AUTISM SPECTRUM DISORDER AND DEPRESSION: TACKLING UNIQUE CHALLENGES IN MENTAL HEALTH

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Abstract. The identification and management of Autism Spectrum Disorder (ASD) and its associated psychiatric comorbidities pose significant clinical challenges. This comprehensive review explores the multifaceted relationship between ASD and depression, suicidality, and borderline personality disorder (BPD), highlighting the intricate interplay between these mental health conditions. The unique complexities of diagnosing and managing comorbid depression and suicidality in individuals with ASD are discussed, including the heightened risks of non-suicidal self-injury and suicidality. Moreover, the review emphasizes the necessity of personalized, innovative treatment approaches, with a focus on the role of antidepressants, cognitive-behavioral therapy (CBT), and the application of electroconvulsive therapy (ECT) in managing treatment-resistant depression. The complexities of co-occurring borderline personality disorder in individuals with ASD are also examined, further underscoring the need for comprehensive, individualized care strategies. This review advocates for multidimensional therapeutic approaches that consider the interplay of psychiatric comorbidities and neurodevelopmental factors, to optimize outcomes and improve the quality of life for individuals with ASD. The findings stress the importance of early diagnosis, tailored interventions, and ongoing research into novel therapeutic modalities to better address the persistent and diverse nature of mental health challenges within the ASD population.
Keywords: *autism, borderline personality disorder, depression, treatment resistant depression*

Introduction

Autism Spectrum Disorder (ASD) represents a multifaceted neuropsychiatric condition, affecting approximately 1 in 59 children in the United States according to the most recent estimates from the Centre for Disease Control and Prevention (CDC) (Lamy and Erickson, 2018). Characterized as a category of enduring neurodevelopmental disorders, ASD exhibits a prevalence of 1.5% in developed nations (Fusar-Poli et al., 2019). The spectrum itself encompasses a broad array of clinical manifestations, spanning from subtle subthreshold presentations and autistic traits to fully manifested ASD within the general population (Dell'Osso et al., 2019). Detection of autism poses unique challenges, particularly in demographic subgroups such as women, individuals from Black and minority ethnic backgrounds, the elderly, and those with coexisting diagnoses of attention deficit hyperactivity disorder (ADHD), obsessive-compulsive disorder (OCD), and learning disabilities. In these populations, identifying autism can prove intricate due to its nuanced presentation. Notably, individuals with autism are predisposed to a heightened risk of diagnostic overshadowing (White, 2019), further complicating accurate and timely recognition within these specific demographic cohorts.

Materials and Methods

In order to highlight the unique challenges and complexity in the management of depression and Autism Spectrum Disorder (ASD), a systematic search was conducted across multiple academic databases. Databases such as PubMed, Web of Science, and Scopus were explored to ensure comprehensive coverage of the relevant literature. Key search terms used included "autism," "autism spectrum disorder," "depression," "comorbid depression in ASD," "treatment-resistant depression," "suicidality in ASD," and "borderline personality disorder in ASD." Boolean operators were used to refine search results, ensuring the inclusion of only peer-reviewed studies, clinical trials, meta-analyses, and review articles. Inclusion criteria required that the studies specifically address either the clinical management of depression in ASD or psychiatric comorbidities such as suicidality and borderline personality disorder. Exclusion criteria involved animal studies, and those that did not provide clear diagnostic frameworks for ASD or depression. The data collected from these studies were categorized based on treatment methodologies employed, including pharmacological interventions, psychotherapeutic approaches, and the application of electroconvulsive therapy (ECT) in treatment-resistant cases. Special attention was given to studies that explored novel therapeutic interventions or personalized treatment strategies in ASD populations. A thematic analysis was conducted to identify common challenges in the management of ASD and depression, and the findings were further corroborated with corresponding literature to ensure accuracy and relevance. Furthermore, a narrative synthesis was applied to summarize the current state of knowledge, gaps in research, and areas where future studies could focus.

Results and Discussion

Autism Spectrum Disorder (ASD) is marked by a notable incidence of psychiatric comorbidities (DeFilippis, 2018), with depression emerging as one of the most prevalent secondary conditions capable of exacerbating ASD symptoms (Smith and White, 2020). Notably, individuals with ASD exhibit a fourfold higher likelihood of experiencing depression throughout their lives when compared to their typically developing counterparts (Hudson et al., 2019). The prevalence of concurrent depression demonstrates a correlation between higher-functioning forms of ASD and the ageing process (DeFilippis, 2018). Recognizing the detrimental impact of comorbid depression on individuals with autism, the imperative for accurate evaluation and timely diagnosis becomes evident. However, the assessment of comorbidity in youth with ASD presents a myriad of challenges, as ASD shares symptomatic commonalities with various other conditions, rendering the differentiation between authentic comorbidity and overlapping symptoms a complex task (Menezes et al., 2018). Moreover, social factors assume a pivotal role in the manifestation of depression among both youth and adults diagnosed with ASD (Smith and White, 2020). Empirical evidence suggests that depression may emerge as a secondary consequence of challenges in social communication, particularly among individuals with high-functioning ASD who face heightened vulnerability to bullying and societal pressures to conform to normative standards (Wigham et al., 2017). Understanding these intricate interplays between psychiatric comorbidity and social dynamics is paramount for a comprehensive comprehension of the challenges faced by individuals with ASD, thereby informing effective intervention strategies.

ASD and suicidality

Individuals with Autism Spectrum Disorder (ASD) confront a heightened susceptibility to suicidality, representing a notable departure from those without ASD (Costa et al., 2020). Patients diagnosed with ASD exhibit an elevated risk of suicidal attempts, with ASD itself serving as an independent factor contributing to this heightened risk (Chen et al., 2017). The prevalence of suicide attempts within this population ranges from 7% to 47%, while suicidal ideation is documented in as many as 72% of cases (Zahid and Upthegrove, 2017). It is noteworthy that, until recently, the topic of suicidality in ASD remained relatively neglected, a surprising oversight considering the substantial risks associated with non-suicidal self-injury, depression, and compromised emotional regulation in individuals with autism spectrum disorder (Maddox et al., 2017). Several studies underscore the elevated rates of comorbidity between ASD and mood disorders, alongside a prevalent occurrence of suicidal ideation among individuals with ASD and distinctive autistic traits (Dell'Osso et al., 2019). This observed proportion surpasses previously reported rates of non-suicidal self-injury among university students, and adult community samples, thereby indicating an augmented risk for non-suicidal self-injury in the adult ASD population (Maddox et al., 2017). These findings emphasize the critical need for increased attention to the complex interplay between ASD, mood disorders, and suicidality, underscoring the urgency for targeted research and intervention strategies within this vulnerable demographic.

Elevated levels of autistic traits, particularly when accompanied by heightened alexithymia, contribute to an increased risk of suicidality (Costa et al., 2020). Noteworthy risk factors include a history of self-harm and depression (Zahid and Upthegrove, 2017), underscoring the multifaceted nature of factors influencing suicidal tendencies in individuals with ASD. The impairment in social communication, a quintessential feature of autism, emerges as a pivotal component in the manifestation of suicidal behaviour (Culpin et al., 2018). In the context of children and adolescents with ASD, the presence of psychotic features and a positive family history of suicide are identified as additional risk factors (Karakoç Demirkaya et al., 2016). Notably, the risk of bullying is associated with heightened suicidality in typically developing teenagers, with factors such as female gender, psychosis, affective disorder diagnoses, and higher intellectual ability being linked to increased suicidality at follow-up (Holden et al., 2020). Additionally, augmented autistic traits, depressive symptomatology, and the use of antidepressants significantly predict suicidality (Costa et al., 2020). The association between specific antidepressants and suicidality is noteworthy, with venlafaxine and paroxetine demonstrating a substantially increased risk, while sertraline is comparably associated with a reduced risk (Boaden et al., 2020).

Recent findings indicate that an elevated risk of self-injurious behaviour is linked to a heightened risk of suicide, particularly in younger individuals at a less advanced developmental stage within the ASD spectrum. Gender differences are also apparent, with women diagnosed with ASD demonstrating a significantly higher likelihood of endorsing non-suicidal self-injury compared to their male counterparts (Maddox et al., 2017). These nuanced associations underscore the necessity for a comprehensive understanding of the interplay between autistic traits, comorbid conditions, and specific risk factors to inform targeted interventions and mitigate the heightened risk of suicidality in individuals with ASD.

ASD and Borderline Personality Disorder (BPD)

The coexistence of personality disorders alongside Autism Spectrum Disorder (ASD) is well-documented, with Borderline Personality Disorder (BPD) being a notably frequent comorbidity (De Cagna et al., 2019). This intersection is not uncommon (Chabrol and Raynal, 2018), as evidenced by the co-occurrence of ASD and BPD in approximately 10% of women diagnosed with either condition (Bringmann and Maidman, 2019). Furthermore, individuals with BPD often exhibit greater autistic characteristics compared to their neurotypical counterparts (Dell'Osso et al., 2018). Discerning between ASD and personality disorders, particularly BPD, in adolescence poses a considerable challenge, as both may manifest with overlapping symptomatology (De Cagna et al., 2019). A shared difficulty experienced by individuals with BPD and ASD revolves around challenges in emotional and relational interactions (Gordon et al., 2020). The cognitive and interpersonal functions of individuals with autism spectrum conditions and BPD are markedly strained, posing additional complexities (Dudas et al., 2017). Additionally, Cluster B personality disorders share commonalities with high-functioning ASD, such as emotionally expressive dysregulation, self-injury, and empathic behaviours (De Cagna et al., 2019).

It is noteworthy that both ASD and BPD are associated with heightened levels of suicidality, emphasizing the critical need for comprehensive assessments and tailored interventions in cases of comorbidity (Chabrol and Raynal, 2018). The intricate interplay between these conditions underscores the necessity for nuanced and individualized approaches to diagnosis and treatment, acknowledging the unique challenges posed by the co-occurrence of ASD and BPD. Consequently, it becomes imperative to consider the potential presence of a personality disorder in the evaluation of adults with ASD, both for differential diagnostic purposes and to enhance the precision of treatment planning (De Cagna et al., 2019). An insufficient or incomplete diagnosis can lead to inadequacies or inappropriateness in the subsequent treatment approach (Gordon et al., 2020). Recognizing the coexistence of ASD and BPD is particularly crucial, as it allows for the adoption of a formulation approach in treatment planning. This approach seeks to provide individualized interventions, beyond a mere descriptive assessment of the encountered challenges (Gordon et al., 2020). The recognition of a neurodevelopmental profile, especially in the context of mental health services for individuals with BPD, holds significant value for early intervention, thereby contributing to improved and enduring outcomes (Stiles, 2018). The integration of such insights into the assessment and treatment process aligns with a holistic perspective that considers the intricate interplay between ASD and personality disorders (Gordon et al., 2020). This comprehensive approach is essential for tailoring interventions to address the unique needs of individuals navigating the complex terrain of comorbid ASD and personality disorders, fostering more effective and targeted therapeutic outcomes.

Antidepressants in ASD with depression

The primary symptoms of ASD, encompassing communication deficits, social interaction deficits, and repetitive behaviours, remain the central focus of care, predominantly addressed through behavioural therapy (Lamy and Erickson, 2018). Notably, no medications have demonstrated efficacy in treating the core symptoms of ASD to date (Goel et al., 2018). However, given the prevalent burden of comorbidities in individuals with ASD, medications are frequently employed to address associated challenges such as irritability, anxiety, and hyperactivity symptoms (Lamy and Erickson, 2018). Despite the absence of pharmacological treatments for the core

symptoms of ASD, there is a notable prevalence of psychotherapy and polypharmacy in the treatment landscape for ASD patients. This trend is likely driven by the necessity to address non-core ASD symptoms and manage psychiatric comorbidities effectively (Jobski et al., 2017). Additionally, the severity of repetitive behaviours has explicitly been associated with polypharmacotherapy, reflecting the multifaceted nature of interventions required for individuals with ASD (Fusar-Poli et al., 2019). This nuanced understanding of the interplay between core symptoms, associated challenges, and pharmacotherapeutic approaches underscores the need for comprehensive, tailored treatment strategies in the complex management of ASD. Antidepressants represent a first-line pharmacological approach commonly prescribed for psychological conditions in children and adolescents (Al Maruf et al., 2019). However, the utilization of antidepressants in this population remains a subject of debate, despite recommendations for their use in the management of various psychiatric disorders (Boaden et al., 2020). The existing evidence for pharmacotherapy in children with ASD is limited, and the potential long-term side effects of antidepressants can pose a substantial burden (Goel et al., 2018).

Regarding the efficacy of antidepressants in children and adolescents, a review indicates that, compared to placebo, fluoxetine demonstrated increased effectiveness in the treatment of major depressive disorder. At the same time, fluvoxamine and paroxetine exhibited superior efficacy in the treatment of anxiety disorders (Boaden et al., 2020). Despite the general effectiveness and tolerability of antidepressants in children, a notable proportion (31% to 48%) do not respond, and adverse drug reactions may occur in up to 25% of cases (Al Maruf et al., 2019). Selective serotonin reuptake inhibitors (SSRIs), although commonly prescribed, are reported to be poorly tolerated and lack compelling evidence for reducing depression in this population (Goel et al., 2018). Moreover, imipramine, venlafaxine, and duloxetine were less well-tolerated in MDD (Boaden et al., 2020). These considerations underscore the complexity of antidepressant interventions in children and adolescents, emphasizing the need for careful evaluation and monitoring due to variable treatment responses and potential adverse effects.

Treatment-Resistant Depression (TRD) in ASD

Individuals experiencing ASD may also be experiencing treatment-resistant depression (TRD) which presents both intriguing and challenging aspects in clinical management (White, 2020). This condition significantly contributes to the global burden of depression, with approximately 50% of depressed patients not receiving adequate care through existing interventions (Taylor et al., 2019; Akil et al., 2018). TRD, therefore, stands as a prominent unmet need in managing MDD (Johnston et al., 2019). Notably, a substantial proportion, around one-fourth, of teenagers with MDD do not respond adequately to their initial antidepressant treatment (Chen et al., 2020). Thus, individuals with ASD with poor response to the antidepressant may also be considered to revise the treatment. The management of TRD often necessitates a trial-and-error approach, even after initial recovery, given the absence of reliable recommendations for matching patients to appropriate treatments. Furthermore, many individuals may resist to treatments over time, further complicating the therapeutic process (Akil et al., 2018). Despite receiving what may be considered sufficient treatment, a significant number of patients still struggle to achieve complete symptom remission (Papadimitropoulou et al., 2017). These challenges underscore the complexity of ASD with TRD and emphasize

the critical need for continued research, innovative treatment approaches, and personalized interventions to address the diverse and persistent nature of depressive symptoms in this population.

Antidepressant augmentation is a recommended strategy for managing treatment-resistant patients, although the outcomes of this approach remain suboptimal. As indicated by six studies, the best-supported predictor of successive treatment outcomes is the early response recorded as early as the second week of treatment (Taylor et al., 2019). In contrast, a systematic review has underscored the potential of cognitive behavioural therapy (CBT) to yield more immediate effects compared to routine antidepressant therapy. Moreover, CBT demonstrates improved mid- and long-term prognoses, along with sustained effects in individuals with treatment-resistant depression (TRD) (Li et al., 2018). These findings highlight the significance of early response monitoring in antidepressant augmentation strategies and underscore the potential benefits of incorporating CBT into the therapeutic arsenal for individuals facing the challenges of ASD with TRD. The synthesis of evidence evaluating efficacy outcomes in the context of TRD revealed superior effectiveness for ketamine compared to other pharmacological and somatic interventions at the 2-week mark following treatment initiation. Notably, the two most efficacious treatments were quetiapine augmentation at 800 mg/day and risperidone augmentation, particularly at the 4, 6, and 8-week intervals (Papadimitropoulou et al., 2017). These findings provide valuable insights into potential interventions for individuals grappling with ASD and TRD, offering a basis for informed treatment decisions and emphasizing the nuanced considerations in selecting appropriate therapeutic strategies based on their comparative efficacy at different time points.

Electroconvulsive Therapy (ECT) in ASD

Electroconvulsive therapy (ECT), despite its historical controversy, has been a fixture in psychiatric practice for over half a century. Its efficacy is noted to be consistent across both youth and adults, with similar indications and contraindications. However, the use of ECT in adolescents is relatively limited due to a scarcity of robust studies in this population. Some consider ECT to be effective in treating autism spectrum disorders associated with catatonia (Zaw, 2006). Case reports involving two adults with ASD and intellectual disability, exhibiting intractable self-harm behaviours and catatonic symptoms, have highlighted a positive response to ECT, even in instances where standard interventions were ineffective (Sajith et al., 2017). The challenge of self-harm behaviour in ASD, often resistant to conventional psychopharmacological and behavioural approaches, has seen a significant reduction in reported instances when electroconvulsive therapy is applied to those diagnosed with agitated catatonia (Wachtel et al., 2018). Moreover, despite the potential impact of comorbidities on treatment response, ECT appears to demonstrate effectiveness even in cases involving multiple psychiatric diagnoses (Karayağmurlu et al., 2019). These observations underscore the utility of ECT in challenging clinical scenarios and suggest its potential role as a therapeutic option in managing severe and treatment-resistant symptoms, particularly in individuals with ASD and associated comorbidities.

Conclusion

Addressing depression in ASD remains a challenge despite various therapeutic approaches. While strategies such as antidepressant augmentation, CBT, and ECT have shown efficacy, controversies persist. Notably, ECT has demonstrated effectiveness even in adolescents, particularly in autism spectrum disorders with catatonia. Furthermore, emerging evidence highlights ketamine, quetiapine, and risperidone augmentation as promising interventions, providing valuable insights into optimizing treatment for TRD in ASD. The nuanced nature of TRD in ASD underscores the importance of personalized and multidimensional approaches to enhance outcomes in individuals facing this complex mental health condition.

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Conflict of interest

The authors confirm that there is no conflict of interest involved with any parties in this research study.

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