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REVIEW ARTICLE

Unravelling Autism: A Holistic Review of Diagnosis, Management, Strength and Future Directions

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Abstract

Autism spectrum disorder (ASD) is a complex neurological state that is marked by difficulties skills and interactions, alongside iterative behaviours and limiting interests. ASD affects around one in the US; one out of every 54 children have a diagnosis. usually coming in early infancy following full assessments by multidisciplinary teams. ASD symptoms vary greatly and are typically shown in two areas: social communication problems and repetitive behaviour. While the actual origins of ASD are unknown, evidence indicates a mix of genetic predispositions and environmental variables. Early intervention with occupational therapy, speech and language therapy and behavioural therapies and support for education is essential for better outcomes. Recent advancements in genetic research, neuroimaging and the growth of innovative ways to treat show promise for improving the understanding and management of ASD. This review seeks to present a complete picture of ASD, including its symptoms, causes and current and developing therapy. It also stresses the need for continued research and raising awareness to help those affected and their families.

Key words: Autism spectrum disorder; Diagnosis; Disease management; Applied behavioural analysis (ABA).

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Introduction

Autism spectrum disorder (ASD) is a complex developmental disease that is marked by recurrent behaviour, not having any interests and having trouble with social communication. People with ASD are very different in the degree to which their functioning is compromised, even though autism is classified as a lifelong condition.[1] Developmental delay in ASD is attributable to alterations in the brain. People with ASD might act, communicate and learn differently from other people. The severity index will determine that they could have trouble interacting and communicating with others both verbally and nonverbally.[2]

There are many different types of autism and no two people with autism have the same profile, even if certain traits may change as a child or adult grows. But problems usually fall into basic areas that can be measured correctly and don't change much over time.[3] These core domains include challenges in interpersonal relations, communication, interaction and confined or reiterating patterns of behaviour and interest. While the manifestation of specific behaviour may evolve as the individual grows, the underlying challenges associated with these core areas tend to persist. For instance, a child may struggle with initiating

conversations or understanding social cues, while an adolescent may face difficulties in forming and maintaining friendships. Understanding these core locations is important to tailor interventions and support plans that meet the specific needs of every individual. ASD is an intellectual disability impairment of considerable community concern for health. Its reach extends beyond the family and the affected child, with both direct and indirect effects for the country's costs, especially in the domains of healthcare, education support and rehabilitation services. Even though it is critical to know, there are few estimates of the prevalence of ASD in India on evidence. With a view to filling the gap, a structured analysis was undertaken in 2021 to determine how prevalent ASD is in the Indian population. The study comprises a meta-analysis of studies that have already been published in evaluating how prevalent ASD is in the community. Some of the databases that were searched for applicable literature were *PubMed*, *OvidSP* and *EMBASE*. STATA MP12 (*StataCorp*, College Station, TX, USA) was employed in examining the data. There were four studies that comprised the assessment, three of which were limited to people living in urban areas and one of which was among metropolitan and rural individuals. The rural study discovered that the aggregate rate among kids of 1–18 years of age was 0.11 % [95 % CI 0.01–0.20]. However, the four urban studies reported an aggregate incidence of 0.09 % (95 % CI 0.02–0.16) for children aged 0–15 years. Early identification of children with ASD is needed to offer them specialised, evidence-based therapies that can improve long-term outcomes.[4]

The phrase 'diagnostic odyssey' that defines the lengthy and difficult journey many families go through before finally getting a formal diagnosis can be avoided through early diagnosis. Much progress has been made in the research of early therapy for ASD. New technologies and designs are being increasingly utilised to better track.[5] Being diagnosed between the ages of two and five allows young children access to therapies that can enable them to enhance their motor skills, social interactions and speech. Early intervention may also reduce frustration and improve the child's overall quality of life.[6] Early intervention programs focus on helping children acquire fundamental skills, including cognitive, social, emotional, communication and physical skills.[7] The objective of the review is to help people understand and accept individuals with autism, to promote awareness among people regarding autism spectrum disorder and to get people involved in finding and treating ASD early on.

Core symptoms of ASD

Social interaction and communication abilities

People with ASD often have problems talking to others and interacting with others. Some common characteristics related to these difficulties consist of a) Evading eye contact, b) By nine months of age, they are not responding to their name, c) No external expression such as pleasure, sorrow, acrimony or amazed by 9 months, d) Disengaged in simple digital games, such as puzzles, e) Using limited body language, f) Absence of interest by 15 months (eg showing an object they like)[8] as seen in Figure 1.

Confined or iterative behaviour or interests

People with ASD may have strange habits or interests. These traits or interests set ASD apart from other diseases that only affect communication and social interaction.

The following are some instances of monotonous or limited ASD-related activities and interests:

- Arranges toys or other items in a line and becomes agitated when the sequence is altered;
- Repetition of words or phrases;
- Always uses toys in the same manner;
- Focuses on certain components of items, like wheels;
- Disturbed by minor changes.

Autism is referred to be a "spectrum" disease because individuals with the condition differ widely in the kind and severity of their symptoms. People of every gender, race, ethnicity and socioeconomic background can be diagnosed with ASD. Even though ASD can be a lifelong disease, as seen in Figure 1, treatments and programs can help improve a person's symptoms and day-to-day functioning.[9]

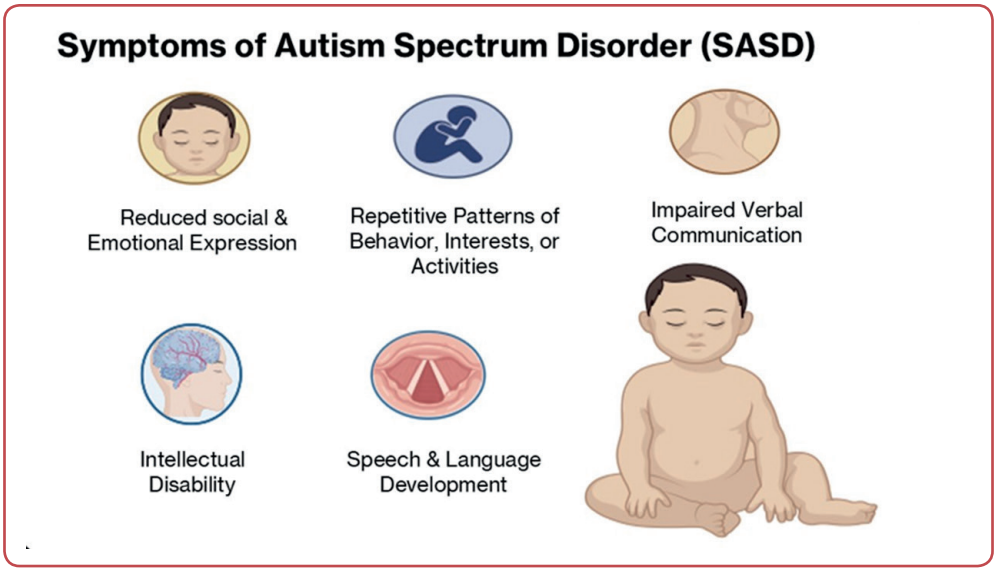

Figure 1: Symptoms of autism spectrum disorder (ASD)

Diagnosis of ASD

Because the signs of ASD are severe and complicated and because they often overlap with those of other psychiatric diseases, it is essential to utilise the right diagnostic tools and scales to properly identify ASD. This ensures better clinical management for ASD patients. Assessment tools often include consultation with parents or nurses, meeting sessions with the patient, direct observations and comprehensive medical evaluations that review family history of ASD or other intellectual disorders.[10] The typical age of diagnosis for ASD is approximately 4.5 years; some people don't get diagnosed until they are adults. You can find out if you have ASD as early as 15 to 18 months. Unfortunately, delayed diagnosis limits early intervention opportunities, which research has shown to greatly enhance the results for people with ASD. To make an ASD diagnosis, psychologists gather information from multiple sources, incorporating: patient consultation, monitoring of the patient's attitude, Tests of cognitive and language abilities, medical diagnosis to rule out other conditions, seeking advice from parents, educators, or other adults who can shed light on the patient's behavioural, emotional and social development.[11] In young children, the diagnosis process usually consists of two steps.

Step 1: Doing a broad development screening at well-child clinics. A doctor or other early childhood health care practitioner should check on every child every year. The American Academy of Paediatrics says that every child should have a developmental delay test at their well-child visits at 9, 18, 24 and 30 months. Also, during their 18- and 24-month well-child exams, children should be checked for autism in a unique way. If a child acts or functions differently throughout this screening process, the healthcare practitioner may propose that they get more tests. Kids who have a family member with ASD, show signs of ASD, have older parents, or have genetic problems are more likely to get ASD.

Step 2: More diagnostic testing finding ASD early and accurately is important since it shows the child's particular strengths and weaknesses. This advance finds caregivers identifying the most suitable services, educational programs and behavioural therapies for their child. A group of healthcare professionals performs diagnostic assessments, having experience in diagnosing ASD, it may encompass occupational therapists, developmental paediatricians, child neurologists, speech-language pathologists, child psychologists, psychiatrists and educational specialists. This thorough assessment may lead to an official diagnosis and treatment suggestions.[12] The assessment typically includes:

- Examination of the nervous system and medicine;
- Evaluation of the child's mental capacity;
- Evaluation of the infantile speech;
- Examination of the child's behaviour;
- Profound conversations regarding the behaviour and growth with caregivers;

- Evaluation of age suitable skills necessary for daily rituals;
- Comprehensive assessment may also involve: complete blood count (CBC tests), audiometry tests.

It has been demonstrated that therapy for people with ASD works best when it involves a lot of different people and focuses on the family. Because ASD is so complicated and different, which impacts speech, social skills, adaptive skills and cognitive abilities, input from specialists across different cores is essential for making a precise diagnosis and creating an operative treatment plan. When working with a child who has autism, A multidisciplinary team may have professionals in the following fields: Applied behaviour analysis (ABA) behavioural therapists, occupational therapists, physical therapists, speech-language pathologists, psychologists, developmental/behavioural paediatricians, neurologists, audiologists and paediatricians/primary care physicians (PCPs).

When dealing with a youngster that has autism, the multidisciplinary team can be strengthened even further by adopting a family-centred strategy. Several studies have demonstrated that family involvement in the child's treatment even throughout the evaluation and intervention has been linked to lower worry levels and higher levels of satisfaction. A multidisciplinary team approach to autism does not imply that experts from various fields see the child and collaborate separately. The team approach works best when there are close collaboration and communication amongst team members. When working with a child who has autism, specialists can cooperate in the following ways: multidisciplinary evaluations, joint debriefing, gathering, coordinating co-treating sessions, consistent communication (exchanging clinical experiences), maintaining current records from various specialists who work with the child. Families can help encourage this conversation. Parents can accomplish this by sharing information regarding their child's visits to other specialists with the professionals working with them, as well as any tactics that appear to perform well during other therapy sessions.[13]

Causes of ASD

ASD is a neurological condition that impacts the growing brain and is affected by both genetic and environmental factors. Although research on there is currently no clear cause of ASD, researchers are still looking at the most likely causes. There haven't been many neuropathological studies, but the ones that have been done have found small malformations, problems with the limbic system, problems with the structure and connections of the cerebellum and changes in the cortex of the frontal and temporal lobes.

Neuroanatomical changes, genetics and pathophysiology in ASD

Studies using animal models revealed that a variety of neuronal proteins have been connected to the rise of ASD, however neuroanatomical studies have discovered abnormal brain connections and macrocephaly in autistic individuals.[14] More recently, alterations in synaptic structure/function and brain circuits have been linked to deficiencies in numerous synaptic proteins in ASD, indicating that "synaptopathy" is a significant contributing factor to ASD[15] as shown in Figure 2. Approximately 20 % of macrocephaly is a condition that some autistic children suffer neuroanatomical abnormality that is commonly seen in the brains of people with ASD.[16] The frontal and temporal lobes are the areas of the brain that are most affected in individuals with ASD. The function of the amygdala in ASD and cognition has been

Figure 2: Strong visual-spatial skills and pattern recognition

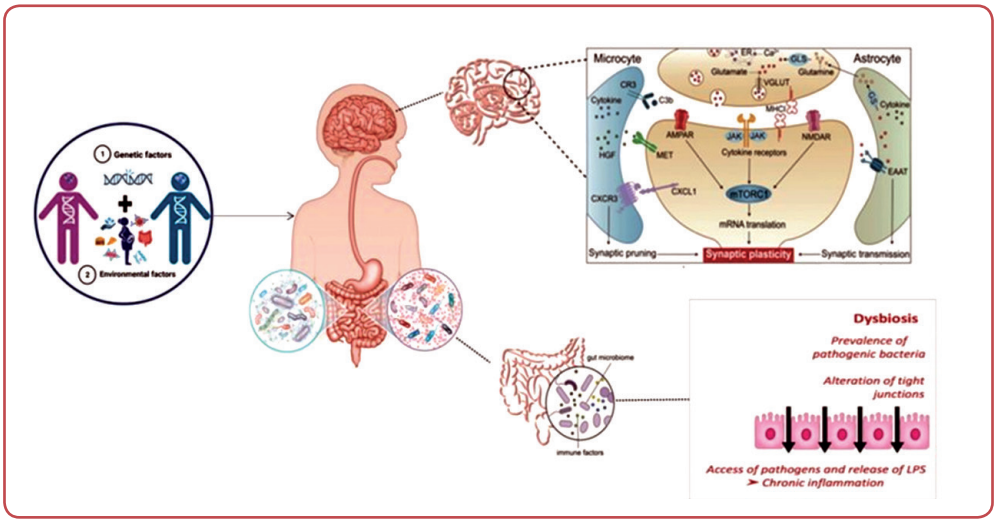

Figure 3: Overview of mechanistic insight into genetic and neurotransmitter imbalance in autism spectrum disorder (ASD)

demonstrated by numerous neuropathological and neuroimaging investigations. The brain regions primarily impacted in people with the frontal and temporal lobes are affected by ASD.

The function of the amygdala in ASD and cognition has been demonstrated by several neuroimaging and neuropathological studies. The amygdala, located in the medial temporal lobe prior to the hippocampus formation, has been thought to be closely linked to social and aggressive behaviours in people with ASD. An essential part of the limbic system and the cortico-striato-thalamo-cortical circuit's emotional loop is the amygdala. These factors by themselves, however, are unlikely to be the cause of autism. Rather, they appear to increase the risk of autism in children when combined with genetic factors. It is important to acknowledge ASD as a complex condition. Numerous studies have provided more evidence that the amygdala and *nucleus accumbens* (NA) play a role in the pathophysiology of ASD, which has a wide range of aetiologies incorporating both hereditary and environmental factors. However, nothing is known about the fundamental structure of ASD development, which may be a target for treatment. More study is needed to improve our understanding of ASD.[17] Cell-adhesion molecules called Neuroligins **(**NLGNs) act as synaptic organisers. NLGNs are anchored in the post-synaptic membrane and contribute to the identity specification and functional maturation of the synapse. These five genes—NLGN1, NLGN2, NLGN3, NLGN4 and NLGN5—located at chromosomes Yq11.2 (NLGN4Y also called NLGN5), Xq13 (NLGN3), Xp22.3 (NLGN4X), 3q26 (NLGN1) and 17p13 (NLGN2). These genes are the source of the human NLGNs[17] as shown in Figure 3.

Genetics is generally acknowledged that ASD is a condition with significant hereditary element based on the many research that has been conducted to clarify the pathogenic mechanisms behind this condition. The fact that concordance rates for autism in monozygotic twins can reach 90 % and in dizygotic twins can reach 10 %[18, 19] lends credence to this idea. Autism is an etiologically heterogeneous disorder, nevertheless, as no single genetic mutation causes more than 1 % to 2 % of cases of ASD.[20] Numerous genes with predisposing mutations and polymorphisms linked to ASD have so far been found by linkage and candidate-gene analyses, genome-wide association studies (GWAS) and evaluations of chromosomal variants.[21, 22] Rare mutations or copy number changes in synaptic proteins, such as neuroligins and *Shanks/ProSAPs*, are among these anomalies.[23-25]

Shank its partners are important targets for ASD's cognitive impairment.[26-28] Corticostriatal glutamatergic synapses are abundant in SHANK, which contacts several postsynaptic density (PSD) proteins, including SAPAP, which binds to PSD-95 to form the postsynaptic complex. SHANK is also linked to group I metabotropic glutamate (mGlu) receptors through its interaction to HOMER.[29, 30] It has been discovered that SHANK3 gene mutations occur often in people with ASD where changes in SHANK3 cause the corticostriatal synapse to malfunction.[31, 32] Neurotransmitter receptor dysfunction has been demonstrated

to be a primary factor in ASD. Since mutations in receptor genes are extremely rare, such dysfunction typically develops indirectly, for instance because of changes caused by additional post-synaptic processes or by the scaffolding proteins already mentioned.[33] Thus far, relatively few ASD patients have had NMDA receptor mutations identified in them, specifically in the GRIN2B and GRIN2A subunits and the GRIK2 kainate receptor subunit.[34, 35] Furthermore, mGlu1 and mGlu5 metabotropic glutamate (mGlu) receptors in group I have been connected to ASD. However, genes encoding the proteins implicated in the mGlu receptor pathway do not experience mutations at the level of these receptors themselves.[36]

Alterations in post-synaptic components or control may interfere with the homeostatic signals associated with activity-dependent processes. The predominant genetic alterations are attributable to SNPs in both coding and non-coding genomic regions, which change trafficking, folding of proteins and gene regulation. The genetics underlying synaptic malfunction may lead to deficiencies in relevant circuits because of improper control of protein-protein interactions and biological processes, although it is unclear how these genetics converge to ASD-phenotypical outcomes.[37]

Environmental causes of ASD

The development of autism spectrum disorder is significantly influenced by environmental circumstances alongside genetic contributions. Genetics is a well-known risk factor, but more data suggests that environmental factors may boost the chance of ASD by interacting with genetic predispositions. The following significant environmental elements have been connected to ASD.[38]

Some environmental pollutants, like pesticides, heavy metals (like lead and mercury), air pollution and endocrine-disruption chemicals, have been associated to a higher risk of ASD when a baby is still in the womb. These drugs have the potential to interfere with neurodevelopmental processes. Plastics contain phthalates and bisphenol A (BPA), which are endocrine disruptors and have been connected to neurodevelopmental problems like ASD. When the brain is developing at its most vulnerable phase, these chemicals can cause a disruption in the hormonal balance.[39]

Pregnancy and birth complications

Maternal state of metabolism including conditions like obesity, diabetes mellitus and hypertension have been connected to an elevated incidence of ASD during pregnancy. These illnesses can impact the brain development of the foetus due to changed metabolic functions. There is evidence that a greater risk for intellectual impairments such as ASD comes with deficiencies in crucial nutrients during pregnancy, including vitamin D, folate and omega-3 fatty acids. Giving birth too early or with a low birth weight increases the risk of ASD. Complications such as hypoxia or inflammation affecting brain development may be present in preterm infants. Birth complications: asphyxia or hypoxia (oxygen loss) during delivery are two examples of incidents that may worsen neurodevelopmental disorders, including ASD. Neurodevelopmental delays, including autism spectrum disorder, have been identified with early postnatal exposure to air pollution, heavy metals and other environmental toxins.[40]

An increased risk of contracting ASD has been linked with both father and mother ages at older levels. Genetic changes in sperm or eggs or pregnancy and delivery problems, which are more prevalent in older adults, may be the cause of the risk. ASD has been linked to immune system dysregulation, whether it occurs in the mother during pregnancy or in the newborn after delivery. Neurodevelopmental abnormalities may result from infections or autoimmune diseases that cause maternal immune activation (MIA) during pregnancy.[41]

Maternal alcohol use and smoking during pregnancy have been associated with an increased risk of ASD. These drugs have the potential to cause neurodevelopmental deficiencies and hinder the development of the embryonic brain. Pregnancy-related stress: High maternal stress levels have been associated with a higher incidence of ASD, regardless of the cause—psychological, socioeconomic, or trauma-related. Prolonged stress can alter the mother's immune system, which could have an impact on the development of the foetus's brain.[42]

A slightly greater frequency of ASD has been linked to *in vitro* fertilisation (IVF) and other assisted reproductive technologies; this might be because of things like multiple births, preterm, or hormone medications utilised during the assisted reproductive technology (ART) procedures.

Medication and infections: a greater frequency of ASD has been linked to prenatal bacterial or viral illnesses (such rubella or CMV). Foetal brain development may be hampered by the immunological reaction and inflammation brought on by these illnesses. Some drugs used while pregnant such as valproic acid (an antiepileptic drug) and an increased risk of ASD has been linked to selective serotonin reuptake inhibitors (SSRIs). However, the advantages and disadvantages of using such drugs must be considered.[43]

Early worries about vaccinations (especially the MMR vaccine) and their connection to ASD fuelled controversy, even though these claims have now been fully disproved. Numerous studies have shown no connection between vaccinations and ASD.

Gut health and ASD

Research has increasingly focused on finding relation between the gut microbiome and brain development disorders, including ASD. Unbalances in the gut microbiota, or dysbiosis, can affect brain development and function through immune modulation, production of neuroactive substances and the gut-brain signalling pathways.

Dietary factors

Certain dietary patterns, including those with imbalanced fatty acids or lacking sufficient nutrients, may contribute to changes in the gut microbiome and potentially influence ASD risk.

Treatment of autism

The involvement of parents and families is seen to be crucial to autism intervention programs for kids.[43] The fundamental theory of behaviour parent training is that parents can be trained to modify their children's learning and maintenance of proper behaviour by altering the conditions that exist within the family setting.[44] Research on early children lends credence to the idea that parent education is a useful strategy for fostering social skills. Not all parents benefit from traditional behavioural parent education programs, so it's important to tailor the curriculum to the specific needs and situations of each family. It looks like parent education works best when it is offered to people who are highly motivated and functional and aren't dealing with any other psychological or life problems that could make it harder for them to learn and practice positive parenting strategies.[45] The research demonstrates how successful parent education initiatives are in improving outcomes for children, especially in interventions for developmental or behavioural disorders. Research shows that when parents actively get involved in their children's intervention programs, significant performance gains can be observed. Conversely, there is a notable lack of these attitude improvements when parents do not engage in the intervention process.[46, 47] These methods and training courses can assist parents and therapists in addressing all the problems related to ASD.

Applied behavioural analysis (ABA)

ABA is a type of behaviour modification that uses approaches based on the principles of operant learning to help people learn new skills and behave in a way that is acceptable in society.[48] The procedure used by ABA starts with the creation of target plans that explain the cause and mechanism of behavioural excesses or deficits, followed by the selection of suitable methods, ongoing assessment and therapy modification through methodical data collection. A related group of evaluation techniques known as functional behavioural assessments offer data on the factors connected to a particular behaviour.[49] The first-line therapy for ASD in young children is now thought to be ABA-based intervention programs.[50] The following operant learning strategies are applied in ABA interventions for children with ASD:

- Encouragement: Using toys, food, snacks and praise to reinforce desired actions;
- Accomplishing target: The practice of rewarding approximate or component elements of a necessary action is known as "shaping," until the desired behaviour is displayed;
- Making independent: Dowering cues to boost self-reliance;
- Extinction: Extinction is when harmful behaviour is maintained by removing reinforcement. Applying an undesirable stimulus to lessen problematic behaviours is known as punishment;
- Differential reinforcement: Rewarding behaviour's absence or an alternative that is socially acceptable.

Pharmacological treatment for comorbidities

The majority of people with ASD throughout their lives receive pharmacological treatment as

an additional treatment strategy.[51, 52] Pharmacotherapy's most well-established objectives are to manage target symptoms that are frequently associated with sleeplessness, hyperactivity, impulsivity, anger, tantrums, anxiety, despair, self- and hetero-aggression, inattention, obsessive symptoms, to vent anger and iterative actions or rituals. This demographic has a higher prevalence of psychiatric comorbidities, according to numerous researches.[53] More than 50 % of autistics exhibit self-assertive and up to 14.6 % engage in severe self-aggression, which can result in hospitalisation, institutionalisation, expulsion from less restricted educational environments and a worse prognosis.[54] There are many different factors that contribute to irritability and aggression, including comprehension issues, a decline in the ability to convey needs and wants and to communicate, a decline in one's ability to confront others, clashes with coworkers and bosses, cognitive and mental impairment unidentified suffering, humour disorders and concern. Finding the source of aggressive behaviour is the first stage in treating it, after which the best therapy strategy (medication or behavioural management) should be chosen. The treatment of aggressive autistic symptoms has shown small to considerable benefits with both first- and second-generation antipsychotics.[55] Reporting on a multicentre clinical trial that evaluated the efficacy of short- and long-term risperidone in treating aggressive, tantrum-prone and self-harming behaviours in children and adolescents with autism, the Research Units in Paediatric Psychopharmacology (RUPP) Autism Network published their findings in 2002. The study included participants aged 5–17.[56] Risperidone treatment was well tolerated for a maximum of six months; adverse effects, which were typically associated with haloperidol in previous studies, were less common when using risperidone. The lowest effective doses were 2 mg on a daily average. After receiving treatment for up to six months, there was no indication of tolerance or the need to raise the dosage in the participants.). The FDA recently approved aripiprazole to treat severe irritability in autistic in the age group (6-17).

The anticonvulsant drugs topiramate and divalproex have demonstrated example for treating irritability in ASD. Majority of research on SSRIs has demonstrated that these drugs are not clinically significant in treating autism spectrum patients' restricted interests and repetitive behaviours.[57, 58] A single research with methodological significance shown modest gains when fluoxetine, an SSRI, was used in place of a placebo.[59] The biggest study evaluating citalopram against a placebo to treat repeated behaviours in ASD found no benefit for citalopram and side effects, including Overactive, sleeplessness and attitude worsening, were frequent.[60] To treat ASD patients' persistent insomnia, it has been demonstrated that exogenous melatonin, which is offered in both immediate-release and extended-release formulations as an over-the-counter supplement, is safe and beneficial in promoting better sleep habits in kids with ASD.[61, 62] According to certain data, kids with ASD may have aberrant circadian rhythms and melatonin secretion in comparison to kids without the disorder.[63] The alpha-2 agonist clonidine has demonstrated potential in lowering nocturnal awakening and sleep onset latency in individuals with ASD.[64]

Occupational therapy

It is a therapeutic approach that addresses personal traits, activities and surroundings that impact an individual's role performance to improve activity participation skills.[65] While several studies have examined the impacts of sensory integration treatment on autistic children, there is still a need for a thorough analysis of the therapy's efficacy because there is a dearth of high-quality evidence-based research. By offering structured sensory experiences in a regulated setting, one kind of occupational therapy that aims to help people with issues relating to sensory processing is sensory integration therapy. Its main goal is to increase the brain's ability to process and respond to sensory information, which can improve daily functioning. Presented study's results lead us to the conclusion that occupational therapy helps children with ASD develop their sensory skills, language proficiency, self-care and social skills, body and object usage and interpersonal skills. Empirical data from study suggest that these advantages are most noticeable in the advanced phases of treatment, even though the rate of progress tends to slow down. According to this, even though occupational therapy can significantly improve children with ASD's quality of life and involvement in daily activities, ongoing and potentially diverse interventions may be required to sustain and expand on these improvements.

Comprehensive education

These interventions are different from those that

target impairments like communication problems, joint attention, or motor planning because they address all three of the key weaknesses that characterise autism. Stated differently, the goals of comprehensive therapies are to decrease ritualistic and/or stereotyped behaviours, address communication issues and develop social skills and interests. Treatment and Education for Children with Autism and Related Communication Handicapped Children (TEACCH) Schools and school districts around the world use TEACCH, the most widely used special education curriculum for children with autism. The curriculum is extensive and addresses a wide range of issues, including social skills, motor skills, imitation, communication, cognition, perception and perception. It places a strong emphasis on having many teachers participate in different classroom environments and TEACH was first implemented in separate, self-contained classrooms; however, these days, the emphasis is on integrating autistic children into inclusive environments with generally functioning students. TEACCH include: visual teaching, visual communication, structured communication, pre academic skills.

Sensory integration therapy

Jean Ayres, a psychologist and occupational therapist, created the sensory integration therapy (SIT) in the 1970s. According to Ayres, sensory issues in children with autism frequently include low arousal, a diminished sensitivity to visual or aural stimuli, poor motor planning and organisation skills and hypersensitivity to touch or sound. SIT aims to address the sensory integration dysfunctions that children with autism display. This is accomplished by giving the vestibular, proprioceptive and tactile systems different kinds of sensory stimulation.[66]

Advances genetic based approach

Genetic variables that contribute to the aetiology of autism include chromosomal abnormalities, insertions, deletions, single nucleotide variants, somatic mutations, de novo mutations, copy number variations and somatic mutations.[67, 68] The ability to remove the genetic abnormalities causing severe neurological disorders like ASD has become possible because to advancements in genome editing technology. However, these variables disrupt several other ASD patient genes which are linked to various vital functions such as transcription, transcription, DNA binding, postsynaptic density, neuroprotection and the genes that code for proteins in the formation of neurons.[69] Any change in known genes linked to ASD may eventually lead to a dysfunction in the brain regions in charge of cognitive processes[70, 71] (SHANK1), contactin-associated protein-like 2 (CNTNAP2) and ubiquitin protein ligase E3A in that order, are implicated in a multitude of processes, including cell proliferation, ubiquitination of proteins, chromatin remodelling, preservation of synaptic activity and cell adhesion.[72] It is also known that some genes (such as MECP2) either control or are controlled by synaptic activity. Genetic study based on the sequencing of the whole genome has shown that missense mutations, including some ASD risk genes, are associated with Missense variants that have increased overall because of single nucleotide and copy number changes.[73] CRISPR-Cas9 can cut the structure and function of crispr-cas9 DNA at specific target locations. Even though the method has already transformed gene editing, scientists are always searching for new applications. Originally discovered as a bacterial defence mechanism against invading viruses, CRISPR-Cas9 has now evolved into a powerful tool for genomic research. The Cas9 protein breaks DNA strands to act as genetic scissors in the type II system.[74]

One of the two structural lobes of the Cas9 protein facilitates recognition (REC), whereas the other one stimulates nuclease activity. REC1 and REC2, which are involved in gRNA recognition, make up the REC lobe. Furthermore, Cas9 binds to the targeted DNA via the nuclease's protospacer adjacent motif (PAM) interaction domain.

The gRNA targets viral DNA in prokaryotes, but when used as a gene-editing tool, it may be synthetically modified to target nearly any gene that needs to be altered. Repair, cleavage and recognition are the processes required in the CRISPR-Cas9 genome editing mechanism, according to genetic research based on whole genome sequencing.[75] One gRNA binds to a complementary area on the targeted DNA to start the recognition process. PAM is an "NGG" pattern sequence consisting of two to five base pairs, where "N" stands for any nucleotide and "G" for two guanine nucleotides. Once the PAM site has been identified, double-stranded DNA starts to melt at the target spot, forming a hybrid. Now, the protein that triggers a double-strand break (DSB) at the targeted DNA location, three base pairs upstream of PAM, is ready.[76] During the NZext stage, cellular machinery uses non-homologous end joining and ho-

mology-directed repair to fix the double-stranded blunt ends that have broken.[77]

The precise gene insertion or substitution is accomplished by homology directed repair; it places a donor DNA template at the anticipated DSB spot that has sequence homology.[78] The transcription factor of gene expression has been regulated by CRISPR-Cas9's ability to either repress or activate genes. Because of its etiological variability, assessing many medication options is the main challenge in treating ASD. To provide a realistic ASD model, an in-lab investigation has been conducted employing the CRISPR tool to introduce mutations in the FOXP1 gene, dead-box helicase 3 X-linked and activity-dependent neuroprotective protein.[79] Comparably, hemizygous CHD8 (CHD8+/–) iPSC lines were created to examine CHD8's function in cellular and molecular aspects of embryonic development. The genome editing technique has developed over time into a specialised gene delivery method for target cells, such as brain and neural cells. One such example was the delivery of engineered Cas9 ribonucleoprotein complex variations to the hippocampal, striatal and cortical regions of mice, which allowed for the demonstration of *in vivo* neuronal gene editing.[80]

Using the CRISPR-Cas9 method, it is possible to target and fix many genes associated with ASD, thereby mitigating the condition. ASD and ASD-associated monogenic syndromes are characterised by mutations in several genes, including reduced arabinose yariv1/suppression of tumorigenicity 8, FMR1 MECP2, TSC1, PTK7, SCN3A, human serotonin transporter gene, γ-aminobutyric acid type A receptor subunit, oxytocin receptor gene, methylenetetrahydrofolate reductase, CHD8, homeobox B1, reelin, inner mitochondrial membrane peptidase subunit 2, oxytocin receptor gene, methylenetetrahydrofolate reductase, SHANK2/3, methylenetetrahydrofolate reductase, homeobox A1, UBE3A, human serotonin transporter gene, POU class 3 homeobox 2, reduced arabinose yariv1/suppression of tumorigenicity 8, FMR1 MECP2, TSC1, SCN3A and CNTNAP2.

The genes that are targeted *in vitro* and *in vivo* use the CRISPR-Cas9 technology for monogenic disorders associated with ASD, but many more need to be studied.[81] Structural magnetic resonance imaging studies - many neuroimaging modalities have been employed to comprehend the neurobiology of the illness. The diversity and lack of agreement in the results seems depressing at first when examining the structural magnetic resonance imaging (MRI) data for ASD, however certain patterns are starting to show. The most consistent conclusion is that early childhood is associated with faster brain volume growth, 10 % increase in brain volume is estimated that peaks between the ages of 2-4. Both grey and white matter appear to be enlarged, with some research indicating that white matter makes a disproportionately big contribution to this volume expansion in the early years of life.[82] These results' variability and dispersion imply that autism is a condition that affects both white and grey matter and is therefore broadly distributed. It is feasible to quantify the white matter and grey matter structures in more detail with newer technology. Now that the cortical grey matter has been characterised in terms of thickness and surface area, the volume of the cortical grey matter can be approximated. Given that these two measurements are thought to be associated with different neurological processes, they are particularly interesting.

Genetic study based on the sequencing of the whole genome has shown that surface area is thought to be dependent on progenitor cell division in the periventricular area during embryogenesis and varies with the degree of cortical folding or gyrification,[83, 84] cortical thickness appears to reflect dendritic arborisation and pruning inside grey matter or changes in myelination at the interface between the white and grey matter.

Case studies in ASD

Studies regarding early inventions based on feeding behaviour

Keen et al investigated feeding difficulties in early infancy among children with autism, focusing on seven cases identified from a cohort of 350. Each child had a BMI below the 0.4th centile, indicating an overrepresentation of low body mass index (BMI) and suggesting a distinct subgroup within the autism population. Although five children eventually achieved normal BMI, two required gastrostomies feeding due to gastrointestinal disorders. Comprehensive assessments found no consistent organic, economic, or social causes for failure to thrive (FTT). Some participants exhib-

ited atypical oral behaviours, though significant oromotor dyspraxia was absent. The findings indicate that early feeding problems and low BMI may reflect phenotypic or behavioural traits rather than medical or environmental factors. The normalisation of BMI in most cases further supports the possibility of developmental rather than pathological origins. Keen et al concluded that feeding difficulties may serve as early behavioural indicators in certain children with autism, underscoring the need for targeted early interventions and further large-scale studies to clarify these associations.[85]

Studies based on students having ASD

Researchers have explored the varied needs and challenges of students with autism.[86, 87] Research identifies not only particular strengths and interests of such students but also how these can be used to inform specific intervention plans. By tapping into individual talent—creativity, maths ability, or single-focused interest—teachers can construct personalised strategies that enhance academic achievement, social interactions and communication. Case studies show some of the challenges students encounter, ranging from emotional regulation and behavioural issues to social and communication delays.[86-88] In general, strength-based, individualised interventions have recorded substantial gains in various areas of development.

Case study 1: Both Chuck, an imaginative and creative student, excelled at drawing but had difficulty with writing because he was frustrated and could not express himself when the work was difficult. A creative student had difficulty with writing because he was frustrated. A visual self-monitoring strategy, the "Horseradish Chart," assisted him in managing feelings and enhancing classroom participation. The visual system allowed Chuck to recognise emotional states, express frustrations and avoid emotional collapse. The intervention improved self-regulation and engagement for him, demonstrating the success of individualised, strength-based practices for assisting students with autism. These innovative, interest-based tools unlock student potential while resolving emotional and academic difficulties.[89]

Case study 2: Eli, a bright and humorous student with a strong aptitude for math, struggled with emotional instability and perfectionism, often reacting to minor frustrations with intense self-blame and withdrawal. To support his emotional regulation, teachers developed "Eli's Success-O-Graph," a two-quadrant grid on his desk where he charted emotions and successes throughout the day. This math-based tool engaged his interests, helping him visualise positive experiences and recognise progress. With time, Eli used the graph autonomously, communicated his emotions more freely and had fewer emotional outbursts. The intervention successfully constructed his self-knowledge, strength and emotional stability. The case of Eli supports the effectiveness of individualised, strength-based interventions in promoting emotional development and self-control in students with autism.[90-93]

Case study 3: But he had difficulty with social interactions and tended to encroach on peers' personal space, leaving others feeling uncomfortable. To resolve this, teachers crafted a visual reminder in the form of his Titanic fascination—equating the collision of the ship with an iceberg with personal boundaries. This ingenious connection taught Jimmy that being "too close" might lead to social issues, much like the Titanic's demise. By connecting the lesson to his interest, teachers enhanced his social awareness and relationships with peers, demonstrating the effectiveness of interest-based interventions in enabling students with autism to develop socially.[94, 95]

Case study 4: Devin, an exceptionally talented student with a strong aptitude for mathematics and fascination with number patterns, exhibited significant behavioural and social challenges in class. Despite his intellectual strengths, he frequently refused to engage in tasks he deemed "boring," disrupted lessons and resisted independent work, affecting both his own learning and the classroom environment. To address these behaviours, teachers implemented a personalised behaviour management system that capitalised on Devin's mathematical interests. Using a point-based rubric, Devin and a peer rated his performance in areas such as participation and task completion, with daily points accumulated toward weekly rewards. This structure encouraged accountability, self-reflection and social interaction through peer feedback. Over time, Devin's engagement and classroom behaviour improved, demonstrating the effectiveness of strength-based, individualised interventions. By integrating his interest in mathematics into behavioural support, educators successfully promoted self-regulation and positive participation.[96] Devin's case underscores how personalised strategies, grounded in students'

strengths and interests, can transform challenging behaviours into opportunities for growth and learning for students on the autism spectrum.[97]

Case study 5: Aaron started receiving early intervention services at the age of two because of severe cognitive and communication delays coupled with problem behaviours like tantrums, opposition to changes in routine and minimal eye contact. Nine months into intervention, he was diagnosed with autism. His speech was minimal and very echolalic, although sporadic appropriate speech testified to his cultural background. Pre-early intervention support consisted of a playgroup and sensory integration therapy to work on developmental and behavioural needs. Structured strategies like visual schedules, the gradual increase in task demands and minimal adult dependence were utilised in his kindergarten year at the Alice H Hayden Early Childhood Centre (AHECC) to enhance transitions and independence. Teachers also made a thorough transition summary and video to assist his transfer to a Jewish day school. With these culturally responsive and individualised supports, Aaron achieved significant academic and social gains. His case highlights the efficiency of early identification, systematic routines and the collaborative planning between families and educators in ensuring successful inclusion and long-term growth of children with autism.[98]

Case study 6: Sean was admitted to the preschool program of AHECC at age three, having been excluded from two childcare placements because of aggressive and noncompliant behaviour. On initial evaluation, there were pronounced social, communication and adaptive delays and he received an autism diagnosis. Interventions across four years in the AHECC program included toileting, sharing, verbal communication and subsequently, peer problem-solving, imaginative play and storytelling. With regular, organised guidance, Sean accelerated development, demonstrating superior intellectual functioning and competent performance in organised activities at age six. Despite these advances, issues with pragmatic language and social interaction continued to require ongoing special education accommodations. Teachers reported significant gains in learning and communication but noted continued difficulties in integrating socially. Sean's development reflects the effectiveness of early, intensive and individualised intervention programs for children with autism. It also illustrates the importance of long-term follow-up to support residual social and communication challenges, securing long-term educational and developmental outcomes.[99, 100]

Case study 7: Ben, one of three children from a bilingual English Chinese family, was referred to school at the age of three for considerable language delay. His main caregiver, a monolingual Chinese-speaking grandmother, continued to restrict exposure to consistent language. Developmental delays, nonverbal communication and self-injurious behaviour were shown through initial assessments, resulting in an ASD diagnosis. When Ben began at the AHECC, intensive, individualised training was provided with functional communication, play and behavioural compliance. Maladaptive behaviours were replaced by reinforcement strategies with positive alternatives. By one year of age, Ben had started imitating teacher behaviours, beginning short play and communicating preferences using symbols. The use of art activities was a major motivational aid that helped him develop. In the second year, he had single-word usage with appropriate meaning and evidenced better independent play, although he still preferred playing alone. Ben generally made significant improvement in all areas of communication, behaviour and development. His case highlights the redemptive potential of early, stable and tailored interventions in promoting communication, play and social development in children with autism.[101, 102]

Conclusion

ASD is a complex neurodevelopmental disorder that requires ongoing multidisciplinary intervention. Future research must strive to integrate genetics, neuroimaging and AI to enable improved and earlier diagnosis, with the exploration of new treatments like CRISPR and microbiome-based treatments. Longitudinal studies and care systems with cultural competence must be implemented to raise worldwide knowledge. Evidence translation to community interventions and practical interventions will maximise the quality of life of individuals with ASD. Multidisciplinary policies and evidence-based practices remain at the centre of advancing effective and inclusive treatment for autism.

Ethics

This study did not directly involve with human participants or experimental animals. Therefore, the ethics approval was not required in this paper.

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Conflicts of interest

The authors declare that there is no conflict of interest.

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Data access

The data that support the findings of this study are available from the corresponding author upon reasonable individual request.

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