World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(REVIEW ARTICLE)

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Psychiatric symptoms and comorbidities in autism spectrum disorder: A narrative review

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World Journal of Advanced Research and Reviews, 2025, 25(01), 1108-1116

Publication history: Received on 06 December 2024; revised on 13 January 2025; accepted on 15 January 2025

Article DOI: https://doi.org/10.30574/wjarr.2025.25.1.0167

Abstract

Autism Spectrum Disorder includes a group of developmental disorders characterized by a delay and deviation in the development of communication, socialization, cognitive skills, and the presence of restricted interests as well as repetitive behaviors. In the present paper, the authors present the psychiatric disorders that can most often be associated with the diagnosis of autism and the most frequent diagnostic means to diagnose comorbidity. Diagnosis can be difficult, especially in mild forms, because individuals with autism are more likely to have comorbid psychiatric disorders than the general population. Moreover, psychiatric comorbidities can worsen the clinical course of autism and determine resistance to pharmacological treatments. Further studies are needed to validate increasingly sensitive psychometric scales in identifying psychiatric comorbidities in people with autism and to use more appropriate medications for the management of core aspects of autism.

Keywords: Autism Spectrum Disorder; Psychiatric symptoms; Psychiatric comorbidities; Diagnostic tools; Pharmacological treatments.

1. Introduction

Autism Spectrum Disorder (ASD) is a group of neurodevelopmental disabilities characterized by persistent difficulties in social-communicative skills, language, behavior, personal skills, and executive functions that impact on quality of life of patients and their caregivers [1,2].

Clinical presentation depends on symptom severity, cognitive and language abilities and co-occurrence of comorbid conditions [3]. In addition to core symptoms, people with ASD often have numerous medical and psychiatric comorbidities that worsen the quality of life of patients and their caregivers [4]. Furthermore, frequently, the symptoms of autism can be mild or subthreshold and overlap with other psychopathological disorders [5]. Subthreshold autistic traits can represent risk factors for the emergence of psychiatric disorders and worsen the trajectory of other comorbid disorders [6,7]. Indeed, people with subthreshold autistic traits often come to clinical attention when comorbid mental disorders arise [8].

Precisely because of the overlapping of symptoms between ASD and other psychopathological conditions, the use of appropriate diagnostic tools and scales appears necessary. In 2016, Vllasaliu et al. [9] published a systematic review of the most widely used diagnostic scales which include: The Developmental, Dimensional, and Diagnostic Interview [10], the Childhood Autism Rating Scale (CARS) [11], the Autism Spectrum Disorder-Observation for Children (ASD-OC) [12], the Autism Diagnostic Interview-Revised (ADI-R) [13], the Asperger Syndrome Diagnostic Interview [14], the Diagnostic Interview for Social and Communication Disorders (DISCO) [15] and the Autism Spectrum Disorder–Diagnosis Scale for Intellectually Disabled Adults (ASD-DA) [16].

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The prevalence of ASD is constantly growing with data that in 2023 in the USA are estimated to be around 1 in 36 children and of 1 in 45 adults [17] also thanks to the increased frequency of screening, improved diagnostic criteria and the use of more accurate behavioral and neuropsychological scales. The prevalence of ASD appears to be four- to five-fold higher in boys than in girls [18].

Many different factors have been identified that may make a child more likely to have ASD, including environmental, biological, and genetic factors [19]. A significant risk factor of ADS is having one or more relatives with ASD. Hence the risk of having a second child with ASD is around 20%; 10 to 20 times more than in the general population [20,21 ,22]. Although the etiopathogenesis of autism has not yet been clarified, the data in the literature agree that the causes of autism are multifactorial [23,24].

Although there are currently no approved medications for the treatment of ASD, psychiatric medications are commonly used in patients with ASD particularly for comorbid psychopathological aspects [25]. Past literature has shown that psychiatric drugs are used in one-third of children and two-thirds of adolescents [26]. However, the effectiveness and tolerability of drug treatments are often questionable [27] and many times drugs are overdosed resulting in numerous side effects [28].

The integration of pharmacological treatment with psychosocial, educational and rehabilitative interventions is a fundamental aspect of the management of ASD [29]. Furthermore, the association of pharmacological therapies with behavioral interventions is reported to be effective in improving functioning [30]. Recently D'Agostino et al. [31] summarized the numerous rehabilitation interventions and treatment models for ASD that have been proposed over the years.

2. Methods

A literature search was conducted on major databases to find useful studies for the aim of this paper.

3. Discussion

Past literature highlighted numerous conditions and disorders frequently associated with ASD. Still, in the present paper, the authors want to focus on the psychiatric comorbidities that most often occur in people with ASD, represented by Attention-Deficit Hyperactivity Disorder (ADHD), anxiety, mood disorders, sleep disorders, eating disorders, obsessive-compulsive disorder, personality disorders and schizophrenia.

ADHD represents the most common neurodevelopmental disorder and is often comorbid with other psychiatric conditions [32]. In 2022, Shoaib et al. [33] showed that ADHD is the most frequent psychiatric comorbidity in people with ASD with a prevalence of co-occurring ranging from 25.7% to 65% [34]. Furthermore, the co-occurrence of ASD and ADHD is associated with more severe impairments in adaptive and executive functioning and quality of life [35]. Psychostimulants are widely used to treat ADHD symptoms comorbid with ASD [36] but are burdened by a reduction in tolerability and efficacy [37].

Anxiety symptoms are very common in people with ASD [38]. Specific phobias and Generalized Anxiety Disorder (GAD) appear to be the most frequent anxiety disorders in ASD, with a lifetime prevalence, respectively, of 31% and 26% [39]. Often, the presence of anxiety disorders generally aggravates psychosocial functional impairment, particularly increasing social avoidance behaviors and withdrawal from school activities [40]. The use of selective serotonin reuptake inhibitors (SSRIs) and serotonin and noradrenaline reuptake inhibitors (SNRIs) for young individuals with ASD and anxiety disorders appear to have relatively good efficacy and low incidence of adverse effects [41].

From a clinical point of view, it is often difficult to recognize mood symptoms and even more so to diagnose a mood disorder in people with ASD. Indeed, Common ASD symptoms can hide symptoms of psychiatric comorbidities. Often, a change or worsening of the core symptoms of autism could be a warning sign for mood disorders. Catatonia may also be an exacerbation of pre-existing mood symptoms [42]. Depressive symptoms may occur in individuals with low-functioning autism (LFA) with mutism, social withdrawal, worsening eye contact, mood swings, increased obsessiveness, and self-injurious behaviors (SIB) [43]. High-functioning autism (HFA) subjects show more feelings of low self-esteem and difficulties in social functioning [44]. On the other hand, bipolar disorder (BD) may manifest with irritability, aggressivity, excessive reactivity, hyperarousal, agitation, increased distractibility, and an increase in laughter [45]. Since mood disorders in ASD are considered negative prognostic factors for a good outcome [46], it is essential to use appropriate diagnostic tools to assess the presence of mood disorders in ASD such as the

Psychopathology in Autism Checklist (PAC) [47]. The only two medications approved for the pharmacological treatment of irritability in ASD associated with mood disorders are aripiprazole and risperidone [48,49]. Lithium and sodium divalproex seem to be effective in the treatment of comorbid manic symptoms and aggression [50]. On the other hand, quetiapine, olanzapine, ziprasidone, tricyclic antidepressants (TCA) and SSRIs showed inconsistent results on effectiveness [51]. Challenging and self-injurious behaviors represent conditions that are difficult to treat [52]. New instrumental approaches have also been attempted [53].

Past literature indicates frequent sleep disorders (SD) in people with autism [54]. SD can worsen autism symptoms, challenging behaviors and general functioning with alterations in the quality of life of patients and caregivers [55,56]. Moreover, medical and psychiatric comorbidities can cause sleep problems [57]. Treatments of SDs in ASD are represented by both pharmacological (melatonin, clonidine) [58,59] and non-pharmacological interventions (behavioral treatments and sleep hygiene) [60,61].

Often, people with ASD may present atypical eating and feeding behaviors, food selectivity, rejecting certain foods, aversion to specific flavors, colors, textures, or temperatures, poor acceptance of new foods, chewing without swallowing and sticking to a diet limited to specific food categories [62,63]. Distinguishing the characteristics of eating behaviors in ASD from a more structured eating disorder can be very difficult. The clinical history and the use of assessment tools such as food diaries, parents' reports questionnaires, such as the Brief Autism Mealtime Behavior Inventory (BAMBI) [64], the Food Frequency Questionnaire (FFQ) [65] or the Eating Disorder Inventory-3 (EDI-3) [66] and are fundamental [67].

The occurrence of OCD in people with ASD has been estimated from 9 to 20% [68,69]. Given the core symptoms of ASD and OCD, determining whether clinical features are present to make a comorbid diagnosis of OCD in individuals with ASD presents a significant challenge to clinicians. Although some differences are based on the content of repetitive thoughts [70], behavior, and ego-syntonicity, the diagnostic tools appear fundamental. Some diagnostic scales are represented by the Children's Yale-Brown Obsessive-Compulsive Scales for ASD (CY-BOCS-ASD) [71], the Autism Diagnostic Interview-Revised (ADI-R), the Repetitive Behavior Questionnaire (RBQ), the Repetitive Behaviour Interview (RBI), and the Repetitive Behaviour Scale-Revised (RRB-R). [72]. An effective pharmacologic strategy for the occurrence of OCD in ASD patients does not exist, but the most utilized psychotropic drugs are fluvoxamine and fluoxetine [73]. Recently, Lee et al. highlighted a possible role of N-acetylcysteine (NAC) [74]. The usage of Deep Brain Stimulation could be a valid tool for the treatment of patients with treatment-refractory OCD and comorbid ASD [53,75].

Personality Disorders (PDs) have an onset in adolescence, appear stable over time, and leads to distress or impairment. PD patients can present impairment of social and emotional regulation, which are also core characteristics of ASD [76].

Cluster A and Cluster C personality disorders are the most frequent co-occurring PD in ASD patients [77], particularly borderline personality disorder, schizotypal personality disorder and Obsessive-Compulsive Personality Disorder. Although there are still few studies, the use of the Personality Assessment Inventory (PAI) may be useful to assess the presence of personality disorders and emotional functioning in adults with ASD [78]. Antipsychotic drugs are widely used for symptomatic interventions in ASD and PDs but show poor evidence of efficacy. Moreover, anticonvulsants are commonly used for aggressive behaviors, but the evidence is poor [79].

Currently, Schizophrenia and ASD are conceptualized as separate disorders but, despite apparent differences, share multiple phenotypic similarities and risk factors and have both been considered neurodevelopmental rather than neurodegenerative disorders [80,81,82] with elevated rates of co-occurrence [83,84,85]. In authors'knowledge, there are no validated assessment tools for differentiating ASD and SSD often causing considerable difficulties in diagnosis. Over the years, researchers have attempted to assess both autistic traits in schizophrenics and schizophrenia in individuals with ASD. Examples of the first attempt are represented by the Diagnostic Interview for Social and Communication Disorders (DISCO) [86], the Social Communication Questionnaire [87], the Autism Screening Questionnaire [88] and the autism spectrum disorder in Adults Screening Questionnaire [89]. Examples of the second attempt, in verbal individuals are the Positive and Negative Symptom Scale (PANSS) [90], the Comprehensive Assessment of the At-Risk Mental State (CAARMS) [91] and the Structured Interview for Prodromal Symptoms (SIPS) [92]. Minimal data exist on the treatment of Schizophrenia in ASD, and to the best of our knowledge, no randomized controlled trials have been conducted to date. Risperidone and aripiprazole appear to be effective for positive and disorganized symptoms [93,94], but efficacy and tolerability on psychotic symptoms appear less favorable than in patients with Schizophrenia alone [95]. While there are numerous studies of rehabilitative interventions in schizophrenia such as cognitive-behavioral therapy, cognitive remediation, psycho-education, and family intervention [96,97], there is a lack of evidence regarding the efficacy of psychosocial interventions for psychotic symptoms in ASD, although there is numerous rehabilitation interventions present in the literature for autism [98].

4. Conclusion

In this paper, the authors have described the symptoms and psychiatric diagnoses most frequently associated with autism. Psychiatric comorbidities can worsen the clinical course of autism and determine resistance to pharmacological treatments. For these reasons, it appears fundamental to recognize symptoms of psychiatric comorbidities to reach an accurate diagnosis and employ correct treatment options. On the other hand, making an accurate diagnosis is not always easy due to the symptomatic overlap and the lack of accurate evaluation tools. Further studies are needed to validate increasingly sensitive psychometric scales in identifying psychiatric comorbidities in people with autism along with the development of dedicated treatment alternatives. Finally, future research must take into account the heterogeneity of phenotypic aspects of autism, as well as transnosographic aspects of autistic symptoms and traits.

Compliance with ethical standards

Acknowledgments

The authors entirely funded this paper, and no pharmaceutical companies were informed of or involved in it. The authors have no potential conflicts of interest directly relevant to the paper's contents.

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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