

Autistic spectrum characteristics as a component of environmental susceptibility in the course of bipolar affective disorder: a narrative review

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Summary

Autism spectrum disorder and bipolar affective disorder exhibit partial symptomatic overlap, which can complicate accurate diagnosis and delay the implementation of appropriate treatment. Increasing research also points to the potential comorbidity of both conditions, further complicating the clinical picture, diagnostics, and therapy planning. The aim of this narrative review is to examine the literature concerning the relationship between autism spectrum disorder and bipolar affective disorder, with particular emphasis on the hypothesis that autistic traits and their associated chronic functional impairments may heighten susceptibility to the development or more severe course of bipolar affective disorder. Epidemiological data, diagnostic challenges, selected neurobiological and genetic mechanisms, as well as practical implications for diagnosis, treatment, and environmental support are discussed. A review of the literature highlights the need for cautious differential diagnosis, longitudinal observation, and interdisciplinary collaboration in the care of individuals with comorbid autism spectrum disorder and bipolar affective disorder. A better understanding of the relationship between these conditions may facilitate earlier recognition of affective symptoms in individuals on the autism spectrum and support more appropriate clinical assessment and management planning.

Key words: autism spectrum disorder, bipolar affective disorder, neurodevelopmental disorders

The autism spectrum – historical overview

The term “autism” originates from the Greek word *autos* (“self”) and was first used by Eugen Bleuler around 1910 in the context of schizophrenia. In 1943, Leo Kanner described early childhood autism, and a year later, Hans Asperger published a paper on autistic psychopathology [1–3]. Today, autism spectrum disorder (ASD)

is recognized as a neurodevelopmental disorder, the symptoms of which include difficulties in social communication and restricted, repetitive patterns of behavior [4]. A significant contribution to understanding the nature of the disorder was also made by Russian psychiatrist Grunya Suchareva, who, as early as the 1920s, described cases corresponding to today's criteria for ASD [5, 6]. For many years, the origins of autism spectrum disorder were thought to lie in the relationship between the parent, primarily the mother, and the child, pointing to the influence of the “cold rearing of refrigerator mothers” on the development of autistic traits in the child. It is now known that the pathomechanism of ASD is a much more complicated phenomenon, with genetic factors, neurological damage, and environmental influences contributing to its occurrence [7]. However, there is no direct link between parental behavior towards the child and the development of autistic traits due to the congenital nature of the disorder [4].

Autism spectrum – symptomatology and diagnosis

ASD is a neurodevelopmental disorder characterized by difficulties in social interactions, communication, and speech, as well as repetitive behavioral patterns [4]. The first symptoms typically appear in early childhood, but they are not always immediately noticeable. Common signs include delayed or atypical speech development, lack of eye contact, limited response to one's name, repetitive movements, attachment to routines, difficulty expressing emotions, impaired symbolic play, and inappropriate sensory reactions [8]. Early diagnosis increases therapeutic opportunities and the chances for compensating functional difficulties [8, 9].

In recent years, there has been an increase in late ASD diagnoses, particularly among adults [10]. This is due to growing social awareness and improved diagnostic standards [11]. For many years, ASD was considered primarily a condition affecting boys, however, it is now known that girls and women are “underdiagnosed”, partly due to the different expression of autistic traits and the phenomenon of masking [8, 12]. It is estimated that around 70% of adults on the spectrum engage in masking, with a higher prevalence among women [13]. Long-term, unconscious masking can lead to psychological exhaustion, identity issues, and delayed diagnoses.

According to the *International Classification of Diseases, 11th revision* (ICD-11, 2019) [14], ASD is diagnosed when there are persistent difficulties in social interactions and communication, as well as limited patterns of behavior, interests, and activities, leading to significant functional limitations. ICD-11 introduces the term “autism spectrum”, discontinuing the previous subdivision into subtypes [15]. The *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5) [16], defines ASD as a neurodevelopmental disorder with persistent deficits in social communication and repetitive behaviors, present from early childhood and limiting daily functioning. However, symptoms may intensify later with increasing social demands.

The contemporary conceptualization of ASD in DSM-5 and ICD-11 represents a significant shift in thinking about autism – from an approach based on rigid, separate diagnostic entities to a spectrum model that considers the variability in clinical presentation and level of functioning. This change is not only classificatory but also

epistemological, as it weakens the traditional dichotomy between normality and pathology, shifting attention to a continuum of traits, severity of difficulties, and diverse support needs. This perspective is particularly important in the context of the emerging concept of neurodiversity, which views some autistic traits not solely as deficits but as an alternative neurodevelopmental pattern. While this does not eliminate the need for clinical diagnosis and support when significant functional difficulties arise, it calls for greater interpretative caution and avoidance of reducing the individual to the category of disorder alone.

In the case of bipolar affective disorder (BAD), the departure from classical nosology is more limited compared to ASD, as it remains strongly rooted in the clinical-symptomatic and episodic model. Nonetheless, the significance of symptom continuity, variability in course, and individual trajectories of the disease is increasingly emphasized within affective disorders. In the context of the comorbidity of ASD and BAD, this suggests the need for a perspective that transcends simple categorical boundaries and considers both the neurodevelopmental profile and affective variability of the patient.

Despite established diagnostic criteria, the picture of ASD is highly diverse. There is no single feature that unequivocally excludes the diagnosis. Individuals within the spectrum can vary in their level of sociability, interests, and abilities – ranging from withdrawn to open and extraverted [15].

Functioning of individuals with autism spectrum disorder

Individuals on the autism spectrum function at very diverse levels – from those with intellectual disabilities and communication disorders who require comprehensive support, to those with intellectual abilities within or above the typical range, leading independent lives with possible adaptations [15]. The level of functioning is heterogeneous – it may be very high in some areas and low in others, with its expression changing over time depending on therapeutic interventions, health status, mental condition, or co-occurring difficulties [17]. Individuals with ASD also differ in the extent and intensity of the support they require, leading to varied life situations and degrees of independence. In relation to such diversity, terms like “high-functioning” and “low-functioning” were used, but due to their oversimplified nature and inadequacy in capturing the complexity of functioning in individuals on the spectrum, their use is now being avoided [18].

Individuals with ASD often face challenges in social relationships and initiating contact. Many identify as non-heteronormative, asexual, non-binary, or transgender. Studies indicate that women on the autism spectrum exhibit a lower level of heterosexuality compared to men [19]. Women and girls with ASD are also particularly vulnerable to psychological, physical, and sexual violence due to difficulties in assessing intentions and taking literal interpretations of communication. Research also confirms a higher risk of peer violence among children with ASD [20].

Despite the intellectual potential of individuals with ASD, obtaining higher education can be a challenge. Students with ASD are less likely to complete their studies

– according to Myrvold et al. [21], only 20% compared to 59% of the general population. At Polish universities, 70.2% of students with ASD report sensory overload, and 63.3% experience loneliness [22]. Employment activity is similarly low – only 2% of individuals with ASD are employed [23]. Barriers include recruitment difficulties, lack of workplace adaptations, and communication issues, which often lead to burnout and depression.

ASD frequently co-occurs with other mental health disorders, such as depression, attention deficit hyperactivity disorder (ADHD), anxiety disorders, and eating disorders. Individuals on the spectrum are also more prone to substance abuse, which may serve as maladaptive coping strategies for stress, sensory overload, or relational difficulties. Particularly concerning are data regarding suicide risk – individuals with ASD experience suicidal thoughts and attempts much more frequently [19, 24]. A meta-analysis by O'Halloran et al. [24] showed that 25% of youth with ASD have suicidal thoughts, and 8% attempt suicide. Among adults, these rates increase – 37% report suicidal thoughts, and over 15% have attempted suicide [25]. Among individuals with ASD without intellectual disabilities, attempts occur in approximately 24%. Scandinavian studies indicate that the risk of suicide attempts and deaths is 3–8 times higher than in the general population [26]. The strongest risk factor remains comorbid depression, affecting nearly 70% of individuals with ASD. Masking of symptoms, chronic feelings of rejection and loneliness, particularly in transgender and non-binary individuals, are also significant factors. Executive function disorders, including difficulties in impulse control, further exacerbate the suicide risk [6, 25].

Bipolar affective disorder (BAD) – historical overview

The origins of describing affective disorders date back to ancient times, when the occurrence of mania and melancholia was noted. For a long time, however, these were considered separate psychopathological phenomena [27]. It was not until the 19th century that the interrelationship and cyclical nature of their course began to be recognized. French psychiatrists Jean-Pierre Falret and Jules Baillarger made significant contributions to this understanding by describing the alternating occurrence of depressive and manic states. However, it was Emil Kraepelin's work in 1899 that introduced the concept of manic-depressive psychosis, laying the foundations for the modern understanding of bipolar affective disorder [27, 28]. In the second half of the 20th century, the development of psychopharmacology, particularly the discovery of lithium's effects and the introduction of mood-stabilizing drugs, significantly impacted the treatment possibilities for this disorder [29]. Today, BAD is understood as a chronic, recurring mood disorder characterized by the occurrence of manic, hypomanic, and depressive episodes, with a multifactorial etiology and varied clinical course.

Bipolar affective disorder – characterization and diagnosis

BAD is a chronic mood disorder characterized by alternating episodes of depression and mania or hypomania, separated by periods of remission [29]. Two main types

are distinguished: Type I, which includes depressive and manic episodes, and Type II, which involves episodes of depression and hypomania [30]. The disorder can also manifest as mixed episodes, where depressive and manic symptoms occur simultaneously, often associated with a high risk of suicide. Additionally, forms such as rapid cycling (≥ 4 episodes per year) and ultra-rapid cycling, where phases change within a week or day, are recognized [30].

BAD has a significant genetic component – the risk of developing the disorder increases with the degree of familial relationship to another affected individual [31]. Environmental risk factors include stress, adverse childhood experiences, prenatal and perinatal burdens, and crisis situations. The condition is diagnosed when at least one depressive and one manic or hypomanic episode occur [30].

Prodromal symptoms of a manic episode can appear up to a year before the full-blown manic episode occurs. Research by Maassen et al. [32] identified the presence of prodromal symptoms in seven areas: behavior (increased activity, impulsivity), physiology (sleep disturbances, increased energy), communication (conflict, increased media activity), thoughts (racing thoughts, excessive self-confidence), cognition (changes in concentration), emotions (euphoria, instability), and personality traits (intensification of existing traits). Early identification of prodromal symptoms in at-risk patients may facilitate earlier intervention and reduce diagnostic delay [33]. However, it should be emphasized that in clinical practice, the diagnosis of BAD is often made only after many years – from the first contact with a physician to the correct diagnosis, an average of 6 to 10 years typically pass [30].

In most patients, the disorder begins with a depressive episode, with manic or hypomanic symptoms appearing later. Diagnostic delays are caused, among other things, by a lack of critical assessment of manic symptoms and misdiagnoses, such as unipolar depression, schizophrenia, ASD, ADHD, or borderline personality disorder [30, 34]. Bipolar disorder can also occur in children and adolescents, further complicating the diagnostic process [35, 36]. Therefore, early recognition of prodromal symptoms and careful differential diagnosis are crucial.

According to Bartoli et al. [37], about two-thirds of patients present a dominant polarity – either manic or depressive. The first episode often determines the course of the disease: mania tends to lead to Type I, while depression results in a predominance of depressive episodes. Patients with dominant mania (more often men) begin the disorder earlier and have more frequent psychotic episodes, while those with dominant depression tend to maintain relationships more often but have a higher suicide risk [30].

The prevalence of BAD in the general population is 1–3% (Type I – approximately 0.8%, Type II – approximately 0.5%), and the annual incidence among adults ranges from 0.3 to 1.2% [38]. Among individuals with ASD, the risk is significantly higher, at 5–8% [39]. In a meta-analysis of adults with ASD, the percentage of BAD was 7.5% (95% CI 5.8–9.5). Among young adults with ASD, the disorder occurs nearly ten times more frequently (7.3% vs 0.9% in the control group) [39]. Varcin et al. [40] indicate that 36% of individuals with ASD have mood disorders, 75% of which are bipolar. These data suggest that the co-occurrence of ASD and BAD is not incidental

but represents a clinically significant pattern of comorbidity, which should be considered both in psychiatric diagnostics and in the long-term monitoring of patients with ASD.

Functioning of individuals with bipolar affective disorder

Understanding the functioning of individuals with BAD, the course of the disease, its challenges, and treatment specifics requires consideration of the concept of neuroprogression. This concept, when applied to mental disorders, posits that the first episode of the disease is triggered by a combination of life-related psychological and social stressors, along with genetic vulnerability. Subsequent episodes, however, are increasingly independent of emerging stressors [41]. The first proponent of this concept was psychiatrist Robert Post, who, in 1921, coined the term *kindling*, referring to the process of “ignition”. According to his theory, psychosocial factors have the greatest influence on triggering the first episode of the disorder. Post also suggested that repeated episodes of the disease could lead to permanent changes in neuron function and activity, which increases susceptibility to relapses and diminishes treatment effectiveness [28]. As a result, subsequent episodes may occur spontaneously, regardless of environmental factors, and the course of the disorder may intensify, taking the form of rapid cycling between phases (rapid-cycling), which is more difficult to treat and exhibits pharmacological resistance [42].

Therefore, one of the most crucial elements influencing the functioning of individuals with BAD is the early and accurate diagnosis (including diagnoses in the case of comorbidities) and the prompt implementation of pharmacological treatment, psychotherapy, and psychoeducation. An important aspect is also psychoeducation for family members and loved ones. Severe cases of BAD often lead to financial debt, breakdowns in marriages, partnerships, or social relationships, strong dependencies on psychoactive substances, sexually transmitted diseases, legal consequences resulting from offenses or crimes, loss of functional capacity, and sometimes complete disability for the entire family unit. This disorder frequently results in partial or total inability to work, difficulty in acquiring education, lack of financial independence, and very commonly in this social group – hospitalizations, suicide attempts, and suicide deaths [33]. Among all mental health challenges, BAD has the highest suicide rate. It is estimated that the risk for individuals with BAD is approximately 30–60% higher compared to the general population. Around $\frac{1}{3}$ to $\frac{1}{2}$ of patients with BAD attempt suicide at least once in their lifetime, and approximately 15–20% die as a result of suicide [43].

Table 1. Comparison of similarities and differences between BAD and ASD [7–25, 30–42]

Criterion	BPAD	ASD
Differences		
Nature of symptoms	Episodic / periodic	Persistent
Time of symptom onset	Typically late adolescence or early adulthood	From birth or early childhood
Nature of the disorder	Mood (affective) disorder	Neurodevelopmental disorder

table continued on the next page

Social interactions	During mania – excessive sociability; during depression – social withdrawal	Persistent difficulties in communication and social interaction
Interests and behaviors	During mania – impulsive, risky behaviors, possible addictions; during depression – loss of interest	Restricted, repetitive interests and routines
Cognitive functioning	During mania – accelerated thinking, tangentiality, “racing thoughts”, word salad, loss of critical judgment During depression – psychomotor retardation, impaired attention and memory functions	Cognitive rigidity, literal interpretation of language, impaired abstract thinking, difficulties understanding irony and humor
Response to medication	High efficacy of mood stabilizers	Often hypersensitivity to neuroleptics; atypical or paradoxical reactions
Similarities		
• Difficulties with emotion regulation (e.g., outbursts of anger, impulsivity, irritability) • Mood fluctuations • Difficulties in interpersonal relationships – individuals with BD may be excessively extroverted during manic phases and withdrawn during depressive phases, while individuals with ASD tend to be socially withdrawn • Sleep disturbances – insomnia, disrupted circadian rhythms, difficulties falling asleep • Increased risk of risky behaviors, self-harm, and suicidal tendencies • Impairments in executive functioning		

Comorbidity of autism spectrum disorder and bipolar affective disorder

The comorbidity of bipolar affective disorder and autism spectrum disorder is increasingly being described in epidemiological and clinical studies. It is estimated that BAD occurs in 5–8% of individuals with ASD, which is several times higher than in the general population, where the prevalence of this disorder is around 1%. A study involving 700,000 children showed that BAD is six times more common in individuals with ASD than in those without the disorder [33]. Other sources suggest that up to 10% of adults with ASD may have comorbid BAD [44].

This comorbidity is associated with significant diagnostic challenges. Some of the characteristics of BAD and ASD overlap, making their differentiation difficult (Table 1) [33]. The diagnostic process depends on factors such as the level of speech and communication development, the ability to recognize and label one’s emotional states, and the capacity to interpret them (as individuals with ASD often exhibit alexithymia) [45]. Even with adequate clinical knowledge and a thorough interview, some symptoms of BAD may remain unnoticed due to communication difficulties and limited insight into one’s mental state, while certain ASD traits might be misinterpreted as symptoms of BAD [45].

An additional source of diagnostic delay is the fact that these patients are more likely to present to mental health specialists during depressive episodes rather than manic or hypomanic phases, whereas a diagnosis of mania or hypomania is crucial for diagnosing BAD [39, 40, 45]. Therefore, early recognition of mania or hypomania symptoms is crucial for accurate diagnosis and treatment planning. The literature also reports that some individuals with ASD may exhibit a different tolerance to certain medications used in the treatment of BAD. Increased adverse effects from mood stabilizers and antipsychotic medications have been described, along with difficulties in early detection of these effects due to limitations in communicating subjective feelings [46].

The co-occurrence of both disorders also leads to greater clinical and psychosocial burden [39]. The literature emphasizes that chronic stress, sensory overload, sleep disturbances, social difficulties, and the masking of autistic traits can increase susceptibility to affective episodes, while episodes of mania, hypomania, and depression can further exacerbate communication difficulties, behavioral disorganization, and adaptive limitations typical of ASD [44, 47, 48]. As a result, the comorbidity of ASD and BAD can lead to a decline in daily functioning, reduced psychological well-being, difficulties maintaining independence, and a deterioration in quality of life. The risk of suicidal behavior and suicide deaths is also elevated, which is high both in individuals with ASD and those with BAD [48].

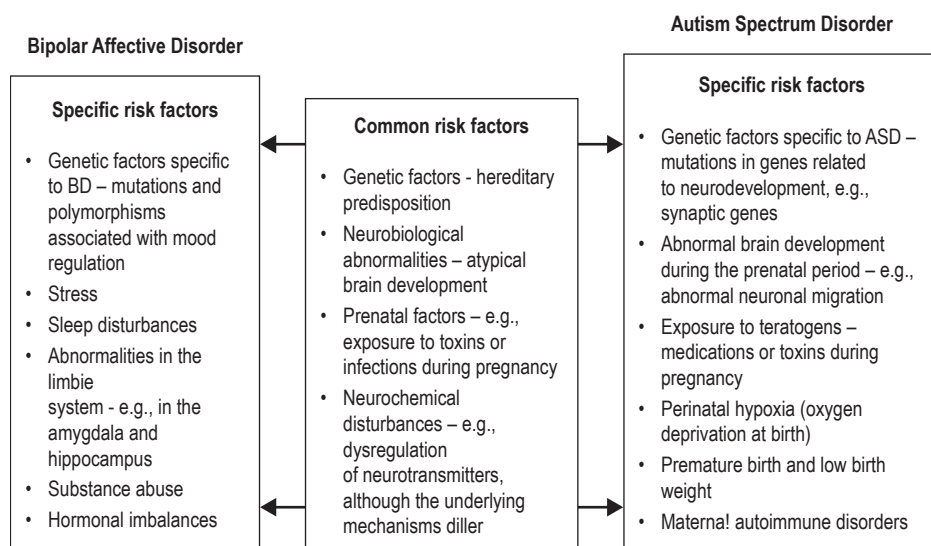


Figure 1. **Shared risk factors for the development of bipolar affective disorder and autism spectrum disorder [7–25, 30–42]**

Autism spectrum as an environmental activator of bipolar affective disorder

Current scientific research suggests that ASD should not be treated as a direct cause of BAD, but rather as a set of neurodevelopmental traits and functional conditions that, under certain circumstances, may increase vulnerability to the development of affective disorders [44, 48]. Chronic stress, sensory overload, sleep disturbances, social difficulties, and limited coping abilities with prolonged burdens are of particular significance in this context (Figure 1) [49].

Given this perspective, developing preventive actions and early interventions targeted at children and adolescents on the autism spectrum seems warranted. Teachers and caregivers can play an important role in preventive interventions, as they observe students in everyday school situations, where changes in emotional, social, and behavioral functioning often manifest earliest. Their role is not to make a diagnosis but to carefully monitor the student's activities and behavior, detect troubling changes, and communicate these observations to parents and specialists. Therefore, teachers can act as intermediaries between daily observation and the initiation of further specialized assistance.

Special attention should be paid to sudden changes in activity, increased irritability, noticeable deterioration in concentration, sleep disturbances reported by the family, increased impulsivity, social withdrawal, or atypical mood swings [47, 49]. In school practice, teachers can also support the student by reducing overload, creating a predictable environment, and flexibly adjusting requirements during periods of functional decline. However, the effectiveness of such support depends on the level of knowledge that the educational staff has about the mental health of students on the autism spectrum and the efficient collaboration between the school, the family, psychologists, and other specialists. Preventive actions carried out at school can complement support efforts but should not replace specialized diagnosis or psychiatric and psychological care [50].

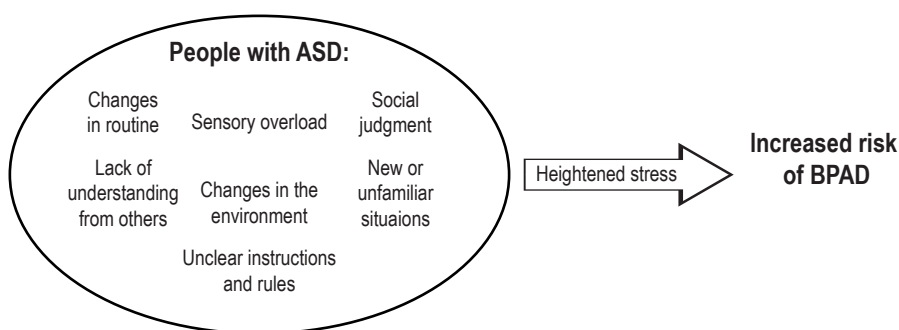


Figure 2. Increased risk of bipolar affective disorder in the context of factors co-occurring with autism spectrum disorder [7–25, 30–42]

The concept of environmental vulnerability in the context of the comorbidity of BAD and ASD can be related to the diathesis-stress model, which posits that genetic

predispositions reveal their clinical significance through interactions with environmental stressors [48]. In this view, ASD is not a causal factor in itself, but rather a set of neurodevelopmental traits that, under specific conditions, may increase sensitivity to chronic stress, disruptions in circadian rhythm, sensory overload, and adaptive difficulties (Figure 2).

According to this model, predispositional genetic factors (e.g., single nucleotide polymorphisms) interact with environmental factors (e.g., air pollution, heavy metals, endocrine-disrupting toxins), increasing the risk of neuropsychiatric disorders [48]. Epidemiological studies have shown that prenatal exposure to PM_{2.5} particles, NO₂, PCBs, and heavy metals like mercury and lead increases the risk of ASD, which may also be relevant for individuals with BAD, as these pollutants induce oxidative stress and neuroinflammatory reactions, affecting the hypothalamic-pituitary-adrenal (HPA) axis and dopaminergic and serotonergic neurotransmission [51]. These factors exert their influence through the effect of excessive neurobiological load – the so-called “double-hit” – particularly in genetically vulnerable individuals with reduced detoxification or compensation abilities [52].

The neurobiological mechanisms linking both disorders include dysfunctions in the dopaminergic axis, as confirmed by over – or under-regulation of DRD1–DRD3 receptors in molecular studies, as well as the involvement of serotonergic pathways associated with the SLC6A4 and HTR2A genes [53]. The dopaminergic axis is responsible for motivation, reward processing, motor control, and social and executive functions. Individuals with ASD exhibit disruptions in mesocorticolimbic and nigrostriatal pathways – decreased dopamine release in the prefrontal cortex and basal ganglia, and increased expression of D2 receptors in the striatum, correlating with social deficits and repetitive behaviors. In patients with BAD, phase instability of the dopaminergic system is observed: hypodopaminergia during depressive phases and hyperdopaminergia during manic phases, which correlates with motivational symptoms and mood changes. This instability in both disorders can reinforce each other, facilitating their comorbidity [53, 54].

The serotonergic axis regulates mood, impulsivity, sleep rhythm, neurogenesis, and immune response. In ASD patients, hyperserotoninemia and abnormalities in serotonin transport are often observed, which may affect the development of the nervous system and social behaviors [55, 56]. In BAD, abnormalities in the methylation of SLC6A4 genes and 5HT receptors have been noted, leading to emotional instability. Additionally, chronic inflammation activates the kynurenine pathway, lowering tryptophan levels and serotonin availability, which exacerbates depressive-manic symptoms and may contribute to the promotion of ASD-like traits [55, 56].

Another aspect is the HPA axis, which regulates the stress response through the secretion of corticotropin-releasing hormone (CRH), adrenocorticotrophic hormone (ACTH), and cortisol. In BAD, chronically elevated cortisol levels and impaired negative feedback of the axis, even during remission phases, can lead to neurotoxicity and disruptions in neuroplasticity [57]. In individuals with ASD, the HPA axis is also hyperreactive, as indicated by increased cortisol responses to psychosocial stress, leading to emotional hypersensitivity and anxiety. Dysregulation of the HPA axis in

both disorders deepens behavioral and emotional deficits, supporting their comorbidity and suggesting a shared pathogenic component at the axis level.

Additionally, both conditions exhibit neuroinflammatory components, including elevated levels of pro-inflammatory cytokines (IL6, TNF α), activation of the NLRP3 inflammasome, and microglia [58]. In BAD, an intensified inflammatory state in the central and peripheral nervous systems correlates with the severity of mood disorder episodes and emotional instability. Chronic inflammation (including microglia activation in the cortex, striatum, and cerebellum) is associated with communication difficulties, stereotypies, and social deficits. These cytokines also interact with the dopaminergic, serotonergic, and HPA axes (e.g., through activation of indoleamine 2,3-dioxygenase and tryptophan degradation, as well as reduced dopamine release), creating a feedback loop that strengthens the simultaneous presence of BAD and ASD traits [58].

Genetically, shared polymorphisms are observed in genes related to ion and synaptic transmission [47]. This includes CACNA1C (SNP rs1006737 and rs1051375), a gene associated with calcium regulation, increased neuronal excitability, and predisposition to BAD and ASD, SHANK3, which encodes a postsynaptic protein, with mutations linked to social and communication deficits in ASD, and synaptic changes observed in behavioral models of mood disorders, as well as GRIN2B, a subunit of NMDA receptors, associated with both ASD and other developmental disorders [59]. Polymorphisms in other glutamate receptor genes (e.g., GRIN2A, GRIK2) and synaptic genes (NRXN1, CNTNAP2) are present in both categories of disorders, as confirmed by molecular pathway analyses [60]. Common mechanisms also include chronic neuroinflammatory glial activation, leading to disrupted neuroplasticity and the formation of suboptimal synaptic connections typical of both mood instability and rhythmic deficits, as well as emotional disorders. Some data also indicate the role of MET gene polymorphisms in modifying sensitivity to prenatal exposure to pollution and interaction with copy number variants (CNVs), as confirmed by epidemiological studies on gender differences in susceptibility to airborne exposure (higher in boys) [47, 59]. At the same time, the expression of synaptic genes is modified due to DNA methylation caused by pollution, affecting, among others, CACNA1C and SHANK3, and influencing the functioning of the HPA axis and dopaminergic and serotonergic neurotransmission. The results suggest that the mechanisms maintaining the balance in the body, particularly glutamatergic-GABAergic, are disrupted in both disorders due to mutations in channel and synaptic genes [47].

The aforementioned data do not allow for the adoption of a simple causal model but collectively support the hypothesis of a partially shared neurodevelopmental and affective vulnerability. From a clinical perspective, it seems more important to acknowledge that the comorbidity of ASD and BAD may result from the overlap of multiple biological and environmental factors.

In a broader context, the comorbidity of ASD and BAD fits within the growing interest in the comorbidity of neurodevelopmental and affective disorders. Modern psychiatry is increasingly moving away from rigidly viewing these diagnoses as completely separate clinical categories, focusing on partially shared genetic, neurobiological, and environmental mechanisms. This approach allows for a better

understanding of both diagnostic challenges and the need for more individualized treatment and support.

Practical recommendations

Differential diagnosis between ASD and BAD represents a substantial clinical challenge, as several features may overlap, particularly irritability, impulsivity, psychomotor agitation, and difficulties in emotion regulation. In clinical practice, it is crucial to determine whether the observed symptoms constitute part of a relatively stable neurodevelopmental phenotype or instead represent a qualitatively new, clearly intensified, and episodic change in the patient's functioning [48].

A thorough developmental history and careful longitudinal assessment of symptom course should form the basis of an accurate diagnosis. In ASD, difficulties typically emerge in early childhood and tend to remain relatively stable over time, whereas in BAD, mood symptoms usually arise later and follow an episodic course [61]. Emotional lability in ASD is more often associated with sensory overload, communicative frustration, adaptive difficulties, or cognitive rigidity rather than with a typical affective episode. For this reason, irritability alone should not be regarded as sufficient grounds for diagnosing BAD in an individual with ASD [61, 62].

Particular diagnostic vigilance is warranted for symptoms suggestive of an evolving manic or hypomanic episode, such as decreased need for sleep, a marked increase in goal-directed activity, pressured or excessive speech, acceleration of thought processes, expansiveness, increased risk-taking behavior, and a significant change in the pace of everyday functioning [32, 62]. These symptoms should always be interpreted in relation to the patient's prior behavioral baseline, as agitation or impulsivity in individuals with ASD may be chronic and related to self-regulatory difficulties rather than to an affective disorder.

In this context, longitudinal observation is of particular importance, since a single psychiatric evaluation may be insufficient to distinguish enduring neurodevelopmental characteristics from episodic affective symptoms. Collateral information obtained from family members, caregivers, or other individuals from the patient's close environment may be especially valuable in identifying changes in sleep, activity level, behavior, and overall functioning. Standardized screening instruments, such as the ADOS-2 or the MDQ, may serve as useful adjuncts in the diagnostic process; however, their results must always be interpreted within the broader clinical context [39, 48, 61–63].

Another essential component of management is the monitoring of pharmacotherapy safety. In individuals with ASD, adverse effects may present atypically or be more difficult to verbalize; therefore, regular assessment of treatment tolerability, changes in sleep, appetite, arousal level, cognitive functioning, and aggressive or self-injurious behaviors is required [39, 61]. Particular attention should be paid to the early identification of paradoxical worsening of irritability, agitation, or self-regulation following treatment initiation, as such manifestations may be erroneously attributed solely to ASD rather than recognized as potential adverse drug reactions [61, 62].

A multidisciplinary approach is warranted in treatment. Ongoing collaboration between the psychiatrist, psychologist, and family increases the likelihood of earlier recognition of prodromal symptoms, more accurate interpretation of behavioral changes, and better tailoring of treatment to the patient's needs. The psychiatrist is primarily responsible for differential diagnosis and pharmacological management, the psychologist for a more in-depth assessment of emotional functioning and environmental determinants, while the family provides crucial information regarding the day-to-day course of symptoms and the circumstances surrounding deterioration in mental state.

In children and adolescents, the school environment also constitutes an important component of the early-support system. Teachers and school-based professionals, by observing the student across a range of social and task-related contexts, may detect sudden changes in activity level, concentration, irritability, social withdrawal, or school adjustment. Although they do not perform a diagnostic role, they may play an important part in identifying warning signs and initiating further psychological or psychiatric referral. Educational support for a student with co-occurring ASD and BAD should be based on predictability of interventions, the provision of a safe and minimally overloading environment, and flexible adjustment of expectations during periods of deterioration in mental functioning.

Conclusions

The literature indicates that the comorbidity of autism spectrum disorder and bipolar affective disorder represents a significant clinical challenge, which should not be understood as a simple sum of two separate diagnoses. Available data suggest that individuals with ASD form a group at increased risk for affective disorders, including BAD. This risk may arise from shared neurobiological and genetic mechanisms, as well as chronic environmental stressors associated with functioning within the autism spectrum. At the same time, the presence of BAD can exacerbate difficulties typical of ASD, worsening emotional regulation, social functioning, and overall quality of life.

There is a need for heightened diagnostic vigilance in cases where individuals with ASD experience episodic changes in mood, sleep, activity levels, and overall functioning. A detailed developmental history, observation of changes over time, and accurate recognition of the true comorbidity of both disorders, rather than just differentiating them, are essential in such cases.

In light of the analyzed studies, an interdisciplinary approach seems justified, combining psychiatric, psychological, developmental, pedagogical, and environmental perspectives. Early identification of prodromal symptoms, collaboration with the family and school, and well-planned psychoeducational support can significantly improve prognosis. Further research should focus on refining the mechanisms linking ASD and BAD and developing more specific diagnostic and therapeutic standards for patients with this complex comorbidity.

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