Pharmaspire

REVIEW ARTICLE

Exploring the interconnection of autism and intellectual disability: Advancements in current research overview

Piyush Anand, Shamsher Singh

Neuropharmacology Division, Department of Pharmacology, ISF College of Pharmacy, Moga, Punjab, India

ABSTRACT

This comprehensive review provides an in-depth examination of the current understanding of the link between autism spectrum disorder (ASD) and intellectual disability (ID). Drawing from empirical research, clinical studies, and theoretical frameworks, the review explores the shared features, etiological factors, diagnostic challenges, and intervention strategies associated with the cooccurrence of ASD and ID. Neurobiological overlaps, including genetic and neurodevelopmental perspectives, are discussed to uncover the complex relationship between these conditions. The review also highlights the phenotypic variability observed in individuals with dual diagnoses, emphasizing the need for personalized approaches to assessment and intervention. Diagnostic considerations, such as diagnostic criteria, assessment tools, and potential biases, are addressed to improve accurate identification and classification. Furthermore, the impact of ASD and ID on various aspects of daily functioning, including cognitive abilities, adaptive skills, social interaction, and academic achievement, is examined. Evidence-based intervention strategies, ranging from behavioral interventions to educational approaches, are explored, along with the importance of early intervention and multidisciplinary collaboration. By synthesizing existing knowledge, this review aims to deepen our understanding of the link between ASD and ID, providing valuable insights for researchers, clinicians, and educators. The review concludes with suggestions for future research directions, highlighting the need for longitudinal studies, advanced neuroimaging techniques, and the development of targeted interventions for individuals with dual diagnoses. Ultimately, this review serves as a comprehensive resource to inform clinical practice, policy-making, and further advancements in supporting individuals with ASD and ID.

KEY WORDS: Autism spectrum disorder, Comorbidity, Diagnosis, Etiology, Intellectual disability, Intervention, Shared features

INTRODUCTION

Autism, also known as autism spectrum disorder (ASD), is a neurodevelopmental disorder that affects social interaction, communication skills, and behavior. It is called a spectrum disorder because it varies widely in its presentation and severity, with individuals experiencing a range of challenges and abilities. It was initially identified in 1943, and its global prevalence has notably increased over time.

Address for Correspondence
Dr. Shamsher Singh, (Ph.D)
Professor and Head
Neuropharmacology Division, Department of Pharmacology, ISF College of Pharmacy.
Email: shamshersinghbajwa@gmail.com

While the exact etiology of autism remains incompletely understood, it is widely accepted that a combination of genetic and environmental factors contributes to its development. These factors include neuroinflammation, oxidative stress, viral or bacterial infections, exposure to various chemicals such as mercury, nickel, cadmium, vinyl chloride, and trichloroethylene, as well as maternal obesity and prenatal exposure to valproic acid (VPA). Extensive

Access this article online

Website: http://isfcppharmaspire.com

DOI: 10.56933/Pharmaspire.2023.15122

Date of Submission: 06 July 2023
Date of Revision: 08 July 2023
Date of Acceptance: 11 July 2023

clinical and statistical studies have consistently identified VPA as a risk factor for ASD.[1-4] Epidemiological data consistently demonstrate a higher prevalence of ASD in boys, with a ratio of approximately four boys diagnosed for every girl. Furthermore, ASD affects approximately one in 100 children globally. The diagnosis of ASD can be made as early as 18–24 months of age, relying on the identification of specific symptoms that differentiate it from typical development and other developmental disorders. This disorder, which begins in early childhood and continues throughout adulthood, is characterized by serious difficulty with social interaction, language, and the use of confined, repetitive behavior. At present, there is no single cause of autism that has been identified. Motor indicators of cerebellar impairment, such as fine and gross motor deficits, eye movement disturbances, altered gait, and balance, as well as coordination, motor learning impairments, and postural instability, seem to be present in the majority of individuals who have autism. Despite the fact that ASD was first described in 1943 and its prevalence has steadily increased around the world ever since, researchers have only recently begun to focus on the possible role that the immune system plays in the disorder's development. Epidemiological studies have shown that males are 4 times more likely than females to experience the symptoms of ASD.[4] Moreover, mental retardation is a cooccurring disorder in 75% of people with ASD.[5] Epidemiological studies have shown that autism has become more common over the world during the past 40 years.[6] Sweden has the highest rate of autism diagnosis at 17.4 per 100 people, followed by Denmark at 12.6 and Italy at 1.6. (11.8–15.5). Between 18 and 24 months of age is the typical window for a diagnosis. Related disorders include attention deficit hyperactivity disorder (ADHD), gastrointestinal distress, anxiety, depression, epilepsy, and fragile X syndrome (FXS).[7] Genetics, environmental variables, neuroinflammation, oxidative stress, and other factors all have a role in autism.

Intellectual disability (ID) refers to significant limitations in intellectual functioning and adaptive behavior that manifest during the developmental period. Previously known as mental retardation, it is a neurodevelopmental condition characterized by significant limitations in intellectual functioning and adaptive behavior. Intellectual functioning: Intellectual functioning refers to an individual's general mental capacity, including their ability to reason, solve problems, learn new information, and apply knowledge to everyday situations. Intellectual functioning is typically assessed using standardized intelligence tests, such as IQ tests.[8,9]. The diagnosis of ID is generally considered when an individual's IQ score falls below a certain threshold, often around 70–75 or lower. Adaptive behavior: Adaptive behavior encompasses the practical skills necessary for everyday functioning and independence. These skills include communication, self-care, social skills, home living, functional academics, work skills, leisure activities, and health and safety.[10] Deficits in adaptive behavior can manifest in difficulties with tasks such as personal hygiene, using public transportation, managing money, or understanding social cues. Onset and developmental period: Intellectual disabilities are typically recognized during the developmental period, which spans from infancy through childhood and adolescence.[11] The limitations in intellectual functioning and adaptive behavior are evident early in life and may persist throughout the individual's lifespan. Levels of ID: ID is often categorized into different levels based on the severity of the condition. The levels include mild, moderate, severe, and profound. These categories are based on the individual's level of intellectual functioning and the amount of support they require for daily living.[12]

ASD and ID are distinct conditions, but they can cooccur in some individuals. The relationship between ASD and ID is complex and multifaceted. While ASD and ID are separate diagnostic categories, there is an overlap in terms of shared characteristics, etiological factors, and clinical presentations.[13] Causes and etiology: ID can have various causes, including genetic factors, prenatal and perinatal conditions, medical conditions, environmental influences, and exposure to toxins. Some genetic conditions associated with ID include Down syndrome, FXS, and other chromosomal abnormalities.[14] However, in many cases, the specific cause of ID remains unknown. Support and interventions: Individuals with Intellectual disabilities may benefit from a range of interventions and supports tailored to their specific needs. These can include educational interventions, behavioral therapies, speech and language therapy, occupational therapy, social skills training, and vocational training.[15] The goal is to enhance the individual's adaptive skills, independence, and overall quality of life. It is important to note that intellectual disabilities is a heterogeneous condition, and individuals with ID can have varying strengths, abilities, and support needs. The diagnosis and management of ID require a comprehensive assessment conducted by qualified professionals, including psychologists, psychiatrists, and other specialists experienced in developmental disabilities.

PREVALENCE RATE OF AUTISM AND ID IN VARIOUS COUNTRIES

The prevalence rates of autism and ID can vary across different countries due to various factors such as diagnostic criteria, access to healthcare, cultural differences, and data collection methods.[6,16] It is important to note that prevalence rates can also change over time as diagnostic practices evolve and awareness increases. Here are some approximate prevalence rates for autism and ID in different countries, based on the available data up until my knowledge cutoff in September 2021 United States: Approximately one in 54 children; United Kingdom: Approximately one in 100 children; South Korea: Approximately one in 38

children; Sweden: Approximately one in 100 children as shown in Table 1.

OVERLAPPING FEATURES AND DIAGNOSTIC CHALLENGES

Common behavioral characteristics and impairments observed in ASD and ID

While ASD and ID are distinct conditions, they can exhibit some overlapping behavioral characteristics and impairments. Understanding these commonalities can help in recognizing the shared challenges faced by individuals with ASD and ID.[17] Here are some common behavioral characteristics and impairments observed in both conditions:

Social interaction deficits

Difficulties in understanding social cues and nonverbal communication, such as facial expressions, body language, and gestures. Challenges in initiating and maintaining age-appropriate social interactions and relationships, limited understanding of social norms, rules, and expectations.[18]

Communication difficulties

Delayed language development or difficulties with expressive and receptive language skills. Deficits in social communication, including difficulty initiating and sustaining conversations, understanding abstract language, and engaging in back-and-forth exchanges. Stereotyped or repetitive use of language, such as echolalia.[19]

Restricted and repetitive behaviors

Engaging in repetitive motor movements, such as hand flapping, rocking, or spinning. Insistence on sameness and resistance to change, resulting in difficulties adapting to new routines or unexpected situations. Highly focused or intense interests in specific topics or objects, often beyond typical developmentally appropriate levels.[20]

Executive functioning challenges

Difficulties with planning, organization, and problem-solving. Impaired cognitive flexibility, leading to rigidity in thinking and resistance to changes in routine or unexpected transitions. Challenges with impulse control and inhibiting inappropriate behaviors.[21]

Sensory sensitivities

Heightened or diminished responses to sensory stimuli, including sounds, lights, textures, tastes, or smells. Overwhelm or discomfort in environments with high sensory input. Preference for specific sensory input or repetitive sensory behaviors.[22]

Adaptive functioning

Difficulties with adaptive skills necessary for independent living, such as self-care, safety awareness, time management, and managing personal finances. Challenges in functional academics, including basic reading, writing, and math skills. Limited ability to generalize skills across different settings or contexts.[23] It is important to note that the severity and specific manifestation of these characteristics can vary widely among individuals with ASD and ID. Additionally, the co-occurrence of ASD and ID can present unique challenges, as the impact of ID can influence the expression and management of ASD-related symptoms.

Recognizing these common behavioral characteristics and impairments can help inform the development of targeted interventions and supports for individuals with both ASD and ID

Table 1: Prevalence rate of autism in different countries

Countries	ASD Prevalence	ID Prevalence	References
United States	Approximately 1 in 54 children	Approximately 1-3% of the population	(CDC, 2020); (AAIDD, 2020)
United Kingdom	Approximately 1 in 100 children	Approximately 1-2% of the population	(NHS, 2019); (Public Health England, 2020)
Australia	Approximately 1 in 70 children	2-3% of the population	(Autism Awareness Australia, 2019); (AIHW, 2018)
Canada	Approximately 1 in 66 children	Approximately 1-3% of the population	(Public Health Agency of Canada, 2018); (CDAC, 2020)
Japan	Approximately 1 in 160 children	Approximately 2.3% of the population	(National Institute of Mental Health, Japan, 2016); (Ministry of Health, Labour and Welfare, Japan, 2012)
Brazil	Approximately 1 in 367 children	Approximately 1-3% of the population	(Ministry of Health, Brazil, 2021)
Germany	Approximately 1 in 100 children (Autism Europe, 2020)	Approximately 1-2% of the population	(Autism Europe, 2020);
Israel	Approximately 1 in 100 children	Approximately 1-3% of the population	(Israel Autism Association, 2021)
South Africa	Approximately 1 in 161 children	Approximately 1-3% of the population	(Statistics South Africa, 2019)

Challenges in differentiating ASD from ID and vice versa

Differentiating ASD from ID and vice versa can be challenging due to several factors. The overlap in some behavioral characteristics and the cooccurrence of these conditions in some individuals can complicate the diagnostic process. Here are some challenges in distinguishing between ASD and ID.[24]

Diagnostic overlap

ASD and ID can exhibit overlapping symptoms and behaviors. For example, both conditions can involve communication difficulties, social interaction deficits, and repetitive behaviors. It can be challenging to determine whether these behaviors are primarily indicative of ASD, ID, or both.[25]

Communication challenges

Communication difficulties are prevalent in both ASD and ID. Individuals with limited language abilities due to ID may exhibit similar communication challenges as those with ASD. This overlap can complicate the diagnostic process and require comprehensive assessments considering various factors, including cognitive abilities, language skills, and social communication patterns.[26]

Intellectual assessment limitations

Traditional intelligence tests may not accurately assess the cognitive abilities of individuals with ASD due to the presence of specific learning profiles and processing differences. The reliance on standardized testing can result in underestimating the intellectual capabilities of individuals with ASD, potentially leading to a misdiagnosis of ID.[27]

Developmental considerations

Developmental trajectories can differ for individuals with ASD and ID. Early developmental delays, including delays in language and social milestones, are common in both conditions. However, as children with ASD grow older, their unique symptomatology, such as social communication challenges and repetitive behaviors, may become more apparent and help differentiate ASD from ID.[28]

Cooccurrence

ASD and ID can cooccur in some individuals, further complicating the diagnostic process. Determining the primary diagnosis and understanding the relative contribution of each condition to the individual's challenges requires careful evaluation by professionals with expertise in both ASD and ID.[29] To address these challenges, a comprehensive and multidisciplinary assessment is crucial. This typically involves gathering information from multiple sources, such as interviews with caregivers, observation in various settings, cognitive assessments, language evaluations, and consideration of the individual's developmental history. Collaboration among professionals from psychology, psychiatry, special education, speech and language therapy, and occupational therapy is essential to ensure accurate diagnosis and appropriate intervention planning for individuals with ASD, ID, or both.

Role of adaptive functioning in distinguishing between ASD and ID

Adaptive functioning plays a significant role in distinguishing between ASD and ID. While both conditions can exhibit overlapping symptoms, evaluating an individual's adaptive skills can provide valuable insights into the nature of their challenges. Here is the role of adaptive functioning in differentiating between ASD and ID.[30]

Concept of adaptive functioning

Adaptive functioning refers to an individual's ability to independently and effectively navigate everyday life tasks and situations. It encompasses various domains, including communication, self-care, socialization, home living, functional academics, work skills, leisure activities, and health and safety. Evaluating adaptive functioning provides a measure of an individual's practical skills and their ability to meet the demands of their environment.[31]

Identification of primary impairments

In the context of distinguishing between ASD and ID, adaptive functioning assessment can help identify the primary impairments contributing to an individual's challenges. Individuals with ID typically exhibit broad-based impairments across multiple areas of adaptive functioning, including communication, self-care, and socialization. In contrast, individuals with ASD may have specific impairments in social communication and interaction while demonstrating relatively stronger adaptive skills in other domains.[32]

Variability of adaptive functioning

Adaptive functioning can vary significantly among individuals with ASD and ID. While individuals with ID generally display global impairments across multiple adaptive domains, those with ASD often exhibit a more uneven profile. For example, individuals with ASD may demonstrate higher adaptive skills in areas like functional academics or self-care while experiencing significant challenges in social communication and interaction. Assessing adaptive functioning can help capture this variability and inform diagnostic differentiation.[33]

Impact on independence and daily living

Evaluating adaptive functioning provides insights into an individual's level of independence and their ability to meet

daily life demands. Individuals with ID typically require substantial support and assistance to navigate various aspects of daily living. In contrast, individuals with ASD may demonstrate uneven adaptive skills but still have the potential to develop functional independence in certain areas with targeted interventions and support.[34]

Differential diagnosis considerations

Assessing adaptive functioning is essential when considering a differential diagnosis between ASD and ID. While individuals with ASD may have cooccurring intellectual challenges, their primary diagnosis is ASD if their social communication and interaction deficits align with the diagnostic criteria. If the impairments primarily reflect global intellectual deficits across adaptive domains, a primary diagnosis of ID may be more appropriate.[35]

ETIOLOGICAL FACTORS

Genetic contributions to ASD and ID

Genetic factors play a significant role in both ASD and ID. There are shared genetic variants that contribute to the development of both conditions, as well as distinct genetic factors that are specific to each condition. Understanding the genetic contributions can provide insights into the underlying biology and potential overlaps between ASD and ID. Here is an overview of the shared and distinct genetic variants associated with ASD and ID [Figure 1].[36]

Shared genetic variants

Copy number variations (CNVs)

Both ASD and ID have been associated with the presence of certain CNVs, which are structural variations in the genome involving deletions or duplications of genetic material. Examples of CNVs associated with both conditions include the 15q11–q13 duplication, 16p11.2 deletion/duplication, and 22q11.2 deletion.[37]

FXS

FXS, caused by a mutation in the FMR1 gene, is a known genetic condition associated with both ASD and ID. It is one of the most common genetic causes of inherited ID and has a higher prevalence among individuals with ASD.[38]

Distinct genetic variants

ASD-specific genetic variants

Several genes have been identified as having specific associations with ASD. These include genes involved in synaptic function (e.g., SHANK3, NLGN3, NRXN1) and genes involved in neuronal development and signaling pathways (e.g., PTEN, TSC1, TSC2). Variants in these genes have been found to be more prevalent in individuals with ASD compared to individuals with ID alone.[39]

ID-specific genetic variants

ID is a heterogeneous condition with various genetic causes. Some genetic syndromes associated with ID, such as Down syndrome (caused by trisomy 21) and FXS, have well-established genetic etiologies. Other genetic variants associated with ID include mutations in genes involved in chromatin remodeling (e.g., CHD7), metabolism (e.g., PKU-related genes), and synaptic function (e.g., SYNGAP1).[40]

It is important to note that while there are shared and distinct genetic factors between ASD and ID, the genetic landscape of these conditions is complex and not fully understood. Genetic factors alone cannot account for all cases of ASD or ID, as environmental influences and gene-environment interactions also contribute to their development.

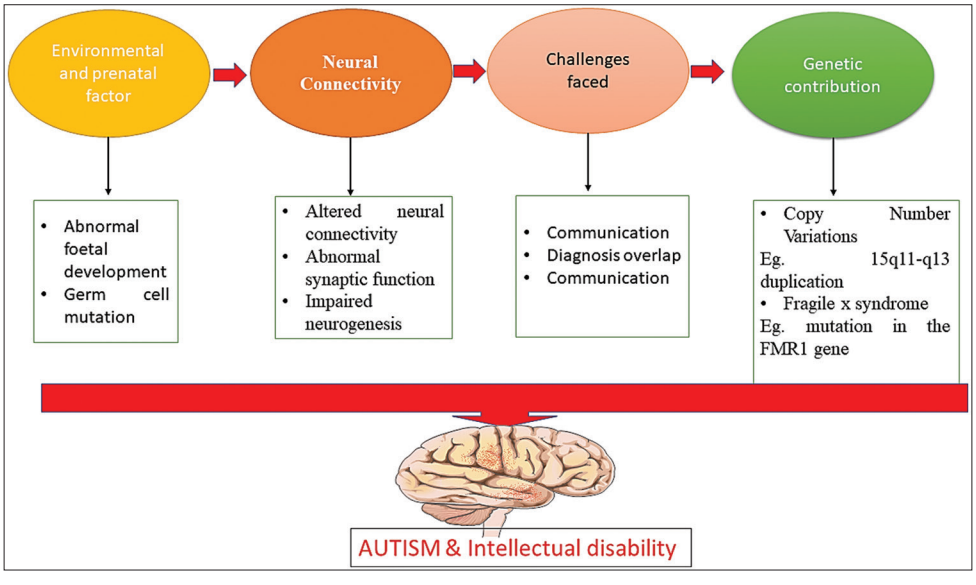

Figure 1: Factors affecting autism and intellectual disability

Gene-environment interactions and their influence on the cooccurrence of both conditions

Gene-environment interactions play a significant role in the cooccurrence of ASD and ID. While genetic factors contribute to the risk of both conditions, environmental influences can modify the expression and severity of symptoms, as well as influence the likelihood of their cooccurrence. Here is an overview of gene-environment interactions and their influence on the cooccurrence of ASD and ID

Genetic susceptibility and environmental triggers

Genetic factors can create a susceptibility to ASD and ID, but the actual development of these conditions often requires the interaction of genetic vulnerabilities with environmental triggers. Environmental factors that have been implicated in the development of ASD and ID include prenatal exposures, perinatal complications, maternal health, and early life experiences.[41]

Prenatal and perinatal factors

Environmental influences during prenatal and perinatal periods can impact brain development and contribute to the cooccurrence of ASD and ID. Factors such as maternal infections, exposure to toxins, prenatal drug or alcohol exposure, and complications during birth (e.g., oxygen deprivation) have been associated with an increased risk of both conditions.[42]

Epigenetic modifications

Epigenetic modifications, which are changes in gene expression without altering the underlying DNA sequence, can occur in response to environmental factors. These modifications can influence how genes are "read" and impact the development of ASD and ID. Environmental factors, such as stress, nutrition, and exposure to toxins, can lead to epigenetic changes that affect gene expression patterns relevant to both conditions.[43]

Shared environmental risk factors

ASD and ID often share common environmental risk factors, such as socioeconomic status, access to early intervention services, and the quality of early caregiving experiences. These shared environmental factors can contribute to the cooccurrence of both conditions. It is important to note that gene-environment interactions are complex and multifaceted, and our understanding of specific interactions is still evolving. The exact mechanisms by which genes and environmental factors interact to influence the cooccurrence of ASD and ID are not fully understood. Further research is needed to unravel the specific gene-environment interplay and its implications for the development, diagnosis, and treatment of these conditions. Overall, recognizing the role of gene-environment interactions is crucial in understanding the complex etiology of ASD and ID and in guiding interventions and support for individuals with these conditions.[44]

NEURODEVELOPMENTAL PATHWAYS IMPLICATED IN ASD AND ID

ASD and ID are both neurodevelopmental disorders that involve atypical brain development and functioning. Several neurodevelopmental pathways have been implicated in the etiology of ASD and ID, providing insights into the underlying biological mechanisms.[45] While there are shared pathways, there are also distinct features that contribute to the unique presentation of each condition. Here are some of the neurodevelopmental pathways implicated in ASD and ID.

Neural connectivity and synaptic function

Altered neural connectivity

Both ASD and ID have been associated with disrupted neural connectivity. Difficulties in establishing and maintaining proper connections between brain regions can lead to impaired information processing and integration.[46]

Abnormal synaptic function

Dysfunction in synapses, the connections between neurons, has been implicated in both ASD and ID. This includes alterations in neurotransmitter systems, such as glutamate and gamma-aminobutyric acid, which play crucial roles in brain development, communication, and plasticity.[47]

Neurogenesis and cell migration

Impaired neurogenesis

Neurogenesis, the process of generating new neurons, is critical for proper brain development. Deficits in neurogenesis have been implicated in both ASD and ID, affecting the formation and organization of brain circuits.[48]

Altered cell migration

Proper migration of neurons to their correct locations is essential for the development of functional brain architecture. Disruptions in cell migration can lead to aberrant brain organization and connectivity, contributing to the pathophysiology of ASD and ID.[49]

Gene expression and regulation

Dysregulated gene expression

ASD and ID involve alterations in gene expression and regulation. Various genetic factors, including mutations and copy CNVs, can disrupt gene expression patterns, leading to altered neurodevelopmental processes.[43]

Epigenetic modifications

Epigenetic mechanisms, such as DNA methylation and histone modifications, can influence gene expression without changing the underlying DNA sequence. Dysregulation of epigenetic processes has been associated with ASD and ID, impacting critical neurodevelopmental pathways.[50]

Brain regions and circuits

Frontal and temporal brain regions

Both ASD and ID often show abnormalities in frontal and temporal brain regions, which are involved in social cognition, language processing, executive functions, and emotional regulation.

Cortical thickness and surface area

Altered cortical thickness and surface area have been observed in individuals with ASD and ID. These changes can affect the structural organization and functional connectivity within the brain.[51] It is important to note that these neurodevelopmental pathways are interconnected, and disruptions in one pathway can have cascading effects on others. In addition, the specific manifestations and severity of these neurodevelopmental abnormalities can vary among individuals with ASD and ID.

Understanding these neurodevelopmental pathways is critical for unraveling the underlying biological mechanisms and informing targeted interventions and treatments for individuals with ASD and ID.

FUTURE DIRECTIONS AND RESEARCH IMPLICATIONS

While significant progress has been made in understanding the neurodevelopmental pathways implicated in ASD and ID, there are still areas that warrant further research and investigation. Advancements in these areas can provide a deeper understanding of the underlying mechanisms, improve diagnostic accuracy, and inform the development of targeted interventions. Here are some key areas for further research.[52]

Genetic architecture

Although genetic factors contribute to the risk of ASD and ID, the full spectrum of genetic variants and their interactions remains to be fully elucidated. Further research is needed to identify additional genetic variants associated with ASD and ID, including rare variants and gene-gene interactions. Large-scale genome-wide association studies (GWAS), whole-genome sequencing, and functional genomics approaches can help uncover novel genetic contributors and clarify the genetic heterogeneity observed in these conditions.[53]

Gene-environment interactions

Investigating the interplay between genetic factors and environmental influences is crucial for understanding the etiology and heterogeneity of ASD and ID. Future studies should focus on identifying specific environmental risk factors, such as prenatal exposures, maternal health, and early life experiences, and examining how they interact with genetic vulnerabilities to influence the development and severity of ASD and ID. Longitudinal studies that incorporate detailed environmental assessments and genetic profiling can provide valuable insights into these interactions.[54]

Biomarkers

Biomarkers hold promise for improving early identification, diagnosis, and monitoring of ASD and ID. Research efforts should focus on identifying reliable and accessible biomarkers, such as genetic markers, epigenetic signatures, neuroimaging markers, or physiological markers (e.g., electroencephalogram, eye-tracking), that can aid in early detection, prognostication, and tracking treatment response. Integrating multiple biomarkers and developing robust predictive models can enhance diagnostic accuracy and inform personalized interventions.[55]

Brain imaging and connectivity

Neuroimaging techniques, such as functional magnetic resonance imaging and diffusion tensor imaging, have provided valuable insights into brain structure and connectivity in ASD and ID. Further research should aim to refine and expand these imaging methods to better understand the neural circuitry disruptions underlying these conditions. Studying brain development and connectivity from infancy through adulthood can shed light on the developmental trajectories and identify critical periods for intervention.[56]

Comorbidity and overlapping conditions

ASD and ID often cooccur with other neurodevelopmental, psychiatric, and medical conditions. Understanding the nature and mechanisms underlying these comorbidities is critical for providing comprehensive care. Future research should investigate the shared and distinct pathways between ASD, ID, and other conditions, such as ADHD, anxiety disorders, epilepsy, and genetic syndromes, to unravel the complex relationships and guide integrated interventions.

By focusing on these areas of research, we can deepen our understanding of the complex neurodevelopmental processes involved in ASD and ID. This knowledge can

inform early identification, improve diagnostic accuracy, guide personalized interventions, and ultimately enhance the quality of life for individuals affected by these conditions.[57]

CONCLUSION

ASD and ID are complex and multifaceted. While ASD and ID are separate conditions, they can cooccur in some individuals, presenting unique challenges. Common behavioral characteristics and impairments, such as social interaction deficits, communication difficulties, restricted and repetitive behaviors, executive functioning challenges, and sensory sensitivities, are observed in both conditions. Differentiating between ASD and ID can be challenging due to diagnostic overlap, communication challenges, limitations in intellectual assessment, developmental considerations, and cooccurrence. Adaptive functioning plays a crucial role in distinguishing between the two conditions, with ID typically involving broader impairments across adaptive domains and ASD exhibiting more uneven profiles. Genetic factors contribute to both ASD and ID, with shared genetic variants, such as copy CNVs and FXS, as well as distinct genetic variants specific to each condition. A comprehensive and multidisciplinary assessment is essential to accurately diagnose and plan interventions for individuals with ASD, ID, or both. Further research is needed to deepen our understanding of the link between ASD and ID and guide effective support for individuals with dual diagnoses.

REFERENCES

1. Upadhyay J, Patra J, Tiwari N, Salankar N, Ansari MN, Ahmad W. Dysregulation of multiple signaling neurodevelopmental pathways during embryogenesis: A possible cause of autism spectrum disorder. Cells 2021;10:958.
2. Bhandari R, Paliwal JK, Kuhad A. Neuropsychopathology of autism spectrum disorder: Complex interplay of genetic, epigenetic, and environmental factors. Adv Neurobiol 2020;24:97-141.
3. Baj J, Flieger W, Flieger M, Forma A, Sitarz E, Skórzyńska-Dziduszko K, *et al*. Autism spectrum disorder: Trace elements imbalances and the pathogenesis and severity of autistic symptoms. Neurosci Biobehav Rev 2021;129:117-32.
4. McPartland J, Volkmar FR. Autism and related disorders. Handb Clin Neurol 2012;106:407-18.
5. Ashwood P, Wills S, Van de Water J. The immune response in autism: A new frontier for autism research. J Leukoc Biol 2006;80:1-15.
6. Zeidan J, Fombonne E, Scorah J, Ibrahim A, Durkin MS, Saxena S, *et al*. Global prevalence of autism: A systematic review update. Autism Res 2022;15:778-90.
7. Al Dera H. Cellular and molecular mechanisms underlying autism spectrum disorders and associated comorbidities: A pathophysiological review. Biomed Pharmacother 2022;148:112688.
8. McIlvane W, Deutsch C. Behavioral phenotypes in neurodevelopmental disabilities: Implications for research and intervention. In: Developmental Disabilities: Etiology, Assessment, Intervention, and Integration. Reno: Context Press; 2004. p. 64-80.
9. Harris, JC, Greenspan S. Definition and nature of intellectual disability. In: Handbook of evidence-based practices in intellectual and developmental disabilities. Cham: Springer; 2016. p. 11-39.
10. McNicholas PJ, Floyd RG, Woods IL, Singh LJ, Manguno MS, Maki KE. State special education criteria for identifying intellectual disability: A review following revised diagnostic criteria and Rosa's Law. Sch Psychol Q 2018;33:75-82.
11. Beesdo K, Knappe S, Pine DS. Anxiety and anxiety disorders in children and adolescents: Developmental issues and implications for DSM-V. Psychiatr Clin North Am 2009;32:483-524.
12. Salvador-Carulla LS, Reed GM, Vaez-Azizi LM, Cooper SA, Martinez-Leal R, Bertelli M, *et al*. Intellectual developmental disorders: Towards a new name, definition and framework for "mental retardation/ intellectual disability" in ICD-11. World Psychiatry 2011;10:175-80.
13. Rice CE, Rosanoff M, Dawson G, Durkin MS, Croen LA, Singer A, *et al*. Evaluating changes in the prevalence of the autism spectrum disorders (ASDs). Public Health Rev 2012;34:1-22.
14. Thapar A, Cooper M, Eyre O, Langley K. Practitioner review: What have we learnt about the causes of ADHD? J Child Psychol Psychiatry 2013;54:3-16.
15. Focht-New G, Clements PT, Barol B, Faulkner MJ, Service KP. Persons with developmental disabilities exposed to interpersonal violence and crime: Strategies and guidance for assessment. Perspect Psychiatr Care 2008;44:3-13.
16. Mojibi N, Ghazanfari-Sarabi S, Hashemi-Soteh SM. The prevalence and incidence of congenital phenylketonuria in 59 countries: A systematic review. J Pediatr Rev 2021;9:83-96.
17. Verma V, Paul A, Amrapali Vishwanath A, Vaidya B, Clement JP. Understanding intellectual disability and autism spectrum disorders from common mouse models: Synapses to behaviour. Open Biol 2019;9:180265.
18. Smith CC, Cihak DF, Morrow MC. Developing social interaction competence. In: Autism Spectrum Disorders: Advancing Positive Practices in Education. United Kingdom: Taylor and Francis; 2022.
19. Tager-Flusberg H, Paul R, Lord C. Language and communication in autism. In: Handbook of Autism and Pervasive Developmental Disorders. Vol. 1. Hoboken: John Wiley and Sons, Inc; 2005. p. 335-64.
20. Gal E, Yirmiya N. Introduction: Repetitive and restricted behaviors and interests in autism spectrum disorders. In: Repetitive and Restricted Behaviors and Interests in Autism Spectrum Disorders: From Neurobiology to Behavior. Berlin: Springer Nature; 2021. p. 1-11.
21. DeGangi GA. Pediatric Disorders of Regulation in Affect

and Behavior: A Therapist's Guide to Assessment and Treatment. Cambridge: Academic Press; 2017.
22. MacLennan K, O'Brien S, Tavassoli T. In our own words: The complex sensory experiences of autistic adults. J Autism Dev Disord 2022;52:3061-75.
23. Kraper CK, Kenworthy L, Popal H, Martin A, Wallace GL. The gap between adaptive behavior and intelligence in autism persists into young adulthood and is linked to psychiatric co-morbidities. J Autism Dev Disord 2017;47:3007-17.
24. Davidson C, O'Hare A, Mactaggart F, Green J, Young D, Gillberg C, *et al*. Social relationship difficulties in autism and reactive attachment disorder: Improving diagnostic validity through structured assessment. Res Dev Disabil 2015;40:63-72.
25. Pedersen AL, Pettygrove S, Lu Z, Andrews J, Meaney FJ, Kurzius-Spencer M, *et al*. DSM criteria that best differentiate intellectual disability from autism spectrum disorder. Child Psychiatry Hum Dev 2017;48:537-45.
26. Fitzpatrick R, McGuire BE, Lydon HK. Improving pain-related communication in children with autism spectrum disorder and intellectual disability. Paediatr Neonatal Pain 2022;4:23-33.
27. Peters-Scheffer N, Didden R, Korzilius H. Maternal stress predicted by characteristics of children with autism spectrum disorder and intellectual disability. Res Autism Spectr Disord 2012;6:696-706.
28. Tsikinas S, Xinogalos S. Towards a serious games design framework for people with intellectual disability or autism spectrum disorder. Educ Inf Technol 2020;25:3405-23.
29. Lukmanji S, Manji SA, Kadhim S, Sauro KM, Wirrell EC, Kwon CS, *et al*. The co-occurrence of epilepsy and autism: A systematic review. Epilepsy Behav 2019;98:238-48.
30. Panerai S, Tasca D, Ferri R, Genitori D'Arrigo V, Elia M. Executive functions and adaptive behaviour in autism spectrum disorders with and without intellectual disability. Psychiatry J 2014;2014:941809.
31. De Bildt A, Sytema S, Kraijer D, Sparrow S, Minderaa R. Adaptive functioning and behaviour problems in relation to level of education in children and adolescents with intellectual disability. J Intellect Disabil Res 2005;49:672-81.
32. Kilmer M, Boykin A. Analysis of the 2000 to 2018 autism and developmental disabilities monitoring network surveillance reports: Implications for primary care clinicians. J Pediatr Nurs 2022;65:55-68.
33. Hodge MA, Boulton KA, Sutherland R, Barnett D, Bennett B, Chan E, *et al*. Predictors of adaptive functioning in preschool aged children with autism spectrum disorder. Autism Res 2021;14:1444-55.
34. Sturrock A, Foy K, Freed J, Adams C, Leadbitter K. The impact of subtle language and communication difficulties on the daily lives of autistic children without intellectual disability: Parent perspectives. Int J Lang Commun Disord 2023;58:1232-50.
35. McClain MB, Mills AM, Murphy LE. Inattention and hyperactivity/impulsivity among children with attention-deficit/hyperactivity-disorder, autism spectrum disorder, and intellectual disability. Res Dev Disabil 2017;70:175-84.
36. Havdahl A, Niarchou M, Starnawska A, Uddin M, van der Merwe C, Warrier V. Genetic contributions to autism spectrum disorder. Psychol Med 2021;51:2260-73.
37. Marshall CR, Noor A, Vincent JB, Lionel AC, Feuk L, Skaug J, *et al*. Structural variation of chromosomes in autism spectrum disorder. Am J Hum Genet 2008;82:477-88.
38. Winarni TI, Utari A, Mundhofir FE, Hagerman RJ, Faradz SM. Fragile X syndrome: Clinical, cytogenetic and molecular screening among autism spectrum disorder children in Indonesia. Clin Genet 2013;84:577-80.
39. Zoghbi HY, Bear MF. Synaptic dysfunction in neurodevelopmental disorders associated with autism and intellectual disabilities. Cold Spring Harb Perspect Biol 2012;4:a009886.
40. Vissers LE, Gilissen C, Veltman JA. Genetic studies in intellectual disability and related disorders. Nat Rev Genet 2016;17:9-18.
41. Yirmiya N, Charman T. The prodrome of autism: Early behavioral and biological signs, regression, peri-and post-natal development and genetics. J Child Psychol Psychiatry 2010;51:432-58.
42. Ornoy A, Weinstein-Fudim L, Ergaz Z. Prenatal factors associated with autism spectrum disorder (ASD). Reprod Toxicol 2015;56:155-69.
43. Grafodatskaya D, Chung B, Szatmari P, Weksberg R. Autism spectrum disorders and epigenetics. J Am Acad Child Adolesc Psychiatry 2010;49:794-809.
44. Durkin MS, Yeargin-Allsopp M. Socioeconomic status and pediatric neurologic disorders: Current evidence. In: Seminars in Pediatric Neurology. Amsterdam: Elsevier; 2018.
45. Delhaye S, Bardoni B. Role of phosphodiesterases in the pathophysiology of neurodevelopmental disorders. Mol Psychiatry 2021;26:4570-82.
46. Dickinson A, Varcin KJ, Sahin M, Nelson CA 3rd, Jeste SS. Early patterns of functional brain development associated with autism spectrum disorder in tuberous sclerosis complex. Autism Res 2019;12:1758-73.
47. Pardo CA, Eberhart CG. The neurobiology of autism. Brain Pathol 2007;17:434-47.
48. Yang G, Shcheglovitov A. Probing disrupted neurodevelopment in autism using human stem cell-derived neurons and organoids: An outlook into future diagnostics and drug development. Dev Dyn 2020;249:6-33.
49. Magdalon J, Mansur F, Teles E Silva AL, de Goes VA, Reiner O, Sertié AL. Complement system in brain architecture and neurodevelopmental disorders. Front Neurosci 2020;14:23.
50. Handy DE, Castro R, Loscalzo J. Epigenetic modifications: Basic mechanisms and role in cardiovascular disease. Circulation 2011;123:2145-56.
51. Postema MC, van Rooij D, Anagnostou E, Arango C, Auzias G, Behrmann M, *et al*. Altered structural brain asymmetry in autism spectrum disorder in a study of 54 datasets. Nat Commun 2019;10:4958.
52. Molinaro G, Huber KM, McCullagh EA, Thomson SR.

Editorial: Recent advances in mechanisms and therapeutics for fragile x syndrome and autism. Front Neurosci 2023;17:1187799.
53. Talkowski ME, Minikel EV, Gusella JF. Autism spectrum disorder genetics: Diverse genes with diverse clinical outcomes. Harv Rev Psychiatry 2014;22:65-75.
54. Bölte S, Girdler S, Marschik PB. The contribution of environmental exposure to the etiology of autism spectrum disorder. Cell Mol Life Sci 2019;76:1275-97.
55. Frazier TW, Coury DL, Sohl K, Wagner KE, Uhlig R, Hicks SD, *et al*. Evidence-based use of scalable biomarkers to increase diagnostic efficiency and decrease the lifetime costs of autism. Autism Res 2021;14:1271-83.
56. Stigler KA, McDonald BC, Anand A, Saykin AJ, McDougle CJ. Structural and functional magnetic resonance imaging of autism spectrum disorders. Brain Res 2011;1380:146-61.
57. Young S, Hollingdale J, Absoud M, Bolton P, Branney P, Colley W, *et al*. Guidance for identification and treatment of individuals with attention deficit/hyperactivity disorder and autism spectrum disorder based upon expert consensus. BMC Med 2020;18:146.