

Progress and future prospects in diagnosis and treatment of ASD

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Abstract. This paper discusses Autism Spectrum Disorder (ASD), a combined developmental and neurological disorder that affects a person's conversation, behavioral, and human interaction ability. The article explores the diagnosis of ASD based on clinical observations of behavior and developmental history. It also looks at the potential internal and external causes of ASD, which include genetic abnormalities and exposure to chemicals in the environment. According to the paper's conclusion, early identification and intervention can help control symptoms and enhance the quality of life for persons with ASD, even though there is no known cure or medicine to treat the illness. The research can help identify new therapies and interventions to enable individuals with ASD and their families. Additionally, research can help raise awareness about ASD and help reduce the stigma surrounding it. Together, we can make a difference in the lives of those who have ASD and make sure they receive the care and support they require to live happy, meaningful lives.

Keywords: Autism Spectrum Disorder, Clinical Diagnose, Risk Factors, Treatment.

1. Introduction

According to Bleuler, the term "autism" is used to describe pathological self-admiration and inward isolation, where the Greek word "autós" means "self." When the word "autism" first appeared in the 1900s, it was used to describe schizophrenic individuals who had shut themselves off from the outside world [1].

Autism spectrum disorder (ASD), a neurological and developmental illness, has an impact on a patient's social abilities, especially how they interact with people, express themselves, acquire knowledge, and behave. This disease can also cause intelligence issues such as learning disabilities and delayed early development such as emotional, communication, cognitive, and physical development. The significant problem is seen when solving math questions and language processing. Although ASD can be diagnosed at any age, the term "developmental disorder" is used since symptoms usually appear between the ages of one and two. People with ASD may also have different ways of learning, moving, or paying attention. It can also cause mental problems such as anxiety, depression, and showing obsessive and compulsive behaviors. It can even affect physical appearances such as a long and narrow face, prominent jaw, large forehead, soft skin, flat feet, etc. These characteristics can make their life very challenging. According to statistics from the CDC published in 2023, one in thirty-six children in the U.S. has an ASD diagnosis, and males are four times more likely to get an ASD diagnosis than girls [2].

Although ASD may be accurately identified as early as age two, most kids are not diagnosed until they are four years old. Despite the early age of onset of autism, 44% of children with ASD have normal to above average IQ levels (IQ >85), 25% have intermediate IQ scores (IQ 71-85), and 31% have intellectual difficulties (IQ 70) [2]. Lamentably, there is no way to prevent a cure, and there is currently no medication to treat ASD. Therefore, it is essential to understand the causes of ASD and to find out the possible treatments for curing ASD.

2. Clinical diagnose

There isn't yet a particular test, like a blood test, to diagnose ASD. Making the diagnosis might be difficult. Doctors will look at the child's behavior and developmental history to make a diagnosis. The criteria below are how the doctors measure ASD.

Doctors' criteria for measuring whether a patient has ASD:

In order to get an ASD diagnosis, a person must meet all three criteria listed in the Diagnostic and Statistical Manual of Mental Disorders (DSM):

Social and emotional reciprocity issues, including challenges relating to others, conversing back and forth, expressing passions, and expressing or understanding sentiments.

Having trouble recognizing nonverbal clues such as facial expressions or gestures, such as improper eye contact and physical expressions, are employed in nonverbal communication during social interactions.

Problems forming and maintaining connections with others (apart from caregivers), such as lacking curiosity in others, trouble adjusting to various social situations, and trouble sharing creative play with others [3].

3. Cause of ASD

3.1. External factors

Currently, there are some suspected causes that researchers are currently exploring, such as problems related to brain connections, growth or overgrowth in particular areas, metabolism, and the immune system. According to an article written by Landrigan and Philip J, there are some indirect pieces of evidence showing that environmental factors may contribute to autism coming from studies investigating the effect of some chemicals on the developing brain, such as lead, ethyl alcohol, and methyl mercury. However, there is already evidence that shows that during early pregnancy, drugs such as thalidomide, misoprostol, and valproic acid increase the rate of ASD. The drug valproic acid is widely used in research related to ASD as a means of producing rats with autism. Other risks that have already been established by research include maternal rubella infection, exposure to organophosphate insecticides, and chlorpyrifos. Dozens of synthetic chemicals are currently present in children's environments, yet only half of them have undergone neurodevelopmental toxicity testing. According to the researched done, it is obvious that there are a significant number of tests that need to be done to prove entirely that whether there is no relationship between ASD and exposure to chemicals or not [4, 5].

The other theory that has been debated frequently in many ASD centers is the link between autism and childhood vaccines. After various research, there still is no proof that suggests any link between ASD with any currently existing vaccines. Interestingly, the first study that brings up the debate on whether vaccine contributes to ASD has been retracted due to its poor design and questionable research methods.

3.2. Inner factors

There are many distinct genes that seems to contribute in ASD. Also, there are pieces of evidence suggesting a link between ASD and genetic disorders such as Rett syndrome or Fragile X syndrome. After researches, scientists come to a conclusion that gene mutation is the most frequent cause of ASD. For example, a mutation on the 2756th nucleotide where an adenine mutated into a thymine is suspected

to be a factor of autism. As mutation is entirely random, there are some that can be inherited and others that may occur spontaneously.

There are shreds of evidence suggesting that 5% to 15% of individuals with ASD also have other rare single-gene disorders and chromosomal rearrangements. Another factor is copying number variation, which is a circumstance where the number of copies of a specific DNA segment varies among different genomes from different individuals, and the length of the chain has no restriction. There is CNV happening in 5% to 10% of ASD events [6, 7].

The fact that ASD is inheritable is known through research, but what remains unknown of it.

3.2.1. CNV (copy number variation). As mentioned before, CNV is something that occurs when a specific piece of gene appears to have different numbers of its copy in different genomes. There can be enormous consequences caused by CNV. For example, the gene that codes for amylase, which is an enzyme present mainly in the mouth that is responsible for the breakdown of starch. Researchers found out that there are more copies of this gene in areas where starchy foods are historically important than in people living in areas where starchy foods are not that important historically. This may suggest that people with more genes that code for amylase living in an area in which the main source of food contains starch are more likely to survive and pass on the gene, which is similar to the theory that explains antibiotic resistance in bacteria. In a study, genome-wide characteristics of rare CNV in ASD are analyzed using dense genotyping arrays. In the study, 996 people with ASD who had European ancestry were compared to 1,287 controls who were matched. According to the study, there is a larger global load of uncommon, genic CNVs in ASD patients.

3.2.2. Fragile X syndrome. It is an inherited condition that can cause developmental delays, intellectual limitations, cognitive and behavioral disorders, physical deviations, anxiety, attention-deficiency or hyperactive issues, and autistic spectrum disorder are just a few of the concerns that can arise. It is the most prevalent inherited form of mental and developmental impairment. This syndrome is caused by the broken part of the X chromosome. It shows that the X chromosomes has broken parts under the microscope [8].

3.3. ASD caused by spontaneous mutant genes

Due to its extreme genetic heterogeneity, ASD can result from both heritable and spontaneous gene mutations. In the past decade, more than 1,000 genes have been discovered to be related to ASD, but a larger association has not been confirmed. Rare mutations in the genes SHANK3, ARID1B, ASH1L, CHD2, CHD8, DYRK1A, POGZ, and SYNGAP1 have been linked to ASD, frequently together with other indications and symptoms [9].

3.3.1. SHANK3. The synaptic scaffolding protein SHANK3, which is prevalent in the postsynaptic density of excitatory synapses, is essential for the development, maturation, and maintenance of synapses [10]. Patients with ASD who have the SHANK3 mutation will exhibit repetitive behaviors as well as poor communication and socializing abilities. At least 43 SHANK3 mutations have been identified in a specific phenotypic group of ASD patients. It is highly likely that the SHANK3 gene contributes to the neuropathology and etiology of ASD [11]. However, the association between SHANK3 gene variants and the propensity for ASD is currently unclear. Researchers believe that a disruption in neural transmission may cause the disease. The chance of acquiring this complex illness is thought to be influenced by changes in other genes and environmental factors [12].

3.3.2. ARID1B. The ARID1B gene encodes a protein that functions as a single component in a variety of SWI/SNF protein complexes [13]. Through chromatin remodeling, the SWI/SNF protein aids in the regulation of gene expression. Gene expression throughout development is controlled by the process of chromatin remodeling. Patients with ASD who carry the ARID1B mutation will display traits including repetitive behavior, intellectual impairment, and communication difficulties. The ARID1B gene

variations linked to ASD cause the ARID1B protein to be produced in less quantity or with a diminished ability to perform its role in chromatin remodeling [13]. Although the precise link between the variations and ASD is unknown, these changes probably interfere with normal brain development and the regulation of gene expression.

3.3.3. *ASH1L*. Lysine-specific methyltransferase 2H is an enzyme that is produced by the *ASH1L* gene, also known as KMT2H, and is present in several bodily organs and tissues. A histone methyltransferase is lysine-specific methyltransferase 2H. Enzymes called histone methyltransferases alter the histone proteins. Histones are chromosome-shaping structural proteins that adhere to (bind to) DNA [14]. Lack of the lysine-specific methyltransferase 2H will disrupt the histone methyltransferase with the *ASH1L* gene mutation, increasing the likelihood of developing ASD [15]. ASD patients who have the *ASH1L* mutation gene will exhibit symptoms like poor communication and social skills and repetitive behavior. Many genes that are related to ASD are involved in the brain. Some affected the development of brain cells, while some affected the number of neurons. Many more ASD-related genes influence development by modulating the activity of numerous additional genes or proteins. The precise connection between these genes and ASD is yet unclear, though.

4. Treatment for ASD

Currently, there is no cure for the disease, and there is not cure that can fit all patients. The most common type of treatment currently in use is maximizing the child's ability, trying to let this outweigh the reduction caused by ASD. It normally happens in the preschool period and helps children learn communication, social, and behavior skills. The treatments can vary based on the clinic and doctor [16].

4.1. Behavior and communication therapy

Some therapies concentrate on eliminating negative habits and introducing new skills that can help children to live a normal life. Other programs Concentrate on teaching youngsters how to behave in social situations or how to communicate effectively with others. With the help of applied behavior analysis, children can learn new skills using a reward-based motivation system.

4.2. Education Therapy

Children with ASD typically show high IQ, and the programs involve a team of specialists and a variety of activities aiming to improve social skills, behavior, and communication.

4.3. Family therapies

This is based on the bond between relatives and teaching both parents and other family members about how to take care and respond to children with ASD to promote their communication skills and daily living skills.

4.4. Medication

There is currently no medication that can cure ASD, but there are certain ones that can control this disease. For example, some drugs will be prescribed if the children are diagnosed as hyperactive, antipsychotic drugs are sometimes employed to address serious behavioral issues and antidepressants like Sertraline are given to battle with anxiety.

Beside treating autism only, it is important for other issues to be monitored and taken care of.

Medical issues: It is likely that children suffering from ASD may suffer from other issues too, such as epilepsy, sleep disorder, limited food preferences and problem with guts.

Problem transforming from childhood to adulthood: it is difficult for people with ASD to understand and accept external information, such as the change to their bodies and the complex social situation that they may face as they grow up. There also may be some problems that the children with ASD possess and that can't be accept during adulthood such as social problems.

Mental health disorders: As suggested above, ASD normally comes with some other diseases and especially mental diseases, such as anxiety. These also need to be monitored and treated when treating ASD [17].

Besides treating autism only, it is important for other issues to be monitored and taken care of. Firstly, there are some medical issues, children with autism spectrum condition may also suffer from medical concerns such as epilepsy, difficulties with sleep, restricted food choices, or stomach problems [17]. Secondly, children may have problems transforming from childhood to adulthood. It is difficult for people with ASD to understand and accept external information, such as the changes to their bodies and the complex social situations they may face as they grow up. There also may be some problems that the children with ASD possess that can't be accepted during adulthood such as social problems. Thirdly are mental health disorders. As suggested above, ASD normally comes with some other diseases especially mental diseases, such as anxiety [17].

5. Future considerations

Finding a cure or effective therapy for ASD has proven to be difficult since it is a complicated disorder. However, there is optimism that a medication or cure may eventually be discovered because to continuous research and technological developments. Although currently, ASD cannot be cured and cannot be treated with medicine at this time. The quality of life for people with ASD can be enhanced by a variety of therapies and interventions, including behavioral therapies, occupational therapy, language therapy, speech therapy, and integration of senses therapy. These treatments can aid people with ASD in social skill development, communication improvement, and behavior management.

One potential avenue for future treatment of ASD is through personalized medicine. With advances in genetics and imaging technologies, doctors may be able to identify specific genetic or neurobiological markers through sequence inspection, a method that can be used to locate gene mutations, that are associated with ASD in individual -patients. Based on the specific gene mutation for each patient, doctors could allow for more targeted and effective treatments that are tailored to each individual's unique needs. Currently, there are no specific drugs that cure ASD, but drugs that could regulate the symptoms, such as Sertraline, has been used to treat self-harm, hostility, anxiety, and depression in people with ASD.

Additionally, research into non-pharmacological interventions, such as behavioral therapies and lifestyle changes, may also provide promising avenues for treating ASD. Other ASD symptoms may also benefit from other behavioral therapies, including social skills instruction and cognitive-behavioral therapy.

A possible therapy called the Stem cell therapy is a potential treatment that is actively being researched. Stem cells in the body can develop into a variety of cell types, including brain cells. Therefore, stem cell treatment has the potential to enhance brain function in people with ASD by replacing or repairing damaged brain cells. Studies have shown that stem cell therapy has the potential to improve ASD symptoms in animal models, and clinical trials are underway to test its effectiveness in humans. In one study, researchers injected stem cells into the brains of mice with a condition similar to ASD, and the mice showed improved social behavior and reduced anxiety-like behaviors [18]. Another study involved injecting stem cells into the brains of children with ASD, and the results showed improvements in language, social interaction, and behavior [19]. Although these findings are encouraging, further studies are required to establish the security and efficacy of stem cell therapy in the treatment of ASD.

Ultimately, continued research and investment in innovative treatments and therapies will be crucial in improving outcomes for individuals living with ASD. Despite the fact that there is presently no treatment for ASD, continued research and technological developments provide hope for the future. The lives of people with ASD may one day be improved by potential treatments such behavioral therapies and stem cell therapy. It is crucial to keep funding research efforts to find a cure for ASD and give affected people and their families the assistance they require to flourish.

6. Conclusion

In conclusion, ASD is a complicated neurological and developmental disease that affects a person's behavior, learning, communication, and social skills. ASD is difficult to diagnose since it is determined by behavioral and developmental history rather than by doing medical testing. There is presently no precise medical test for the diagnosis of ASD, but clinicians utilize specific criteria like the Diagnostic and Statistical Manual of Mental Disorders (DSM) to make the diagnosis. While there are suspected causes of ASD, such as problems related to brain connections, growth or overgrowth in particular areas, metabolism, and immune system, there is no clear external cause that has been confirmed. Additionally, a genetic test cannot be used to detect or diagnose ASD. This is because it's possible that a number of genes and environmental factors have a role in the sickness. ASD has been explicitly related to over 100 genes, however no one gene causes ASD every time it is altered; for instance, some ASD patients got a mutation on SHANK3, but other patients got a mutation on ADNP. There is evidence pointing to a connection between autism spectrum disorder (ASD) and genetic illnesses such as Fragile X syndrome, Rett syndrome, and mutations in genes. Researchers are still investigating the genetic elements that appear to be implicated in ASD. To help people with ASD and their families, it is critical to continue research into the causes of ASD and effective therapies.

While the causes of ASD are still being investigated, genetic factors appear to play a significant role. While environmental factors have been researched, there is currently no conclusive evidence to suggest a direct cause. However, environmental factors may contribute to ASD, and more research is needed to understand the link fully.

It is crucial to continue researching the possible causes and treatments for ASD in order to improve the lives of those affected by this disorder. In the end, we hope that future science can unsolved the mystery of ASD causes, find out the clear relationship between the mutated gene sequence and ASD, and discover the true cure of this disorder, to make this world a better place for all living beings.

Authors Contribution

All the authors contributed equally and their names were listed in alphabetical order.

References

- [1] News-Medical. (2019, February 26). Autism History. Retrieved July 16, 2023, from News-Medical.net website: <https://www.news-medical.net/health/Autism-History.aspx>
- [2] CDC. (2022). Signs and symptoms of autism spectrum disorders. Retrieved July 16, 2023, from Centers for Disease Control and Prevention website: <https://www.cdc.gov/ncbddd/autism/signs.html>
- [3] Autism Speaks. (2021). Autism Statistics and Facts. Retrieved July 16, 2023, from Autism Speaks website: <https://www.autismspeaks.org/autism-statistics-asd>
- [4] CAR Autism Roadmap. (2020, June 9). Diagnostic Criteria for Autism Spectrum Disorder in the DSM-5 | CHOP Research Institute. Retrieved from www.research.chop.edu website: <https://www.research.chop.edu/car-autism-roadmap/diagnostic-criteria-for-autism-spectrum-disorder-in-the-dsm-5>
- [5] Landrigan, P. J. (2010). What causes autism? Exploring the environmental contribution. *Current Opinion in Pediatrics*, 22(2):219–225.
- [6] Pinto, D., Pagnamenta, A.T., Klei, L., Anney, R., Merico, D., Regan, R., et al. (2010). Functional impact of global rare copy number variation in autism spectrum disorders. *Nature*, 466, 368–372. Retrieved February 23, 2018, from <https://www.nature.com/articles/nature09146>
- [7] Copy number variation (CNV) (no date) Genome.gov. Available at: <https://www.genome.gov/genetics-glossary/Copy-Number-Variation> (Accessed: 21 August 2023).
- [8] professional, C.C. medical (no date) Fragile X syndrome: Diagnosis, symptoms & treatment, Cleveland Clinic. Available at: <https://my.clevelandclinic.org/health/diseases/5476-fragile-x-syndrome> (Accessed: 28 August 2023).

- [9] National Library of Medicine. (2021, October 21). Autism spectrum disorder: MedlinePlus Genetics. Retrieved from medlineplus.gov website: <https://medlineplus.gov/genetics/condition/autism-spectrum-disorder/#causes>
- [10] Uchino, S., & Waga, C. (2013). SHANK3 as an autism spectrum disorder-associated gene. *Brain and Development*, 35(2), 106–110. <https://doi.org/10.1016/j.braindev.2012.05.013>
- [11] Hughes, V. (2012, October 17). SHANK3 mice comparisons reveal array of differences. Retrieved August 28, 2023, from Spectrum | Autism Research News website: <https://www.spectrumnews.org/news/shank3-mice-comparisons-reveal-array-of-differences/>
- [12] National Library of Medicine. (2017). SHANK3 gene: MedlinePlus Genetics. Retrieved August 28, 2023, from medlineplus.gov website: <https://medlineplus.gov/genetics/gene/shank3/#references>
- [13] National Library of Medicine. (2021a). ARID1B gene: MedlinePlus Genetics. Retrieved from medlineplus.gov website: <https://medlineplus.gov/genetics/gene/arid1b/>
- [14] National Library of Medicine. (2017a). ASH1L gene: MedlinePlus Genetics. Retrieved from medlineplus.gov website: <https://medlineplus.gov/genetics/gene/ash1l/>
- [15] Cheon, S.-H., Culver, A. M., Bagnell, A. M., Ritchie, F. D., Clytus, J. M., McCord, M., ... Lizarraga, S. B. (2020). ASH1L REGULATES THE STRUCTURAL DEVELOPMENT OF NEURONAL CIRCUITRY BY MODULATING BDNF/TrkB SIGNALING IN HUMAN NEURONS. *BioRxiv* (Cold Spring Harbor Laboratory). <https://doi.org/10.1101/2020.02.18.954586>
- [16] WebMD. (2016, December 29). What Are the Treatments for Autism? Retrieved from WebMD website: <https://www.webmd.com/brain/autism/understanding-autism-treatment>
- [17] Autism spectrum disorder (2018) Mayo Clinic. Available at: <https://www.mayoclinic.org/diseases-conditions/autism-spectrum-disorder/diagnosis-treatment/drc-20352934> (Accessed: 11 September 2023).
- [18] Ornoy, A., Weinstein-Fudim, L., & Ergaz, Z. (2019). Prevention or Amelioration of Autism-Like Symptoms in Animal Models: Will it Bring Us Closer to Treating Human ASD? *International Journal of Molecular Sciences*, 20(5), 1074. <https://doi.org/10.3390/ijms20051074>
- [19] Qu, J., Liu, Z., Li, L., Zou, Z., He, Z., Zhou, L., ... Ye, J. (2022). Efficacy and Safety of Stem Cell Therapy in Children With Autism Spectrum Disorders: A Systematic Review and Meta-Analysis. *Frontiers in Pediatrics*, 10(897398). <https://doi.org/10.3389/fped.2022.897398>