Behavioral and Psychiatric Observations in Autism

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Autism spectrum disorder (ASD) consists of a group of heterogeneous genetic neurobehavioral disorders associated with developmental impairments in social communication skills and stereotypic, rigid or repetitive behaviors. Behavioral and psychiatric disorders are more prevalent in autistic individuals compared to the general population, and their symptom overlap with core features of autism can create diagnostic challenges.

autism spectrum disorder behavior psychiatry co-occurring disorders

1. Introduction

Autism spectrum disorder (ASD) is a complex neurodevelopmental condition with onset in infancy or early childhood, in which genetic and non-genetic influences acting either alone or in combination contribute to the development of ASD. According to the World Health Organization, ASD is characterized by impairments in social and communication skills, rigid or repetitive behaviors, atypical interests and differences in the perception of sensory stimuli [1]. The neurodiversity paradigm diverges from the traditional medical model's understanding of autism as a disorder, viewing common traits in autism as neurological differences instead of deficits, thus shifting attention away from a disease model, while highlighting unique autistic strengths and embracing autism as a manifestation of neurological diversity that needs no cure [2].

Behavioral and psychiatric disorders in individuals with ASD are prevalent, and their impact is significant. A growing body of research reveals evidence of the frequent association between ASD and irritability, aggression, self-injurious behaviors, ADHD, anxiety, obsessive compulsive disorder, gender dysphoria, mood disorders, suicidality, substance use disorders, catatonia, psychosis and schizophrenia spectrum disorders. The symptoms associated with many behavioral and psychiatric disorders that commonly occur in individuals with ASD can overlap with core characteristics of ASD, which results in diagnostic challenges [3].

The risk for co-occurring behavioral and psychiatric disorders is influenced by individual differences including age, intellectual functioning, sex and genetic factors [4], with a majority of existing studies focusing on children and adolescents with ASD [5]. It has been shown that older autistic adults are at lower risk for having a co-occurring psychiatric diagnosis compared to their younger cohorts, a pattern similar to that found in the general population [6]. There is even less that is known about co-occurring conditions in autistic individuals with intellectual developmental disabilities. Although about one-third of people historically diagnosed with ASD have an intellectual disability [7], this subgroup is often excluded in the literature describing behavioral and psychiatric disorders in ASD [8].

2. Behavioral and Psychiatric Conditions Often Associated with Autism

2.1. Irritability, Aggression and Self-Injurious Behaviors

Autistic individuals often experience elevated levels of irritability (e.g., temper tantrums, frustration or angry outbursts) and problem behaviors (e.g., physical aggression toward others, self-injurious behaviors or property destruction). Deficits in emotional self-regulation (e.g., using maladaptive emotion regulation strategies such as perseveration or shutting down) are common in autism and may result in anger being experienced more intensively, and in turn, strong negative emotions can trigger aggressive behaviors. Additionally, impairments in social cognition including inaccurate assessments or misinterpretation of social intent can promote aggressive behaviors [9].

Self-injurious behaviors (SIBs) are acts of physical harm inflicted upon oneself that have the potential to result in injury. Examples include hitting, pinching, scratching, biting, head banging and hair pulling. In contrast, stereotyped self-stimulatory behaviors typically involve repetitive or ritualistic movements, gestures, or vocalizations (e.g., repeated sounds, words or phrases) [10]. These behaviors can be persistent or episodic, spontaneous or repetitive, often without any identified cause, or may tend to occur within specific contexts or in response to certain triggers or situations. Risk factors for more serious and persistent SIBs include intellectual disability, limited communication skills, lower adaptive functioning, impairments in impulse control [11], sensory processing deficits or chronic sleep problems [12].

2.2. ADHD and Executive Functioning Deficits

Attention Deficit Hyperactivity Disorder (ADHD) is characterized as a neurodevelopmental disorder manifested by core symptoms of distractibility and impulsivity, either with or without hyperactivity. In comparison to typically developing peers, limitations of executive functioning are common in both ASD and ADHD, suggesting that both may be conceptualized through an “executive functioning deficit model” [13]. Executive functions are cognitive control mechanisms that modulate perceptual experiences, motor responses, emotion regulation and behavioral reactions, as well as enable cognitive skills providing the ability to sequence, prioritize, plan, make decisions, anticipate novel situations, evaluate risks, utilize effective problem solving and develop adaptive coping strategies [14].

Developmentally appropriate social skills are commonly underdeveloped or impaired in both ASD and ADHD. The evaluation of social functioning involves an assessment of the individual’s social skills within the context of a particular interpersonal encounter. Social skills deficits in ADHD typically include a lack of attention to or disregard of situational or non-verbal cues, as well as intrusive or impulsive tendencies in communication and social interactions. In comparison, ASD related social challenges tend to manifest as either poorly developed or awkward social skills, with an apparent indifference to or lack of awareness for social cues, and for some individuals, this includes active avoidance of social engagement [15].

2.3. Anxiety and Anxiety Disorders

Anxiety involves the expectation of a future threat, whether it is real or imagined. Anxiety disorders differ from what is considered to be age-related normal anxiety or fear as they cause significant distress, are functionally impairing, are excessive for the situation, or persist beyond developmentally appropriate periods. Leo Kanner [16], in 1943, described excessive anxiety in autistic individuals around unanticipated changes in the environment, alterations in schedules or unexpected events, viewing the behaviors of an autistic child as driven by an intense desire for maintaining sameness. His view was that difficulties with adapting occur in response to obsessive, restricted and perseverative features associated with autism. Rigid behaviors, including verbal rituals, compulsive routines (e.g., ordering and lining up objects), restrictive or rule-based preferences (e.g., eating only foods of one color), if interfered with or prevented, tend to trigger anxious distress.

Among the anxiety disorders associated with ASD, the most common ones are specific phobias and generalized anxiety disorder, followed by social anxiety disorder and separation anxiety disorder [17]. It can be clinically challenging to diagnose specific anxiety disorders in the context of ASD due to shared features associated with both autism and anxiety disorders. For example, social anxiety disorder which is characterized principally by a fear of negative evaluation by others, and therefore, often leads to a lack of active engagement in social situations, which can manifest similarly to the core social communication deficit seen in autism [18]. Children with ASD often experience emotional and behavioral difficulties when they are overwhelmed with sensory stimulation. Deep pressure is a therapeutic modality utilized in occupational therapy to have a calming effect on the child by decreasing sympathetic arousal. An inflatable wrap called an autism hug machine portable seat has been shown to reduce neurobiological stress as measured by the sympathetic response, which in turn reduces problematic behaviors in children with ASD [19][20].

2.4. Repetitive Behaviors versus Obsessive Compulsive Disorder

According to the *Diagnostic and Statistical Manual of Mental Disorders, fifth ed. (DSM-5),* the symptoms associated with ASD include restricted, repetitive patterns of behavior, interests or activities [21]. Repetitive behaviors in ASD can include recurrent vocalizations such as repeating certain noises, words or phrases, fixating on topics of special interest, rigid behaviors such as inflexible insistence on specific routines in everyday life, listening to the same song or watching the same videos repeatedly, or ritualistic stereotyped movements such as symmetric flapping or twirling of the hands, rocking of the body or the spinning of objects. Repetitive behaviors characteristic of ASD may appear to be very similar to the compulsive rituals often associated with obsessive compulsive disorder (OCD) [22].

OCD is characterized by a pattern of obsessive thoughts and compulsive behaviors that interfere with daily activities and cause significant distress. Obsessions in OCD consists of intrusive thoughts, either driven by an intense need for organization or symmetry, in response to fear of disease or contamination, or as an attempt to ward off unwanted urges or morally unacceptable thoughts or images that trigger significant anxiety. Compulsive behaviors in OCD are typically performed in response to intrusive thoughts in an unconscious effort to relieve distress. In comparison to OCD, repetitive behaviors in ASD are generally preferred, performed for the purpose of

self-soothing, and do not typically cause distress. Repetitive behaviors in both OCD and ASD are often disruptive or time consuming and can lead to behavior problems including tantrums or aggression, particularly when others attempt to alter or interrupt the behavior [23].

2.5. Gender Dysphoria

Gender dysphoria is caused by a misalignment between a person's biological or birth-assigned sex and their personal experience of gender identity, whereas gender variance (or gender diversity) describes when an individual's gender role and behaviors deviate from the culturally defined or socially expected gender norms [24]. Autistic individuals report a higher number of gender dysphoric traits compared to that of non-autistic peers [25]. Multiple studies report that ASD is over-represented in those with gender dysphoria and in gender-affirming specialty care clinics [26][27]. Strang et al. published clinical guidelines to help guide evaluation and treatment considerations for adolescents with co-occurring gender dysphoria and ASD [28].

Gender-diverse autistic adolescents and adults are known to have increased rates of mental health problems, including elevated risks for depression and suicidality compared to those of either autistic or transgender persons individually [29]. Due to associated social and communication differences associated with autism, they can face significant challenges in advocating for their gender-related healthcare needs. To optimize the success in patient outcomes, it is essential that medical providers become familiar with established standards of care for gender-diverse autistic individuals, help them to enlist family and social support, provide guidance in accessing gender-affirming healthcare, actively partner with other members of the patient's care team to coordinate treatment interventions and obtain effective mental health consultation when it is needed [30].

2.6. Depression and Bipolar Disorders

Major depressive disorder (MDD) consists of a predominantly depressed or irritable mood, accompanied by a loss of interest or pleasure in previously enjoyed activities, as well as a host of other distressing psychological and somatic symptoms, lasting for a period of at least 2 weeks [21]. An approximately two-fold risk for developing major depression in autistic young adults was reported in a population-based cohort study, which also found that MDD is more common in those with ASD than it is in their non-autistic siblings. ASD, particularly ASD without intellectual disability, is associated with elevated rates of major depression in young adulthood, and it is likely that the explanation is related to both shared genetic and environmental factors [31]. Identifying a major depression when it occurs in the context of ASD can be challenging given the overlap of common depression symptoms and features of ASD, as well as by a lack of evidence supporting the validity of commonly used assessment instruments for diagnosing MDD in autistic individuals [32].

Bipolar Affective Disorder (BAD) has two main subtypes. Bipolar I Disorder, which closely aligns with the classically described manic-depressive illness, involves both full-blown manic and major depressive episodes, and if the patient is not stabilized with effective treatment, it tends to evolve into a pattern of recurrent episodes that have the potential to escalate, with an associated risk for brief periods of psychosis. Bipolar II Disorder tends to follow a less

severe course, defined by one or more episodes of major depression and hypomania [21]. BAD is more likely to occur in association with autism than it is in the general population. Not only is the risk of bipolar disorder greater for those with ASD compared to age- and sex-matched controls from the general population, but the risk is also higher in family members with ASD than it is in non-autistic siblings [33]. Diagnostic challenges exist because when BAD occurs in the context of autism, it may have an atypical presentation, thus causing either a lack of recognition or worse, an incorrect diagnosis, given that when psychotic symptoms are present, the clinical picture can be easily mistaken for schizophrenia [34].

2.7. Suicidality

The elevated risk for suicidality in ASD has been historically under-recognized. The majority of studies evaluating suicidality in ASD have been conducted only in recent years [35]. A landmark study that assessed suicidality in a sizable clinic population of autistic adults formerly diagnosed with Asperger syndrome (an outdated diagnosis defining a sub-group of individuals with ASD with normal intelligence and greater impairment in social skills compared to those with other autistic traits) found that about two-thirds of them endorsed a history of suicidal ideation, with one-third having previously planned or attempted suicide [36]. Similarly, a population study in Sweden found that individuals diagnosed with ASD were significantly more likely to have suicide listed as the cause of death compared to the average proportion of suicide deaths reported in the general population [37].

The stress associated with “camouflaging” (a term used to describe those with ASD who intentionally mask their autistic traits or adapt their behavior with the goal conforming to neurotypical expectations) in autistic adolescents and adults contributes to increased stress, depression and suicidal behaviors in ASD [38]. Additional risk factors for suicidality in ASD include a history of behavioral problems, bullying, victimization, male gender, minority identity and lower socioeconomic status or educational attainment. Finally, the associated risks for suicidal thoughts and behaviors shared with the general population include recurrent self-injurious behaviors, psychiatric disorders and unstable employment, all of which occur at a greater frequency for individuals with ASD [39].

2.8. Substance Use Disorders

An emerging body of research suggests that ASD is associated with double the risk for developing a substance use disorder (SUD). There is no clinical evidence explaining the lack of attention to the risk for SUD in ASD. The fact that SUDs were historically thought to be rare among individuals with ASD may be understood in considering the divergent culturally constructed narratives for the two conditions. The albeit naïve or simplistic ASD narrative portrays the individual as blameless and innocent, whereas the judgmental and moralistic narrative of SUD depicts the person as corrupt and unworthy, with the opposing narratives leading to cognitive discordance, and hence, bias. Clinicians need to remain vigilant when adopting the routine practice of screening individuals with ASD for SUD in the same manner they would for other patients and provide appropriate treatment for this common and potentially life-threatening co-occurring morbidity [40].

With regard to the susceptibility for developing SUDs, autistic individuals share common risk factors that exist in the general population including a genetic predisposition, environmental effects, stressful family events, early nicotine or other substance use, psychological distress and co-occurring emotional (i.e., depression) and behavioral conditions (i.e., ADHD, conduct disorder and anti-social personality disorder). Additional risk determinants that are more likely to be relevant in autistic individuals include low social support, dysfunctional coping strategies and poorer executive functioning. Social isolation compounded by social communication deficits may lead to difficulties with self-management, including a higher risk for establishing a pattern of substance abuse. The evidence suggests that autistic persons are at increased risk for developing substance use disorders, potentially via self-medicating with the goal of seeking relief from the multitude stressors they are commonly faced with or using drugs or alcohol to calm social anxiety or reduce the stress experienced in social interactions [41].

2.9. Catatonia

Catatonia is a neuropsychiatric syndrome which has two subtypes. The akinetic (or retarded) type is the most frequent one and is characterized by a slowing or reduction of motor movements, immobility, rigidity, staring, mutism, withdrawal or refusal to eat. It may also include bizarre features such as posturing, grimacing, negativism, waxy flexibility, echolalia, echopraxia, stereotypy, verbigeration and automatic obedience. Hyperkinetic (or excited) catatonia is a less common presentation, in which there are prolonged periods of psychomotor agitation characterized by rigidity, autonomic dysregulation and altered mental status, and it can lead to life-threatening complications, including death, if it is not rapidly identified and treated [42].

There is an increased risk for catatonia in ASD, as well as other neurodevelopmental disorders, compared to that of the general population, occurring most often in adolescence and young adulthood [43]. Diagnostic challenges exist when catatonia develops in the context of autism given the overlap of behavioral features between the two conditions. Catatonic symptoms, including mutism, stereotypic speech, repetitive behaviors, echolalia, posturing, mannerisms, purposeless agitation and rigidity, can be misidentified as core features of ASD [44]. Catatonia should be considered in autistic individuals when there is an obvious and marked deterioration in movement, vocalizations, pattern of activities, self-care and daily life skills. When accurately diagnosed catatonia can be medically treated in a timely manner, improved outcomes are demonstrated, and a full recovery is seen in most cases [45].

2.10. Psychosis and Schizophrenia Spectrum Disorders

Psychosis is defined by a loss of reality orientation, with symptoms including hallucinations, paranoid or delusional thoughts (defined as fixed, false beliefs), and can occur as a result of a coexisting medical or psychiatric disorder. It is assumed that there is an underlying vulnerability to developing psychosis in ASD, which is likely related to overlapping genetic findings in ASD and primary psychotic (schizophrenia spectrum) disorders [46]. The risk factors for developing psychosis in ASD, when present, include major depressive disorder, anxiety disorders and the emotional trauma caused by bullying and other victimization, social bias, discrimination, unemployment, disability or other stressors commonly experienced by autistic individuals.

Schizophrenia is a serious and chronic mental illness that, in addition to psychotic symptoms, is defined by cognitive impairments, as well as persistently disordered ideas, beliefs, perceptions and behaviors [47]. Zheng et al. conducted a systematic review and meta-analysis of studies published over 10 years, demonstrating a significantly increased prevalence of schizophrenia in ASD [48]. The overlap in clinical features, which can superficially appear to be similar between ASD and schizophrenia, increases the possibility of a mistaken diagnoses. The idiosyncratic ideas of a person with ASD, for example, can be mistaken for the delusional beliefs which occur in psychosis. Likewise, cognitive rigidity and behavioral inflexibility in ASD can be interpreted as delusional in nature, potentially leading to a misdiagnosis of mental illness [49].

References

1. World Health Organization. ICD-11: International Classification of Diseases (11th Revision). 2019. Available online: https://icd.who.int/ (accessed on 30 October 2022).
2. Kapp, S.K.; Gillespie-Lynch, K.; Sherman, L.E.; Hutman, T. Deficit, difference, or both? Autism Neurodivers. Dev. Psychol. 2013, 49, 59–71.
3. Genovese, A.; Ellerbeck, K. Autism Spectrum Disorder: A Review of Behavioral and Psychiatric Challenges Across the Lifespan. SN Compr. Clin. Med. 2022, 4, 217.
4. Rosen, T.E.; Mazefsky, C.A.; Vasa, R.A.; Lerner, M.D. Co-occurring psychiatric conditions in autism spectrum disorder. Int. Rev. Psychiatry 2018, 30, 40–61.
5. Matson, J.L.; Cervantes, P.E. Commonly studied comorbid psychopathologies among persons with autism spectrum disorder. Res. Dev. Disabil. 2014, 35, 952–962.
6. Lever, A.G.; Geurts, H.M. Psychiatric Co-occurring Symptoms and Disorders in Young, Middle-Aged, and Older Adults with Autism Spectrum Disorder. J Autism Dev Disord. 2016, 46, 1916–1930.
7. Christensen, D.L.; Baio, J.; Braun, K.V.N.; Bilder, D.; Charles, J.; Constantino, J.N.; Daniels, J.; Durkin, M.S.; Fitzgerald, R.T.; Kurzius-Spencer, M.; et al. Prevalence and characteristics of autism spectrum disorder among children aged 8 years—Autism and developmental disabilities monitoring network, 11 sites, United States, 2012. Morb. Mortal. Wkly. Rep. Surveill. Summ. 2016, 65, 1–23.
8. Lerner, M.D.; Mazefsky, C.; Weber, R.J.; Transue, E.; Siegel, M.; Gadow, K.D. Verbal ability and psychiatric symptoms in clinically referred inpatient and outpatient youth with ASD. J. Autism Dev. Disord. 2018, 48, 3689–3701.
9. Mazefsky, C.A.; White, S.W. Emotion regulation: Concepts & practice in autism spectrum disorder. Child Adolesc. Psychiatr. Clin. N. Am. 2014, 23, 15–24.

10. Minshawi, N.; Hurwitz, S.; Fodstad, J.; Biebl, S.; Morris, D.; McDougle, C. The association between self-injurious behaviors and autism spectrum disorders. Psychol. Res. Behav. Manag. 2014, 7, 125–136.
11. Gulsrud, A.; Lin, C.E.; Park, M.N.; Hellemann, G.; McCracken, J. Self-injurious behaviours in children and adults with autism spectrum disorder (ASD). J. Intellect. Disabil. Res. 2018, 62, 1030–1042.
12. Soke, G.N.; Rosenberg, S.; Hamman, R.F.; Fingerlin, T.; Rosenberg, C.R.; Carpenter, L.; Lee, L.C.; Giarelli, E.; Wiggins, L.D.; Durkin, M.S.; et al. Factors associated with self-injurious behaviors in children with autism spectrum disorder: Findings from two large national samples. J. Autism Dev. Disord. 2017, 47, 285–296.
13. Doyle, A.E.; Vuijk, P.J.; Doty, N.D.; McGrath, L.M.; Willoughby, B.L.; O'Donnell, E.H.; Wilson, H.K.; Colvin, M.K.; Toner, D.C.; Hudson, K.E.; et al. Cross-Disorder Cognitive Impairments in Youth Referred for Neuropsychiatric Evaluation. J. Int. Neuropsychol. Soc. 2018, 24, 91–103.
14. Miyake, A.; Friedman, N.P. The Nature and Organization of Individual Differences in Executive Functions: Four General Conclusions. Curr. Dir. Psychol. Sci. 2012, 21, 8–14.
15. Reiersen, A.M.; Constantino, J.N.; Richard, T.D. Co-occurrence of motor problems and autistic symptoms in attention-deficit/hyperactivity disorder. J. Am. Acad. Child Adolesc. Psychiatry 2008, 47, 662–672.
16. Kanner, L. Autistic disturbances of affective contact. Nervous Child 1943, 2, 217–250.
17. Zaboski, B.A.; Storch, E.A. Comorbid autism spectrum disorder and anxiety disorders: A brief review. Future Neurol. 2018, 13, 31–37.
18. van Steensel, F.J.; Bögels, S.M.; Perrin, S. Anxiety disorders in children and adolescents with autistic spectrum disorders: A meta-analysis. Clin. Child Fam. Psychol. Rev. 2011, 14, 302–317.
19. Afif, I.Y.; Farkhan, M.; Kurdi, O.; Maula, M.I.; Ammarullah, M.I.; Setiyana, B.; Jamari, J.; Winarni, T.I. Effect of Short-Term Deep-Pressure Portable Seat on Behavioral and Biological Stress in Children with Autism Spectrum Disorders: A Pilot Study. Bioengineering 2022, 9, 48.
20. Afif, I.Y.; Manik, A.R.; Munthe, K.; Maula, M.I.; Ammarullah, M.I.; Jamari, J.; Winarni, T.I. Physiological Effect of Deep Pressure in Reducing Anxiety of Children with ASD during Traveling: A Public Transportation Setting. Bioengineering 2022, 9, 157.
21. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, 5th ed.; American Psychiatric Association: Washington, DC, USA, 2013.
22. Scahill, L.; Challa, S.A. Repetitive behavior in children with autism spectrum disorder: Similarities and differences with obsessive-compulsive disorder. In Psychiatric Symptoms and Comorbidities

in Autism Spectrum Disorder; Mazzone, L., Vitiello, B., Eds.; Springer: Berlin/Heidelberg, Germany, 2016.

23. Postorino, V.; Kerns, C.M.; Vivanti, G.; Bradshaw, J.; Siracusano, M.; Mazzone, L. Anxiety Disorders and Obsessive-Compulsive Disorder in Individuals with Autism Spectrum Disorder. Curr. Psychiatry Rep. 2017, 19, 92.
24. Davy, Z.; Toze, M. What is gender dysphoria? A critical systematic narrative review. Transgender. Health 2018, 3, 159–169.
25. George, R.; Stokes, M.A. Gender identity and sexual orientation in autism spectrum disorder. Autism 2018, 22, 970–982.
26. Warrier, V.; Greenberg, D.M.; Weir, E.; Buckingham, C.; Smith, P.; Lai, M.; Allison, C.; Baron-Cohen, S. Elevated rates of autism, other neurodevelopmental and psychiatric diagnoses, and autistic traits in transgender and gender-diverse individuals. Nat. Commun. 2020, 11, 3959.
27. Thrower, E.; Bretherton, I.; Pang, K.C.; Zajac, J.D.; Cheung, A.S. Prevalence of autism spectrum disorder and attention-deficit hyperactivity disorder amongst individuals with gender dysphoria: A systematic review. J. Autism Dev. Disord. 2020, 50, 695–706.
28. Strang, J.F.; Meagher, H.; Kenworthy, L.; de Vries, A.; Menvielle, E.; Leibowitz, S.; Janssen, A.; Cohen-Kettenis, P.; Shumer, D.E.; Edwards-Leeper, L.; et al. Initial clinical guidelines for co-occurring autism spectrum disorder and gender dysphoria or incongruence in adolescents. J. Clin. Child Adolesc. Psychol. 2018, 47, 105–115.
29. van der Miesen, A.; Hurley, H.; Bal, A.M.; de Vries, A. Prevalence of the wish to be of the opposite gender in adolescents and adults with autism spectrum disorder. Arch. Sex. Behav. 2018, 47, 2307–2317.
30. Genovese, A.C.; Singh, S.C.; Casubhoy, I.; Hellings, J.A. Gender Diverse Autistic Young Adults: A Mental Health Perspective. Arch. Sex. Behav. 2022.
31. Rai, D.; Heuvelman, H.; Dalman, C.; Culpin, I.; Lundberg, M.; Carpenter, P.; Magnusson, C. Association Between Autism Spectrum Disorders with or without Intellectual Disability and Depression in Young Adulthood. JAMA Netw. Open 2018, 1, e181465.
32. Chandrasekhar, T.; Sikich, L. Challenges in the diagnosis and treatment of depression in autism spectrum disorders across the lifespan. Dialogues Clin. Neurosci. 2015, 17, 219–227.
33. Selten, J.P.; Lundberg, M.; Rai, D.; Magnusson, C. Risks for nonaffective psychotic disorder and bipolar disorder in young people with autism spectrum disorder: A population-based study. JAMA Psychiatry 2015, 72, 483–489.
34. Vannucchi, G.; Masi, G.; Toni, C.; Dell'Osso, L.; Erfurth, A.; Perugi, G. Bipolar disorder in adults with Asperger´s Syndrome: A systematic review. J. Affect Disord. 2014, 168, 151–160.

35. Veenstra-VanderWeele, J. Recognizing the problem of suicidality in autism spectrum disorder. J. Am. Acad. Child Adolesc. Psychiatry 2018, 57, 302–303.
36. Cassidy, S.; Bradley, P.; Robinson, J.; Allison, C.; McHugh, M.; Baron-Cohen, S. Suicidal ideation and suicide plans or attempts in adults with Asperger's syndrome attending a specialist diagnostic clinic: A clinical cohort study. Lancet Psychiatry 2014, 1, 142–147.
37. Hirvikoski, T.; Mittendorfer-Rutz, E.; Boman, M.; Larsson, H.; Lichtenstein, P.; Bölte, S. Premature mortality in autism spectrum disorder. Br. J. Psychiatry 2016, 208, 232–238.
38. Cassidy, S.; Bradley, L.; Shaw, R.; Baron-Cohen, S. Risk markers for suicidality in autistic adults. Mol. Autism 2018, 9, 42.
39. Segers, M.; Rawana, J. What do we know about suicidality in autism spectrum disorders? A systematic review. Autism Res. 2014, 7, 507–521.
40. Butwicka, A.; Långström, N.; Larsson, H.; Lundström, S.; Serlachius, E.; Almqvist, C.; Frisén, L.; Lichtenstein, P. Increased risk for substance use-related problems in autism spectrum disorders: A population-based cohort study. J. Autism Dev. Disord. 2017, 47, 80–89.
41. Adhia, A.; Bair-Merritt, M.; Broder-Fingert, S.; Nunez Pepen, R.A.; Suarez-Rocha, A.C.; Rothman, E.F. The critical lack of data on alcohol and marijuana use by adolescents on the autism spectrum. Autism Adulthood 2020, 2, 282–288.
42. Rasmussen, S.A.; Mazurek, M.F.; Rosebush, P.I. Catatonia: Our current understanding of its diagnosis, treatment and pathophysiology. World J. Psychiatry 2016, 6, 391–398.
43. Dhossche, D.M.; van der Steen, L.F.; Shettar, S.M. Catatonia in autism spectrum disorders: Review and case-report. Tijdschr. Psychiatr. 2015, 57, 89–93.
44. Mazzone, L.; Postorino, V.; Valeri, G.; Vicari, S. Catatonia in patients with autism: Prevalence and management. CNS Drugs 2014, 28, 205–215.
45. Kakooza-Mwesige, A.; Wachtel, L.E.; Dhossche, D.M. Catatonia in autism: Implications across the life span. Eur. Child Adolesc. Psychiatry 2008, 17, 327–335.
46. Larson, F.V.; Wagner, A.; Jones, P.B.; Tantam, D.; Lai, M.-C.; Baron-Cohen, S.; Holland, A.J. Psychosis in autism: Comparison of the features of both conditions in a dually affected cohort. Br. J. Psychiatry 2017, 210, 269–275.
47. McGrath, J.; Saha, S.; Chant, D.; Welham, J. Schizophrenia: A concise overview of incidence, prevalence, and mortality. Epidemiol. Rev. 2008, 30, 67.
48. Zheng, Z.; Zheng, P.; Zou, X. Association between schizophrenia and autism spectrum disorder: A systematic review and meta-analysis. Autism Res. 2018, 11, 1110–1119.

49. Lugo Marín, J.; Alviani Rodríguez-Franco, M.; Mahtani Chugani, V.; Magán Maganto, M.; Díez Villoria, E.; Canal Bedia, R. Prevalence of Schizophrenia Spectrum Disorders in Average-IQ Adults with Autism Spectrum Disorders: A Meta-analysis. J. Autism Dev. Disord. 2018, 48, 239–250.