was incorporated. More study is needed to determine how new technology might improve adaptive abilities in kids and adolescents with NDD, as well as minimize the strain on families and caregivers. It is important to consider both evaluation and rehabilitation aims. Telemedicine and virtual reality can benefit people with neurological problems (Jackson & Mackillop, 2016).

Conclusion

Considering the above pieces of information, a few considerations must be given importance: (a) participant behavior and technological amplification; (b) follow-up, maintenance, preference assessment, and generalization phases; and (c) social validation procedures that involve external raters who have personal experience with or professional knowledge about the subject matter being evaluated. For example, an initial study might focus on using new technologies – like serious games – for children who have developmental disabilities different from those included in the examined

studies. When making these efforts, one must be aware of (a) the vast amount of literature available regarding using intervention methods in other areas of rehabilitation, such as acquired or pathological conditions; (b) ethical concerns surrounding whether & when it is appropriate for legal representatives to make decisions regarding their clients' treatment options; and lastly, but not least importantly — there needs to be more rigorousness in terms of how we design our experiments if we want them to show us anything new about what works best where.

Abbreviations used:
ADHD- Attention Deficit Hyperactive Disorders, **ASD-** Autistic Spectrum Disorders.

Acknowledgement

The authors like to extend their sincere thanks to the Institute Guru Nanak Institute of Pharmaceutical Science and Technology for their active support and initiative to encourage such research.

Conflict of Interest:

The authors declare no conflict of interest.

References

Airaksinen, M., Räsänen, O., Ilén, E., Häyrinen, T., Kivi, A., Marchi, V., ... & Vanhatalo, S. (2020). Automatic posture and movement tracking of infants with wearable movement sensors. *Scientific reports*, *10*(1), 1-13. https://doi.org/10.1038/s41598-019-56862-5

Akin, N. T. A., &Gokturk, M. (2019). Comparison of theory of mind tests in augmented reality and 2D environments for children with neurodevelopmental disorders. *Advances in Intelligent Systems and Computing*, *781*, 257–264. https://doi.org/10.1007/978-3-319-94334-3_26

American Psychiatric Association, D. S. M. T. F., & American Psychiatric Association, D. S. (2013). *Diagnostic and statistical manual of mental disorders: DSM-5* (Vol. 5, No. 5). Washington, DC: American psychiatric association.

Bailey, B., Bryant, L., & Hemsley, B. (2022). Virtual reality and augmented reality for children, adolescents, and adults with communication disability and neurodevelopmental disorders: a systematic review. *Review Journal of Autism and Developmental Disorders*, *9*(2), 160-183. https://doi.org/10.1007/s40489-020-00230-x

Barkley, R. A., & Peters, H. (2012). The earliest reference to ADHD in the medical literature? Melchior Adam Weikard's description in 1775 of "attention deficit"(Mangel der Aufmerksamkeit, AttentioVolubilis). *Journal of attention disorders*, *16*(8), 623-630. https://doi.org/10.1177/1087054711432309

Berenguer, C., Baixauli, I., Gómez, S., Andrés, M. D. E. P., & De Stasio, S. (2020). Exploring the impact of augmented reality in children and adolescents with autism spectrum disorder: A systematic review. *International Journal of Environmental Research and Public Health*, *17*(17), 1–15. https://doi.org/10.3390/ijerph17176143

Bernini, S., Stasolla, F., Panzarasa, S., Quaglini, S., Sinforiani, E., Sandrini, G., ... &Bottiroli, S. (2021). Cognitive telerehabilitation for older adults with neurodegenerative diseases in the COVID-19 era: a perspective study. *Frontiers in Neurology*, *11*, 623933. https://doi.org/10.3389/fneur.2020.623933

Billeci, L., Tonacci, A., Narzisi, A., Manigrasso, Z., Varanini, M., Fulceri, F., ... & Muratori, F. (2018). Heart rate variability during a joint attention task in toddlers with autism spectrum disorders. *Frontiers in physiology*, *9*, 467. https://doi.org/10.3389/fphys.2018.00467

Bishop, D. V. (2010). Which neurodevelopmental disorders get researched and why?. *PloS one*, *5*(11), e15112.https://doi.org/10.1371/journal.pone.0015112

Campbell, C. D., & Eichler, E. E. (2013). Properties and rates of germline mutations in humans. *Trends in Genetics*, *29*(10), 575-584. https://doi.org/10.1016/j.tig.2013.04.005

Caprì, T., Nucita, A., Iannizzotto, G., Stasolla, F., Romano, A., Semino, M., ... & Fabio, R. A. (2021). Telerehabilitation for improving adaptive skills of children and young adults with multiple disabilities: a systematic review. *Review Journal of Autism and Developmental Disorders*, *8*, 244-252. https://doi.org/10.1007/s40489-020-00214-x

Clark, C. C. T., Bisi, M. C., Duncan, M. J., &Stagni, R. (2021). Technology-based methods for the assessment of fine and gross motor skill in children: A systematic overview of available solutions and future steps for effective in-field use. *Journal of Sports Sciences*, *39*(11), 1236-1276.https://doi.org/10.1080/02640414.2020.1864984

Colombini, G., Duradoni, M., Carpi, F., Vagnoli, L., &Guazzini, A. (2021). LEAP motion technology and psychology: a mini-review on hand movements sensing for neurodevelopmental and neurocognitive disorders. *International journal of environmental research and public health*, *18*(8), 4006. https://doi.org/10.3390/ijerph18084006

Danielson, M. L., Bitsko, R. H., Ghandour, R. M., Holbrook, J. R., Kogan, M. D., & Blumberg, S. J. (2018). Prevalence of parent-reported ADHD diagnosis and associated treatment among US children and adolescents, 2016. *Journal of Clinical Child & Adolescent Psychology*, *47*(2), 199-212. https://doi.org/10.1080/15374416.2017.1417860

Davidson, T. M., Bunnell, B. E., Saunders, B. E., Hanson, R. F., Danielson, C. K., Cook, D., ... & Ruggiero, K. J. (2019). Pilot evaluation of a tablet-based application to improve quality of care in child mental health treatment. *Behavior therapy*, *50*(2), 367-379. www.sciencedirect.com, www.elsevier.com/locate/bt

Dellazizzo, L., Potvin, S., Luigi, M., & Dumais, A. (2020). Evidence on virtual reality–based therapies for psychiatric disorders: meta-review of meta-analyses. *Journal of medical Internet research*, *22*(8), e20889. https://doi.org/10.2196/20889

Di Palma, S., Tonacci, A., Narzisi, A., Domenici, C., Pioggia, G., Muratori, F., ... & MICHELANGELO Study Group. (2017). Monitoring of autonomic response to sociocognitive tasks during treatment in children with Autism Spectrum Disorders by wearable technologies: A feasibility study. *Computers in biology and medicine*, *85*, 143-152. https://doi.org/10.1016/j.compbiomed.2016.04.001

Drechsler, R., Brem, S., Brandeis, D., Grünblatt, E., Berger, G., & Walitza, S. (2020). ADHD: Current concepts and treatments in children and adolescents. *Neuropediatrics*, *51*(05), 315-335. https://doi.org/10.1055/s-0040-1701658

Edwards, S., Rudaizky, D., Toner, M., & Chen, W. (2021). A qualitative study of factors perceived by parents as promoting personal recovery in children and young people with attention deficit hyperactivity disorder. *Advances in Neurodevelopmental Disorders*, *5*, 102-115. https://doi.org/10.1007/s41252-020-00187-2

Fabio, R. A., Gangemi, A., Semino, M., Vignoli, A., Priori, A., Canevini, M. P., ... &Caprì, T. (2020). Effects of combined transcranial direct current stimulation with cognitive training in girls with Rett syndrome. *Brain Sciences*, *10*(5), 1-15. https://doi.org/10.3390/brainsci10050276

Fischer, B. A. (2012). A review of American psychiatry through its diagnoses: the history and development of the Diagnostic and Statistical Manual of Mental Disorders. *The Journal of nervous and mental disease*, *200*(12), 1022-1030. https://doi.org/10.1097/NMD.0b013e318275cf19

Franceschini, S., Bertoni, S., Gianesini, T., Gori, S., &Facoetti, A. (2017). A different vision of dyslexia: Local precedence on global perception. *Scientific reports*, *7*(1), 1-10. https://doi.org/10.1038/s41598-017-17626-1

Frank, S. A. (2014). Somatic mosaicism and disease. *Current Biology*, *24*(12), R577-R581. https://doi.org/10.1016/j.cub.2014.05.021

Gilissen, C., Hehir-Kwa, J. Y., Thung, D. T., Van De Vorst, M., Van Bon, B. W., Willemsen, M. H., ... & Veltman, J. A. (2014). Genome sequencing identifies major causes of severe intellectual disability. *Nature*, *511*(7509), 344-347. https://doi.org/10.1038/nature13394

Gillberg, C. (2010). The ESSENCE in child psychiatry: early symptomatic syndromes eliciting neurodevelopmental clinical examinations. *Research in developmental disabilities*, *31*(6), 1543-1551. https://doi.org/10.1016/j.ridd.2010.06.002

Girirajan, S., Rosenfeld, J. A., Coe, B. P., Parikh, S., Friedman, N., Goldstein, A., ... & Eichler, E. E. (2012). Phenotypic heterogeneity of genomic disorders and rare copy-number variants. *New England Journal of Medicine*, *367*(14), 1321-1331. https://doi.org/10.1056/nejmoa1200395

Girirajan, S., Rosenfeld, J. A., Cooper, G. M., Antonacci, F., Siswara, P., Itsara, A., ... & Eichler, E. E. (2010). A recurrent 16p12. 1 microdeletion supports a two-hit model for severe developmental delay. *Nature genetics*, *42*(3), 203-209. https://doi.org/10.1038/ng.534

Gorman, P., Dayle, R., Hood, C. A., &Rumrell, L. (2003). Effectiveness of the ISAAC cognitive prosthetic system for improving rehabilitation outcomes with neurofunctional impairment. *NeuroRehabilitation*, *18*(1), 57-67. https://doi.org/10.3233/NRE-2003-18107

Griffiths, Y., & Stuart, M. (2013). Reviewing evidence-based practice for pupils with dyslexia and literacy difficulties. *Journal of Research in Reading*, *36*(1), 96-116.https://doi.org/10.1111/j.1467-9817.2011.01495.x

Gualniera, L., Singh, J., Fiori, F., & Santosh, P. (2021). Emotional behavioural and autonomic dysregulation (EBAD) in Rett syndrome–EDA and HRV monitoring using wearable sensor technology. *Journal of psychiatric research*, *138*, 186-193. https://doi.org/10.1016/j.jpsychires.2021.03.052

Hansen, B. H., Oerbeck, B., Skirbekk, B., Petrovski, B. É., & Kristensen, H. (2018). Neurodevelopmental disorders: prevalence and comorbidity in children referred to mental health services. *Nordic journal of psychiatry*, *72*(4), 285-291. https://doi.org/10.1080/08039488.2018.1444087

Hickie, I. B., Scott, E. M., Cross, S. P., Iorfino, F., Davenport, T. A., Guastella, A. J., ... & Scott, J. (2019). Right care, first time: a highly personalised and measurement-based care model to manage youth mental health. *Medical Journal of Australia*, *211*, S3-S46. https://doi.org/10.5694/mja2.50383

Hoischen, A., Krumm, N., & Eichler, E. E. (2014). Prioritization of neurodevelopmental disease genes by discovery of new mutations. *Nature neuroscience*, *17*(6), 764-772. https://doi.org/10.1038/nn.3703

Iannizzotto, G., Nucita, A., Fabio, R. A., Caprì, T., & Lo Bello, L. (2020). Remote eye-tracking for cognitive telerehabilitation and interactive school tasks in times of COVID-19. *Information*, *11*(6), 1-9. https://doi.org/10.3390/info11060296

Jackson, J. N., & MacKillop, J. (2016). Attention-deficit/hyperactivity disorder and monetary delay discounting: a meta-analysis of case-control studies. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, *1*(4), 316-325. https://doi.org/10.1016/j.bpsc.2016.01.007

Jeste, S. S. (2015). Neurodevelopmental behavioral and cognitive disorders. *CONTINUUM: Lifelong Learning in Neurology*, *21*(3), 690-714. www.ContinuumJournal.com

Kayabinar, B., Alemdaroğlu-Gürbüz, İ., & Yilmaz, Ö. (2021). The effects of virtual reality augmented robot-assisted gait training on dual-task performance and functional measures in chronic stroke: a randomized controlled single-blind trial. *Eur J Phys Rehabil Med*, *57*(2), 227-237. https://doi.org/10.23736/S1973-9087.21.06441-8

Kieling, C., Baker-Henningham, H., Belfer, M., Conti, G., Ertem, I., Omigbodun, O., ... & Rahman, A. (2011). Child and adolescent mental health worldwide: evidence for action. *The lancet*, *378*(9801), 1515-1525. https://doi.org/10.1016/S0140-6736(11)60827-1

Kim, E. J., Park, J. M., Kim, W. H., Lee, K. L., Kim, H. N., Lee, K. E., ... & Ahn, K. O. (2012). A learning set up for detecting minimally conscious state (MCS). *Annals of Rehabilitation Medicine*, *36*(3), 428-431. https://doi.org/10.5535/arm.2012.36.3.428

Kirk, S. A., & Bateman, B. (1962). Diagnosis and remediation of learning disabilities. *Exceptional children*, *29*(2), 73-78. https://doi.org/10.1177/0014402962029002

Kong, A., Frigge, M. L., Masson, G., Besenbacher, S., Sulem, P., Magnusson, G., ... & Stefansson, K. (2012). Rate of de novo mutations and the importance of father's age to disease risk. *Nature*, *488*(7412), 471-475. https://doi.org/10.1038/nature11396

Lancioni, G. E., Bosco, A., O'Reilly, M. F., Sigafoos, J., & Belardinelli, M. O. (2017). Assessment and intervention with patients with severe disorders of consciousness. *Advances in Neurodevelopmental Disorders*, *1*, 196-202. https://doi.org/10.1007/s41252-017-0025-5

Leblond, C. S., Heinrich, J., Delorme, R., Proepper, C., Betancur, C., Huguet, G., ... & Bourgeron, T. (2012). Genetic and functional analyses of SHANK2 mutations suggest a multiple hit model of autism spectrum disorders. *PLoS genetics*, *8*(2), 1-17. https://doi.org/10.1371/journal.pgen.1002521

Lee, I. S., Jung, W. M., Lee, Y. S., Wallraven, C., & Chae, Y. (2021). Operant and classical learning principles underlying mind–body interaction in pain modulation: a pilot fMRI study. *Scientific reports*, *11*(1), 1-11. https://doi.org/10.1038/s41598-021-81134-6

Linnet, K. M., Dalsgaard, S., Obel, C., Wisborg, K., Henriksen, T. B., Rodriguez, A., ... &Jarvelin, M. R. (2003). Maternal lifestyle factors in pregnancy risk of attention deficit hyperactivity disorder and associated behaviors: review of the current evidence. *American Journal of Psychiatry*, *160*(6), 1028-1040. https://doi.org/10.1176/appi.ajp.160.6.1028

Liu, R., Salisbury, J. P., Vahabzadeh, A., & Sahin, N. T. (2017). Feasibility of an autism-focused augmented reality smartglasses system for social communication and behavioral coaching. *Frontiers in pediatrics*, *5*, 1-8. https://doi.org/10.3389/fped.2017.00145

Lussier-Desrochers, D., Dupont, M. È., Lachapelle, Y., Massé, L., Martineau, A., & Pépin-Beauchesne, L. (2020). Creation process for a technology design model promoting active participation of end users with neurodevelopmental disorders: achievements and pitfalls. In *Universal Access in Human-Computer Interaction. Applications and Practice: 14th International Conference, UAHCI 2020, Held as Part of the 22nd HCI International Conference, HCII 2020, Copenhagen, Denmark, July 19–24, 2020, Proceedings, Part II 22* (pp. 48-57). Springer International Publishing. https://doi.org/10.1007/978-3-030-49108-6_4

Manta, O., Androutsou, T., Anastasiou, A., Koumpouros, Y., Matsopoulos, G., &Koutsouris, D. (2020). Innovative technological advancements to improve cognitive and social skills of students with neurodevelopmental disorders. *Technology and Disability*, *32*(4), 243-253. https://doi.org/10.3233/TAD-200288

Masi, A., Mendoza Diaz, A., Tully, L., Azim, S. I., Woolfenden, S., Efron, D., & Eapen, V. (2021). Impact of the COVID-19 pandemic on the well-being of children with neurodevelopmental disabilities and their parents. *Journal of Paediatrics and Child Health*, *57*(5), 631-636. https://doi.org/10.1111/jpc.15285

Matamala-Gomez, M., Bottiroli, S., Realdon, O., Riva, G., Galvagni, L., Platz, T., ... &Tassorelli, C. (2021). Telemedicine and virtual reality at time of COVID-19 pandemic: an overview for future perspectives in neurorehabilitation. *Frontiers in Neurology*, *12*, 1-9. https://doi.org/10.3389/fneur.2021.646902

McArthur, G., Sheehan, Y., Badcock, N. A., Francis, D. A., Wang, H. C., Kohnen, S., ... & Castles, A. (2018). Phonics training for English-speaking poor readers. *Cochrane Database of Systematic Reviews*, (11). https://doi.org/10.1002/14651858.CD009115.pub3

Mesa-Gresa, P., Gil-Gómez, H., Lozano-Quilis, J. A., & Gil-Gómez, J. A. (2018). Effectiveness of virtual reality for children and adolescents with autism spectrum disorder: an evidence-based systematic review. *Sensors*, *18*(8), 1-15. https://doi.org/10.3390/s18082486

Morrow, E. M., Yoo, S. Y., Flavell, S. W., Kim, T. K., Lin, Y., Hill, R. S., ... & Walsh, C. A. (2008). Identifying autism loci and genes by tracing recent shared ancestry. *science*, *321*(5886), 218-223. https://doi.org/10.1126/science.1157657

Neale, B. M., Kou, Y., Liu, L., Ma'Ayan, A., Samocha, K. E., Sabo, A., ... & Daly, M. J. (2012). Patterns and rates of exonic de novo mutations in autism spectrum disorders. *Nature*, *485*(7397), 242-245. https://doi.org/10.1038/nature11011

Nepon, J., Belik, S. L., Bolton, J., & Sareen, J. (2010). The relationship between anxiety disorders and suicide attempts: findings from the National Epidemiologic Survey on Alcohol and Related Conditions. *Depression and anxiety*, *27*(9), 791-798. https://doi.org/10.1002/da.20674

Oerbeck, B., Overgaard, K. R., Aspenes, S. T., Pripp, A. H., Mordre, M., Aase, H., ... & Zeiner, P. (2017). ADHD, comorbid disorders and psychosocial functioning: How representative is a child cohort study? Findings from a national patient registry. *BMC psychiatry*, *17*, 1-9. https://doi.org/10.1186/s12888-017-1204-7

O'Roak, B. J., Deriziotis, P., Lee, C., Vives, L., Schwartz, J. J., Girirajan, S., ... & Eichler, E. E. (2011). Exome sequencing in sporadic autism spectrum disorders identifies severe de novo mutations. *Nature genetics*, *43*(6), 585-589. https://doi.org/10.1038/ng.835

Perrachione, T. K., Del Tufo, S. N., Winter, R., Murtagh, J., Cyr, A., Chang, P., ... & Gabrieli, J. D. (2016). Dysfunction of rapid neural adaptation in dyslexia. *Neuron*, *92*(6), 1383-1397. https://doi.org/10.1016/j.neuron.2016.11.020

Pessoa, L. (2017). The emotional brain. In *Conn's translational neuroscience* (pp. 635-656). Academic Press.https://doi.org/10.1016/B978-0-12-802381-5.00046-4

Pistoia, F., Sacco, S., Sarà, M., &Carolei, A. (2013). The perception of pain and its management in disorders of consciousness. *Current pain and headache reports*, *17*, 1-10. https://doi.org/10.1007/s11916-013-0374-3

Poduri, A., Evrony, G. D., Cai, X., & Walsh, C. A. (2013). Somatic mutation, genomic variation, and neurological disease. *Science*, *341*(6141), 1237758. https://doi.org/10.1126/science.1237758

Ponsford, J., Janzen, S., McIntyre, A., Bayley, M., Velikonja, D., & Tate, R. (2014). INCOG recommendations for management of cognition following traumatic brain injury, part I: posttraumatic amnesia/delirium. *The Journal of Head Trauma Rehabilitation*, *29*(4), 307-320. https://doi.org/10.1097/HTR.0000000000000074

Rahman, M. M., Usman, O. L., Muniyandi, R. C., Sahran, S., Mohamed, S., & Razak, R. A. (2020). A review of machine learning methods of feature selection and classification for autism spectrum disorder. *Brain sciences*, *10*(12), 1–23. https://doi.org/10.3390/brainsci10120949

Renemane, L., Kivite-Urtane, A., &Rancans, E. (2021). Suicidality and its relation with physical and mental conditions: Results from a cross-sectional study of the nationwide primary care population sample in Latvia. *Medicina*, *57*(9), 1-9. https://doi.org/10.3390/medicina57090970

Rey-Casserly, C., McGuinn, L., Lavin, A., LaMonte Askew, G., Baum, R., Berger-Jenkins, E., ... & Committee On Psychosocial Aspects of Child and Family Health. (2019). School-aged children who are not progressing academically: considerations for pediatricians. *Pediatrics*, *144*(4), 1-18. https://doi.org/10.1542/peds.2019-2520

Ricchi, I., Tarun, A., Maretic, H. P., Frossard, P., & Van De Ville, D. (2022). Dynamics of functional network organization through graph mixture learning. *Neuroimage*, *252*, 1-13. https://doi.org/10.1016/j.neuroimage.2022.119037

Sanders, S. J., Ercan-Sencicek, A. G., Hus, V., Luo, R., Murtha, M. T., Moreno-De-Luca, D., ... & Devlin, B. (2011). Multiple recurrent de novo CNVs, including duplications of the 7q11. 23 Williams syndrome region, are strongly associated with autism. *Neuron*, *70*(5), 863-885. https://doi.org/10.1016/j.neuron.2011.05.002

Schmidt, U. (2003). Aetiology of eating disorders in the 21 st century: new answers to old questions. *European child & adolescent psychiatry*, *12*, i30-i37. https://doi.org/10.1007/s00787-003-0309-3

Selander, H., Strand, N., Almberg, M., &Lidestam, B. (2021). Ready for a learner's permit? Clinical neuropsychological off-road tests and driving behaviors in a simulator among adolescents with ADHD and ASD. *Developmental neurorehabilitation*, *24*(4), 256-265. https://doi.org/10.1080/17518423.2020.1869339

Sgandurra, G., Beani, E., Giampietri, M., Rizzi, R., Cioni, G., &CareToy-R Consortium Francesca Cecchi Maria Luce Cioni Carlo Dani Paolo Dario Marco Di Galante Ugo Faraguna Patrizio Fiorini Paolo Ghirri Irene Mannari Martina Maselli Valentina Menici Filomena Paternoster. (2018). Early intervention at home in infants with congenital brain lesion with CareToy revised: a RCT protocol. *BMC pediatrics*, *18*(1), 1-9.https://doi.org/10.1186/s12887-018-1264-y

Sharif, H., & Khan, R. A. (2022). A novel machine learning based framework for detection of autism spectrum disorder (ASD). *Applied Artificial Intelligence*, *36*(1), e2004655-369- e2004655-401. https://doi.org/10.1080/08839514.2021.2004655

Sheehan, R. (2017). Mental illness in children: Childhood illness and supporting the family. *Brain sciences*, *7*(8), 1-4. https://doi.org/10.3390/brainsci7080097

Snowling, M. J. (1996). Dyslexia: a hundred years on. *BMJ*, *313*(7065), 1096-1097. https://doi.org/10.1136/bmj.313.7065.1096

Sokolova, E., Oerlemans, A. M., Rommelse, N. N., Groot, P., Hartman, C. A., Glennon, J. C., ... &Buitelaar, J. K. (2017). A causal and mediation analysis of the comorbidity between attention deficit hyperactivity disorder (ADHD) and autism spectrum disorder (ASD). *Journal of autism and developmental disorders*, *47*, 1595-1604. https://doi.org/10.1007/s10803-017-3083-7

Sridhar, C., Bhat, S., Acharya, U. R., Adeli, H., &Bairy, G. M. (2017). Diagnosis of attention deficit hyperactivity disorder using imaging and signal processing techniques. *Computers in Biology and Medicine*, *88*, 93-99. https://doi.org/10.1016/j.compbiomed.2017.07.009

Stasolla, F., &Bottiroli, S. (2020). Fostering daily life skills in young and older adults with neurodegenerative diseases through technological supports. *International Journal of Ambient Computing and Intelligence (IJACI)*, *11*(4), 1-15. https://doi.org/10.4018/IJACI.2020100101

Stasolla, F., Caffò, A. O., Damiani, R., Perilli, V., Di Leone, A., & Albano, V. (2015). Assistive technology-based programs to promote communication and leisure activities by three children emerged from a minimal conscious state. *Cognitive Processing*, *16*, 69-78. https://doi.org/10.1007/s10339-014-0625-1

Toro, R., Konyukh, M., Delorme, R., Leblond, C., Chaste, P., Fauchereau, F., ... & Bourgeron, T. (2010). Key role for gene dosage and synaptic homeostasis in autism spectrum disorders. *Trends in genetics*, *26*(8), 363-372. https://doi.org/10.1016/j.tig.2010.05.007

Tsampalas, E., Dimitrios, S., Papadimitropoulou, P., Vergou, M., &Zakopoulou, V. (2018). Learning Paths and Learning Styles in Dyslexia: Possibilites and Effectiveness--Case Study of Two Elementary School Students Aged 7 Years Old. *Online Submission*, *3*(1), 25-41. https://doi.org/10.5281/zenodo.1095187

Valentine, A. Z., Brown, B. J., Groom, M. J., Young, E., Hollis, C., & Hall, C. L. (2020). A systematic review evaluating the implementation of technologies to assess, monitor and treat neurodevelopmental disorders: A map of the current evidence. *Clinical psychology review*, *80*, 1-16. https://doi.org/10.1016/j.cpr.2020.101870

Varela-Aldás, J., Buele, J., Ramos Lorente, P., García-Magariño, I., & Palacios-Navarro, G. (2021). A virtual reality-based cognitive telerehabilitation system for use in the COVID-19 pandemic. *Sustainability*, *13*(4), 1–24. https://doi.org/10.3390/su13042183

Wiguna, T., Wigantara, N. A., Ismail, R. I., Kaligis, F., Minayati, K., Bahana, R., &Dirgantoro, B. (2020). A four-step method for the development of an ADHD-VR digital game diagnostic tool prototype for children using a DL model. *Frontiers in Psychiatry*, *11*, 1-7. https://doi.org/10.3389/fpsyt.2020.00829

Yerys, B. E., Wallace, G. L., Sokoloff, J. L., Shook, D. A., James, J. D., & Kenworthy, L. (2009). Attention deficit/hyperactivity disorder symptoms moderate cognition and behavior in children with autism spectrum disorders. *Autism Research*, *2*(6), 322-333. https://doi.org/10.1002/aur.103

Yuzaidey, N. A. M., Din, N. C., Ahmad, M., Ibrahim, N., Razak, R. A., & Harun, D. (2018). Interventions for children with dyslexia: A review on current intervention methods. *Med J Malaysia*, *73*(5), 311-320.

Zamin, N. Jamil, N. Norwahi, MD.N.(2019). Make Me Speak: A Mobile Apps for Children with Cerebral Palsy. *Journal of Engineering and Science Research*, *3*(2), 21–26. https://doi.org/10.26666/rmp.jesr.2019.2.4

Zhang, M., Vallabhajosyula, R., & Fung, D. (2020). Emotional bias modification for individuals with attention deficit hyperactivity disorder: protocol for a co-design study. *JMIR Research Protocols*, *9*(12), 1-6. https://doi.org/10.2196/24078

Zhu, X., Need, A. C., Petrovski, S., & Goldstein, D. B. (2014). One gene, many neuropsychiatric disorders: lessons from Mendelian diseases. *Nature neuroscience*, *17*(6), 773-781.https://doi.org/10.1038/nn.3713