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New Pathways of Brain Plasticity in People with Williams Syndrome: A Brief Review of Technology-Based Cognitive Interventions

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Abstract

Evidence from behavioral and neurophysiological studies shows marked asymmetry in the brain and behavioral performance of people with neurodevelopmental disorders in both verbal and nonverbal abilities. In these studies, individuals with developmental disabilities exhibited normal behavior but showed atypical neurological signatures, indicating that they had the ability to achieve normal performance through a distinct neurological network. This review article investigates neural plasticity in terms of computer-based interventions as new pathways for training people with neurodevelopmental disorders and points out possible rehabilitation on people with Williams syndrome. Several possible intervention methods are discussed, including computer-assisted programs, virtual reality, and robotics. Each method has its own advantages for the intervention approach. With training, people with neurodevelopmental disorders can achieve normal-like behavioral performance and function in typical neurological mechanisms.

Keywords: Brain plasticity; Cognitive interventions, Robotics; Computer-based technology; Virtual reality

Introduction

Speech therapy is believed to benefit people who need articulation adjustment and speech training. The same concept is applicable when cognitive interventions are implemented for people with developmental disabilities. Several studies have reported improvements after behavioral or computer-assisted cognitive training programs were used as intervention tools for patients. The positive influence of such interventions has been observed in people with developmental disabilities and neurological disorders. This article addressed a possible research direction for assisting people with Williams syndrome (WS), a rare genetic disorder caused by gene mutation on chromosome 7q11.23 that results in mental retardation. Individuals with WS have an average IQ score of 55 [1]. Previous research efforts mainly focused on investigating the uneven cognitive profiles of this clinical population, with relatively good language and face processing skills but other cognitive functions such as visuospatial perception are relatively limited [2,3]. Few studies have examined the potential cognitive interventions for people with WS. A growing body of evidence shows that there is an asymmetry in the brain and behavioral performances in both verbal and nonverbal domains of people with WS, suggesting that they behave normally but exhibit atypical brain signatures both for processing language [4] and faces [5,6].

Neural plasticity is applicable to a wide range of neurodevelopmental disorders. The basic concept is an experience-dependent process for shaping learning and memory in both animals and humans. There is abundant evidence on neural plasticity and impact on behaviors, such as visual deprivation in animals with reduced visual acuity [7], nutritional deficiency during development, stressful events, adverse experiences during early life, maternal separation, maternal deprivation, and low maternal care [8]. This evidence points out general patterns of boosted neuronal and synaptic activities. These biological changes and findings demonstrate the impact of enriched environments and stimulation from various surroundings. In addition, early development plays an important role in brain plasticity due to early intervention program improves cognitive performance in preterm infants and parent-infant relationships. In caring for preterm infants, kangaroo care or skin-to-skin contact helps to build emotional bonding between mothers and preterm infants.

This contact improves maternal behaviors and response to infants' needs. Other programs such as a newborn individualized developmental care and assessment program creates short-term benefits and has a significantly positive influences on brain function and motor development [9]. Other interventions on neurodevelopmental disorders such as the program for creating opportunities for parent empowerment facilitate parental care and parent-infant interaction. Early intervention is one of the methods to fulfill this purpose. The basic rationale for early intervention is to create enriched environments for cared children. Toward this, many home-based and family-centered practices and programs have been developed. The concept of epigenetics relates to the interaction between genes and environments, and these two factors influence development and take effect on intervention on neurodevelopmental disabilities.

Li et al. [10] used a meta-analysis method on 17 studies, including studies on people with mild cognitive impairment (MCI) to identify potential improvements in cognitive abilities after training. The results revealed improvements in overall cognition and self-reported ratings on depression and anxiety. The overall improvement in cognition included language, episodic memory, semantic memory, executive functions, working memory, visuospatial ability, attention, processing speed, quality of life, and activities of daily life. Cognitive interventions have proven to be efficient tools for enhancing the cognitive and functional abilities of people with MCI. Neuroimaging studies can demonstrate in the future the pre- and post-training states of the MCI brain.

Bauminger's study [11] aimed to improve understanding on social and emotional information and social interactions with appropriate ways for people with high-functioning autism. An intervention program was structured into a three-hour per week format over a seven- month period, and it was applied to 15 clinical individuals. This intervention program involved cooperation with the clinical child, his or her age-equivalent peer, a schoolteacher, and the child's parents. The teachers taught planned topics on social knowledge weekly in class, and autistic children practiced learning essential social skills with peers after school and during school recess. At home, parents interacted with children based on their social skills. Significant improvements in understanding social and emotional cues and social interactions with participants' peers with high-functioning autism emerged. It is predicted that more participants would increase generalization on the usefulness of this intervention program.

In this review article, several possible intervention methods are discussed, including computer-assisted programs, virtual reality, and robotics. Each method has its own advantages for the intervention approach. Aiming at hoping these intervention methods can be useful tools on people with neurodevelopmental disabilities. With rehabilitation-based intervention on neuronal changes, normal-like behaviors on people with special needs could be reached.

Cognitive Interventions using Computer-Assisted Programs

Bauminger [11] conducted a 7-month cognitive behavioral intervention program on children with high-functioning autism (HFA) and evaluated the efficacy of this intervention in improving social cognition and social interaction of individuals with WS. As part of this intervention, children with HFA received three different types of training aimed at improving their social and cognitive shortcomings. First, they were trained in problem-solving skills by composing stories that required cognitive reasoning. Their stories were evaluated into five categories: activity (active vs. passive), relevance, number of solutions, variety, and content. Second, they were trained to recognize complex emotions (e.g., guilt, embarrassment, loneliness) and asked to identify a specific event related to that emotion and include an audience who witnessed the emotional display. Third, this intervention was geared toward interpersonal interaction with peers, with guidance from teachers and parents. For example, children were taught to initiate a conversation, deal with confronting a friend, and share with a friend. In addition, these children were involved in peer meetings that emphasized reciprocity and continuity in communication, such as making a phone call to practice social skills and initiate conversations. These interventions improved problem solving skills, understanding complex emotions, and engaging in pro-social behaviors. Although this study lacked a control group, the significant improvement after treatment, compared to the previous condition, indicates that these children with HFA were able to learn and recognize emotions and understand social cognition through training.

In the study by Golan & Baron-Cohen [12], individuals with Asperger Syndrome (AS) and HFA were trained using computer-based programs to recognize the contexts of face and voice emotions. This training aimed at improving socio-emotional abilities of these clinical individuals. Participants in the intervention group underwent a 2-hour training every day for 10 to 15 weeks to recognize complex emotions such as insincerity and other mental states. Participants were evaluated before and after the intervention. Each participant was evaluated using several software programs, including the Cambridge Mind-Reading Face-Voice Battery, psychometric analysis to recognize mental states using formats such as reading the mind in the eyes, voice, and films. Two control groups included individuals with same syndrome (AS and HFA) who did not receive the interventions and those with typical development. It was hypothesized that the two clinical groups would perform worse before the intervention than typical developers and AS individuals and HFA individuals would improve after taking the training with software programs. These results confirmed the hypotheses. Individuals with AS and individuals with HFA who received training using interactive, multimedia, and educational software improved to recognize complex emotions and mental states, proving that computer-based interventions can help people with neurodevelopmental

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disabilities.

A study by Diamond & Lee [13] investigating the executive function of 4-year-old children with attention deficit hyperactivity disorder showed improvements in working memory and reasoning after training with computer games. Similar benefits were observed in a selective attention task in 4- and 6-year-old children. These participants also showed improvements in two of the three inhibition tasks. Other interventions that are considered effective in improving executive function include aerobic exercises, traditional taekwondo, mindfulness training (e.g., yoga), and appropriate curriculum design for children with specific needs. This qualitative change in cognitive behavior after using technology-based training programs can be observed not only in people with developmental disabilities but also in people with neurological disorders. A study of people with Alzheimer's disease (AD) using computer-assisted training programs showed domain-specific effects after six weeks of intensive practice [14]. These clinical participants received intervention assignments, including listening, reading, and playing a visuospatial oriented computer game to recover their brain plasticity. Their memory (and/or learning), language (and/or visuospatial cognition), and attention (and/or executive function) were tested before and after the training to assess the outcome of this intervention. Participants with AD showed improved memory and learning compared to a control group, but they exhibited less improvement in visuospatial cognitive functioning (except for the spatial span test). Further studies are necessary to clarify why certain domains are amenable to training, whereas others are not, these results indicate that computer-based interventions are an effective approach for people with neurological disorders. For instance, another study by Cipriani, Bianchett & Trabucchi [15] on cognitive rehabilitation for people with AD showed that computer-based cognitive training improved participants' neuropsychological functioning in outcomes such as attention, memory, perception, visuospatial cognition, language, and nonverbal intelligence. A 16-day training program spread across 4 weeks evaluated participants' performance before and after the intervention based on their total score, time taken, and number of errors. Another group of people with mild cognitive impairment (MCI) was recruited for this study. The results showed that both people with AD and those with MCI benefited from receiving the computer-based neuropsychological training program.

Schizophrenia, another neurocognitive disorder, has also been shown to benefit from computer-assisted cognitive remediation [16,17]. Kurts et al. [16] reported that patients undertook a 100-hour, yearlong intervention program aimed at improving their attention in verbal and non-verbal memory and language processing in visual and auditory modalities. The pre- and post-training assessments were compared to evaluate the impact of the intervention. The results showed significant improvement in the working memory of patients with schizophrenia, particularly in digit span and arithmetic assessments. This finding further supports the use of computer-assisted cognitive remediation for people with neurocognitive deficits. Additionally, Bellucci et al. 's study [17] shows that the negative symptoms of patients with schizophrenia were largely reduced after they participated in computer-based rehabilitation for cognitive functioning.

Computer-based intervention has proven beneficial to people with autism, who pay more attention, learn more vocabulary, improve motivation, and stay focused for longer periods. This effect persisted even after 30 days of training, indicating the efficacy of computer-based interventions in people with autism [18]. Ploog, Scharf, Nelson & Brooks [19] reviewed studies on interventions for people with autism spectrum disorders (ASD) using computer-based assistance. The results indicated positive outcomes with technological interventions, such as increased vocabulary and grammar in reading and phonological awareness. In a study assessing the efficacy of learning in people with ASD by comparing teacher-alone, computer assisted technology (CAT)-alone, and teachers with CAT approaches, the results revealed that people with ASD benefited from teachers using the CAT approach as the control mechanism. However, while healthy controls did not show an advantage from the teacher-alone approach, people with ASD showed equivalent efficacy to teacher-alone methods as they gained from teachers using the CAT approach but failed to benefit from the CAT-alone method. Another study examined whether face is an important factor in interventions other than voice-only language training in people with ASD. The results showed that bimodal training of face and voice is superior to the voice-only training method in enhancing the language abilities of clinical individuals; for example, learning better and memorizing vocabulary. Thus, visual cues have proven to be a trainable facet in people with special needs. Computer-assisted technology interventions are a useful tool in improving the abilities of people with ASD, partially because of the enjoyment and low anxiety induced by playing computer games. Interventions with CAT have been demonstrated to be efficient in training the theory of mind. However, caution must be exercised with a more rigorous research design. Controlled groups should be recruited and the number of participants with ASD must be increased while conducting research on people with ASD to generate valid conclusions [19].

Preschoolers (3-5 years of age) are capable of using computers, and it has been demonstrated that they benefited from interactions with computers on the development of various cognitive abilities. Cochran & Nelson [20] made an extremely important suggestion of using developmentally appropriate software to train preschoolers. The inclusion of computer- based interventions is essential in speech and language therapy. These programs must be educational, interactive, and multimedia covering vocabulary, syntax, phonological awareness, narratives, contextual comprehension to improve narrative skills. Animations help preschoolers to retell stories compared to narrative text. Computer-based training programs are tools that enhance rather than replace interventions. Clinicians play an important role in

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assisting people with developmental disabilities with primary enhancement in their abilities before and after taking computer activities.

Schery & O'Connor [21] reviewed earlier studies to compare the effectiveness of computer-assisted intervention programs with traditional training programs on children with special needs and revealed that no differences were observed between the two programs, implying that computer-assisted interventions are as useful as the conventional methods. The possible factor resulting in the indifference between the two groups could be the presence of a paraprofessional accompanying person or a clinician in both training programs. Later, three experiments were conducted to investigate vocabulary growth, general linguistic skills, and interpersonal relationships. One of the pairs received a computer enhancement program and the other pair took a computer training program. Each computer training program with 16 participants lasted 10 weeks, twice a week, and was of 30 minutes. After the planned computer-assisted program ended, each participant received traditional classroom training programs. The results showed that children with developmental disabilities in language and cognition benefited from computer training, even during the middle of the training program (around five weeks). Positive effects on vocabulary growth, interpersonal social interactions, and language skills emerged among the participants with developmental disabilities. It is suggested that cautious planning of intervention programs, specifically tailored to meet children's needs with the selection of software and designed contexts for intervention is required in developing computer-assisted interventions on language and cognition in special populations.

Cognitive Interventions Using Virtual Reality

Virtual reality (VR) is a promising intervention tool that can be used in individuals with autism. Children with autism may benefit from this interactive technology in various aspects of everyday life, such as pedestrian safety while crossing streets. However, VR is not a common tool, and it is not easy to conduct a study using this technology. This tool can be used to train people with neurodevelopmental disabilities on everyday skills such as face recognition and differentiating family members from strangers. A study compared active video games with sedentary video games with objective indexes, such as waist size and screen time of players. The comparison confirmed that children participating in active video games have less sedentary time (more active activity) and is associated with smaller waist size circumference after the intervention. The intervention period varied from one week to six months. An issue left would be stability after intervention [22].

Virtual Reality Social Cognition Training (VR-SCT) is used to train people with ASD to gain social abilities in three aspects, including verbal and nonverbal emotional recognition, theory of mind, and conversation skills. In verbal and nonverbal emotional recognition, advanced clinical solutions for the Wechsler Adult Intelligence Scale–Fourth Edition (WAIS-IV) and Wechsler Intelligence Scale for Children–Fourth Edition (WSIC-IV) social perception subtests were used to test social affect and social prosody in individuals with ASD. In the theory of mind test, mindreading and triangular tests were used to probe the mentalizing abilities of individuals with ASD. In the conversation skills test, role-played semi-structured conversations were tested. Using VR as an intervention, Kandalaft et al. [23] used a pre-test and post-test method to probe social cognition ability in people with ASD. Several social settings are included in social cognition training, such as initiating conversations, addressing conflicts with roommates, and attending job interviews. The results revealed improved performances in social affect, social prosody recognition, mindreading, and triangular animation comprehension in people with ASD. Overall, VR-SCT is a valid tool for training social abilities in individuals with ASD. Generally speaking, VR is a promising tool in rehabilitation that trains patients to shape neural responses. After brain damage, patients were changed in their neural pathways or cognition capabilities, including attention, working memory, and executive function. Rehabilitation with VR can take advantage of learning and reshape the development of neural processes [24].

VR can have a wide range of applications, including cognitive, vocational, and social for patients with special needs. VR seems like a paradigm shift in interventions from traditional assessments to computers and information training. This new type of intervention for human-machine interaction shows a new direction in revolution of rehabilitation. There are several advantages to the application of VR interventions in neurodevelopmental disorders. First, VR helps create real-world environments that are natural to patients and similar to their daily life. Second, it makes hazardous situations possible in training, such as driving intervention with simulation of brain trauma injury. Third, it provides immediate feedback from trials without the limitations of funding resources or the availability of specialists. Fourth, it combines homebound and external environments, which contribute to patients' training with major benefits. Fifth, the most important point is creating individualized learning. Patients have individual differences in the severity of illness, type of injuries, and duration of emotion expression. Put together, individualized training is reasonable and necessary. Schultheis & Rizzo [25] reported successful interventions with VR while evaluating the driving ability of patients with brain injury and classroom education in children with attention deficit and hyperactivity disorders (ADHD). VR is an important training tool, which is inexpensive compared to the traditional assessment in rehabilitation. More systematic and scientific research is required.

Morina, Ijntema, Meyerbröker & Emmelkamp [26] demonstrate the effectiveness of virtual reality exposure treatment (VRET) psychotherapy as a useful treatment method, which has been proven to be useful in the treatment of anxiety disorders and various phobias. Fifteen studies were selected as a small database to analyze their effect sizes. Patient outcomes improved to reduce

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phobias in those who received VRET. No difference was observed between the post-assessments after VRET and in vivo treatments. Thus, it was concluded that VRET changes behavior in real life. However, a small database is a limitation that must be considered.

For people with cerebral palsy and traumatic brain injuries, VR is a useful intervention tool. After training, patients with cerebral palsy can improve their capacity for physical activity and performance. Wii and Mitti software programs are demonstrated to be able to improve patients' physical activity and performance [27].

Application of VR is a relatively young technological advancement [24]. Successful interventions depend on several factors, including repetitive and intensive training, patients' motivation and engagement, interaction with the environment, and severity of impairments. More serious impairments are, and more repetitive and stronger intensive interventions should be received. Indeed, the advent of technologies has boosted intervention, but more scientific evidence should be provided to clinical practitioners. VR enriches the environment for patients to interact with the external world naturally without limitations of time and space. Promising developments in VR interventions in rehabilitation can be expected in future.

Goldsmith & LeBlanc [18] observed the potential for integrating robotic developments with research on developmental disorders. This is a relatively new multidisciplinary research field that requires researchers from various specialties. More scientific research must be conducted to explore possible interventions using technologies.

Cognitive Interventions Using Robotics

Robotics is another potential intervention tool for children with ASD because robotic therapy provides a simplified social environment and improves their social interaction ability. The mechanistic characteristics of computers increase autistic children's willing to interact with robotics. Children with ASD view robotics as partners or playmates and are motivated to interact with them. This therapeutic intervention shows potential for future investigations of social interactions [18]. The AuRoRA project in the United Kingdom has been conducting studies on this issue. Researchers have developed several versions of robots to train social interactions of children with ASD. Non-human characteristics improve the social interactions of autistic people with robots; for instance, one of the invented versions was a car with a face-like front to train eye contact of autistic children.

Robotic technology has proven to be a useful tool for treating people with ASD. Various types of robots are invented, and the effects of intervention in social and emotional improvement are obvious. Many robots have been invented for this purpose, such as ROBOTA for training social skills, joint attention impairments, and body movements. The KASPAR was designed to train autistic children to learn to collaborate with adults, recognize visual perspective skills, and learn from other people's perspectives. Other robots, such as TITO, were invented to train autistic people to recognize facial expressions. This robot-assisted therapy has been working well with different intervention levels on many social skills and interactions. Robots have a positive impact on children's engagement. Even the QUEBALL robot helped children with autism enhance their learning and playing abilities through distinct modalities, including kinetics, vision, audio, and tactile. Other robots trained children with autism to reduce stereotyped behaviors and refine their social skills. Robot-assisted treatment is important and useful in interventions for people with autism. In fact, people with autism are willing to interact with robots and are comfortable with them. However, robotic technology has ethical issues as it seems inappropriate to replace humans with robots in therapy. Though ethnic issues remain unresolved, it cannot be denied that robots have the potential to enhance the social and emotional cognition of people with autism. Comparisons of healthy controls have demonstrated that more visual perception leads to better emotion recognition. These results suggest possible directions for future interventions [28].

Intervention robots were further divided into three types: humanoid, non-humanoid, and non-biological. Syriopoulou-Delli [29] used a car-type non-biological robot as an intervention tool to train people with autism, aimed at improving their social skills. With this objective, the EDISON robot was invented with several play scenarios included in a 6-month intervention program. After interacting with this robot, children with autism got along with teachers and others for longer periods, preferred to be isolated less, and reduced negative behaviors. Hence, robots contributed to interventions that improved autistic individuals' social skills and enabled them to follow instructions. How can this intervention be applied to other neurodevelopmental disorders? How can this intervention shape neural plasticity of the brain of neurodevelopmental disabilities?

Asymmetry of Brain and Behavioral Performances in Williams Syndrome

People with Williams syndrome (WS) show local preference but global ignorance in processing perceptions, including visuospatial construction, emotional identification, and facial recognition. For instance, in visuospatial constructive problems, people with WS drew only parts of objects that were shown to them as images, such as a bicycle and a swimming pool in a copying task [2]. Meanwhile, in block-design tasks, people with WS focused only on parts of the object rather than the object as a whole. Generally, individuals with WS lack the form of configurations in arrangements. In terms of emotional recognition, Gagliardi et al. [30] presented to individuals with WS animated facial expressions that mimicked human emotions, such as anger, disgust, happiness, sadness, and fear. The results showed that participants with WS performed as well as the mental age-matched healthy children but were inferior to chronological age-matched healthy adults

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in their sensitivities to different emotional expressions. The study concluded that the limited ability of individuals with WS to recognize facial expressions was due to a deficiency in coding configural information. Moreover, although the healthy controls showed a correlation between age and the recognition of emotional expressions, people with WS failed to show this pattern. Instead, their intelligence, rather than age, correlated with correctness of recognition, indicating that their ability to recognize expressions would not improve with age. These studies revealed that people with WS processed facial expressions in atypical manner.

This processing preference was also observed in facial identification. Hsu & Chen [5] asked individuals with WS to detect facial configuration. A model face was displayed on the screen, followed by a target face with changed features (eyes, mouth) and configurations. The participants had to judge whether each face probe was the same as or different from the target face. This study showed that WS individuals recognized feature-changed faces fairly easily compared with the controls, but they had difficulty in recognizing faces in which the configuration had been changed. This normal-like behavioral finding in face recognition is similar to observations in a study on face identification [6]. In this study, two faces were displayed consecutively with one face as the prime and the other as the target. Target faces were presented in upright or inverted orientations. As inverted faces lose configuration information but retain featural cues [31], it was hypothesized that normal participants would have difficulty in processing inverted faces. The results showed that people with WS have longer response times and make greater number of errors in processing inverted faces compared to the controls, suggesting that people with WS process faces exactly like normal controls. However, the neurological signatures recorded from event-related potentials between people with WS and controls were different. In Hsu and Chen's study [5], although the control group exhibited a difference in the left hemisphere when processing faces with changed facial features from configuration, participants with WS did not show this pattern; in the right hemisphere, the control group processed the two types of changed facial features differently, whereas individuals with WS did not show a significant difference in their brainwaves in processing these two distinct types of changed faces.

Mills et al. [6] demonstrated this asymmetry between the brain and behavioral performance in facial processing for people with WS. A difference was observed at the beginning of processing the task. Although the healthy controls responded to prime faces with a large N100 and a small N200, participants with WS showed a small N100 and a large N200. The difference was also observed when the target faces were shown to the two groups. Additionally, the controls showed an N320 negativity to upright faces, whereas the participants with WS showed this negativity when viewing both upright and inverted faces. Beyond behavioral performance, these neurophysiological findings show that people with WS have atypical face processing strategies.

People with WS showed a unique processing pattern in a verbal conceptual formation study with a false memory paradigm [4]. The behavioral performance of people with WS was the same as that of the controls, who showed a high number of false positives to non-presented semantically related items (i.e., lures). This suggests that both groups misrecognized the lures as old items that were presented during the acquisition stage. However, the brain signatures of the two groups showed distinct patterns. People with WS differentiated old from new items in a manner that was similar to controls, but they responded differently to the lure items. The controls processed lures as old items, whereas participants with WS recognized lures as new items. In both the verbal and non-verbal domains, individuals with WS exhibit an asymmetry between the apparent normality of the behavior and the difference in the brainwaves compared to controls. These results indicate that people with WS achieve a normal-like performance (compared to chronological age-matched or mental age-matched controls) via a distinctly different brain mechanism. The asymmetry demonstrates that people with developmental disabilities, such as WS, are able to react typically like developing controls through the use of cognitive interventions such as computer-assisted training programs that have been shown to be effective for individuals with developmental and neurological disorders.

Based on this review of cognitive impairments in visuospatial construction and emotional recognition in the non-verbal domain for people with WS, a possible intervention direction maybe the use of a computer-based training program to improve the cognitive abilities of this clinical group to reach a normal-like behavioral performance. Furthermore, based on these findings related to verbal and face processing in nonverbal domains, computer-assisted educational software may benefit WS individuals who exhibit an asymmetry between their behavior in the normal range and atypical neurological signatures compared to controls. It is hoped that people with WS may develop neurological mechanisms similar to those of typically developing individuals or reach normal-like behaviors with distinct neurological processing as compensatory strategies. Computer-assisted intervention training takes a short period and yields remarkable improvement in the cognitive abilities of people with developmental disabilities, such as high-functioning ASD, ADHD, and neurological disorders such as Alzheimer's disease and schizophrenia. Hence, people with WS may benefit from well-designed cognitive training, and effective rehabilitation on people with WS may be achieved in the future.

Rehabilitation-Based Interventions on Neuronal Changes

Calderoni et al. [32] reported considerable evidence proven in the early altered developmental trajectory of global and regional brain structures that shape brain modifications in people with ASD using fMRI after interventions based on reviewing studies

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from 2006 to 2015 on non-pharmacological interventions. Neuroimaging measurements can be considered objective in functional and structural plasticity due to rehabilitation therapy in autistic people. For instance, compensatory mechanisms have been observed in face processing in autistic individuals. These clinical populations showed activation at right superior parietal lobe rather than fusiform gyrus as in typically developing controls. This review confirmed that computer-assisted programs using neuroimaging techniques can improve intervention effects. Neurological level compensatory mechanisms activated the bilateral insula, posterior language regions, right postcentral gyrus, right subcortical regions, and connectivity among the frontal, parietal, and temporal regions. These compensatory mechanisms demonstrate critical plasticity in early life, even though developmental stages are so important in interventions, including school-age children and adults.

The term ASD covers the concepts of heterogeneity and complexity, which pose serious challenges in their studies. To date, the genetic origins of this disorder are controversial, including discoveries of 1p, 2q, 7q, 17q, and 19q. Some genetic models of ASD propose that gene mutation carriers are risk factors for ASD. Environmental factors, such as toxins, viruses, and immune functions, contribute to abnormal immunity in ASD. Dawson [33] proposed that there is a need to investigate how genes relate to environmental responses. Other neurobiological factors related to autistic traits have been identified, such as reduced Purkinje cells in the cerebellar cortex and increased cerebellar lobe size, leading to heightened repetitive behaviors and reduced social play. Brain abnormalities have been observed in individuals with ASD such as enlargement of the brain in the early stage and increased cerebral cortical gray matter causing atypical social and emotional behaviors. Neocortical and cerebellar development in atypical courses results in ASD. Put together, it is believed that early interventions are necessary for people with neurodevelopmental disorders. Early treatment can alter the developmental trajectories of ASD individuals in brain development and behavioral outcomes. The key point is how early the interventions should be. It is clear that neural atypicality changes the brain circuitry. In typically developing controls, the fusiform face area was activated in face processing; however, people with ASD showed the same activation in object processing. Moreover, people with ASD failed to differentiate familiar from unfamiliar faces and fearful faces from neutral faces. Early intensive interventions can prevent and make treatment effective in people with ASD to reduce the impact of genetic and environmental risk factors on behavioral and biological developments.

Developing the brain in different stages of life in people with neurodevelopmental disorders makes neuronal plasticity possible. Brain plasticity requires behavioral intervention for people with neurodevelopmental disorders. Previous studies have mainly focused on individuals experiencing neurodevelopmental disabilities for a long time. This sheds light on potential interventions for neurodevelopmental disorders in the future. This paper reviewed highlighted points with potential interventions on behavioral and neurological level with technologies in people with neurodevelopmental disorders, especially people with WS. These interventions could be new pathways leading to brain plasticity at behavioral and neurological levels.

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