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Comorbid Behavioral Problems and Psychiatric Disorders in Autism Spectrum Disorders

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Abstract

Behavioral problems and psychiatric disorders are common among individuals with Autism Spectrum Disorders (ASD), including those often regarded nonspecifically as "autistic behaviors," rather than specific psychiatric comorbidities. This article summarizes several symptoms or syndromes that significantly interfere with adjustment and functioning, and reviews current treatment evidence, as well as potential future interventions. These symptoms or syndromes are impairments outside of the core diagnostic features — impaired communication, impaired social skills and restricted interests / repetitive movements — that may significantly impede the implementation of behavioral or other non-medical interventions. Early identification of these comorbidities could aide in the development of successful targeted treatments.

Keywords: Autism spectrum disorder; Asperger disorder; Comorbidity; Treatment

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Introduction

Lifelong functional impairment related to core autism features, such as social and communication deficits are well documented. A less studied source of impairment in Autism Spectrum Disorders (ASD) relates to psychiatric comorbidity.

This article addresses the assessment and management of several symptoms or syndromes that significantly interfere with adjustment and functioning in individuals with ASD. These impairments are outside of the core diagnostic symptoms of communication and social skills deficits, and restrictive interest / repetitive movements; nevertheless, they are associated with significant impact and may impede the implementation of behavioral or other non-medical interventions [1, 2].

Advances in genetics and neuroscience have led to the identification of promising target molecules and neurophysiological pathways involved in ASD [3]. The research evidence for symptomatic relief in ASD outside of core symptoms has grown substantially in recent years. Identifying such targets for treatment can certainly improve overall patient functioning and family wellbeing.

The identification of psychiatric comorbidity remains a significant challenge for clinicians: The nature of ASD makes it difficult to assess thoughts and emotions for reasons that include impaired reciprocity in the conversational process, difficulty identifying emotions, impaired theory of mind, and lack of empathy. The affected person may not be able gauge the impact of their own behavior on others. Distinct genetic syndromes may also underlie heterogeneous presentations [4]. Separately, core features and comorbidities may have overlapping symptoms, obscuring the comorbidity. The phenotype of comorbidities may differ from the disorder outside of the context of ASD. The comorbidity may be further modified by the severity of core symptoms and degree of intellectual disability. Finally, environmental factors and stressors may alter both core symptoms and comorbidity phenotype.

In order to reduce diagnostic complexity and develop consensus interventions, validated scales to investigate comorbidity are needed. The Autism Comorbidity Interview-Present and Lifetime version (ACI-PL) [5], Children's Interview for Psychiatric Syndromes-Parent version (P-ChIPS) [6] and, Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS) modified for ASD are some helpful tools. The newly available Anxiety Scale for Children - ASD, Parent and Child versions (ASC-ASD) shows promise [7]. Semi-structured, interviewer-rated tools, such as the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) performed by a clinician experienced in the field of autism may be more valid than highly structured responder-dependent tools [8]. The lack of gold standard instruments to assess comorbidity

may explain the wide range of findings regarding prevalence and outcomes [9]. A reliable developmental history, family history, comprehensive phenotype of the patient, and functional behavioral assessment of target symptoms are necessary to develop effective, well-tolerated therapeutic interventions that would lead to sustained overall improvement. Ideally, treatment recommendations are evidence-based, but personalized through knowledge of each patient's unique needs.

Comorbidity should be suspected when core features fail to explain impairment, when there is noticeable change from baseline, or when the patient is not responding to therapeutic interventions as expected [9]. Simonoff et al. used structured assessments in a population-derived sample of 255 children with ASD, reporting 70.8% of children studied had at least one other current psychiatric disorder. The most common disorders were social anxiety disorder (29.2%, three-month point prevalence), Attention-Deficit / Hyperactivity Disorder (28.1%), and Oppositional Defiant Disorder (28.1%). Other disorders with prevalence greater than 10% were Generalized Anxiety Disorder (13.4%), Panic Disorder (10.1%) and Enuresis (11%). Rates of Major Depressive Disorder (0.9%), Dysthymic Disorder (0.5%), Obsessive compulsive Disorder (8.2%) and Conduct Disorder (3.2%) appeared low [10].

Mattila et al., studied comorbidity in a sample of 50 children, ages 9 to 16 years with Asperger Syndrome (AS) and High Functioning Autism (HFA). The study reported prevalence for psychiatric disorders of 74% and often found multiple disorders. Behavioral problems were most prevalent (44%). Diagnostic criteria for ADHD were met by 38%. Anxiety was present in 42% and tic disorders in 26% with 13% prevalence for Tourette syndrome. Two or three different current anxiety disorders were diagnosed in 14% of participants. Tic disorders and behavioral problems were more common in primary school age children. Oppositional defiant disorder, anxiety and major depressive disorder were found to significantly impair general functioning [11].

Lugnegard et al. [8], studied comorbidity in young adults with AS. He found increased prevalence of anxiety disorders 50%. As many as 70% had experienced at least one episode of major depression. Fifty percent had suffered from recurrent depressive episodes. Psychosis had a lower prevalence at 4%, compared with other reports [12, 13], which offered rates between 12 to 20%. Bulimia nervosa was found in 4% of participants. Even though the rates of substance abuse were low in the ASD group, prevalence was higher if ADHD was present.

Mukaddes et al., compared rate and type of comorbidity in a population diagnosed with HFA and AS. Both groups were found at high risk of developing psychiatric conditions with AS found to be at higher risk to develop depression [2].

Age of diagnosis and core symptom severity seems to increase risk of psychiatric comorbidity with the exception of depression, as recent studies indicated individuals with more subtle social impairments may actually be more likely to develop depressive symptoms [14]. Similar findings are found for anxiety disorders. Those patients who are more aware of their disability in interpreting social cues are postulated to be more vulnerable to suffer anxiety [8].

Aggression and Self-Injurious Behavior

In the presence of maladaptive behaviors, to include aggression and self-injurious behaviors, underlying medical problems should be considered as causal factors. Seizures, sleep apnea, gastrointestinal problems, menstruation, pain, and iron or zinc deficiencies are some examples. It is also important to evaluate the presence of environmental stressors that may precipitate this behavior. Functional analysis is imperative in the identification of factors that may trigger, perpetuate, or reinforce the unwanted behavior. Functional analysis would help to establish specific behavioral interventions or therapeutic environmental modifications [15].

For those patients with severe functional impairment secondary to disruptive behavior, safety concerns, or no response to behavioral interventions, pharmacological treatment is recommended. Interventions should be guided by evidence and appropriate treatment guidelines [16]. Pharmacological agents should be used at the lowest effective dose, and polytherapy — potentially worsening behavioral symptoms — should be avoided [17].

Typical neuroleptics such as haloperidol have been used to treat severe aggression in autistic children, but significant side effects including acute dystonia and dyskinesia may limit its use [18].

In Huffman et al.'s review of medical treatment in children with ASD, there was strong evidence for the use of risperidone for irritability [9]. Risperidone is approved by the US Food and Drug Administration (FDA) for the treatment of irritability, aggression, self-injurious behavior and severe tantrums in ASD [17, 19]. Aripiprazole is approved by the FDA for the treatment of irritability in children with ASD from age 6 to 17 years [20]. A one-year follow-up study of 124 children with ASD has proved risperidone and aripiprazole to be highly effective in the treatment of these symptoms and examined the additive effect of their combination with Parent Training in behavioral management [21].

In several randomized controlled trials, lesser evidence of efficacy and significant side effects were found for other atypical antipsychotics such as clozapine, olanzapine and ziprasidone [22-24].

Obsessive-Compulsive Disorder

Obsessive-compulsive disorder (OCD) is characterized by recurrent intrusive thoughts or images, and repetitive behaviors. The disorder frequently starts in childhood and adolescence, as much as diagnosis is often delayed by many years.

Studies found increased incidence of OCD in the ASD population, as well as increased ASD among those diagnosed with OCD [3, 16]. Family studies have reported an association between repetitive behaviors in children with autism and obsessive compulsive features in parents [25, 26]. The concurrent diagnosis is sometimes controversial, considering rituals; repetitive behavior and rigid adherence to routines are among core criteria for Autism [8, 27, 28]. Compulsions are best considered related to OCD if they are distressing and unwanted (egodystonic), are preceded by anxiety-inducing thoughts, and serve to relieve anxiety. Rituals common to autism are seen as most likely to be rewarding and pleasant for the child, voluntarily engaged, egosyntonic, and not closely linked

with preceding anxiety or subjective suffering. In ASD, little insight (which can be understood as the awareness of the unreasonable nature of repetitive thoughts and behavior) is expected [29]. Others report this would not apply to OCD in children, who may lack sufficient cognitive awareness for judgment [30].

Ruta et al. [31] did not find differences in insight between the two groups, but children and adolescent with AS and OCD engaged in different types and frequencies of repetitive thoughts and behaviors. Specifically, the OCD group reported significantly higher frequencies of contamination and aggressive obsessions and checking compulsions and the AS group displayed slightly higher frequencies of saving / hoarding and ordering clusters compared with the OCD group. Mack et al. [28] compared the clinical characteristics and symptom severity of children with OCD plus ASD to those children with OCD plus Tourette Syndrome (TS) and OCD alone. The authors reported comparable levels of symptom severity and impairment. Children with OCD plus TS reported more ordering compulsions and obsessions with sexual content compared with children with OCD plus ASD and OCD alone. The OCD plus ASD group tended to report fewer games and superstitious behaviors, as well as less somatic complaints.

Anholt et al. report that adults with OCD show increased frequency of ADHD and autism symptoms. The authors speculate common etiological factors to ASD, ADHD and OCD [32].

It is well worth the effort to distinguish the presence of OCD in children with ASD, as the comorbidity may be subject to specific treatments, such as Cognitive Behavioral Therapy. Nevertheless, further work is needed to validate existing therapies in the context of developmental characteristics of children with ASD.

The use of selective serotonin reuptake inhibitors (SSRI) in children with ASD is based on the effectiveness of SSRI in individuals with OCD alone as exemplified in a meta-analysis of randomized controlled trials [33]. Similarities between OCD and the repetitive behaviors of ASD led researches to investigate the use of SSRI in the autism core domain [34]. In a randomized placebo-control crossover study of 44 children with ASD, fluoxetine was beneficial in reducing repetitive behaviors [35]. Fluvoxamine had limited efficacy and was poorly tolerated [36]. Open label trials with sertraline in adults have noted improvement [37]. The strength of evidence for the effect of citalopram and escitalopram is insufficient [17]. Ongoing and promissory research is currently addressing the benefits of drugs such as memantine with a role in OCD [38]. Riluzole was found to be effective in the treatment of OCD and in severe behavioral problems [39].

Attention-Deficit / Hyperactivity Disorder

Attention-Deficit / Hyperactivity Disorder (ADHD) is characterized by symptoms of inattention, hyperactivity, and impulsivity across multiple settings. ADHD and ASD frequently co-occur [40], which demands routine reciprocal assessment. ADHD is present in ASD as frequently as 30 to 80% of cases, whereas the presence of ASD is estimated in 20 to 50% of children with ADHD [41]. Van der Meer et al. [41] studied three proposed groups: comorbid ADHD plus ASD, predominant ASD plus ADHD, and ADHD alone. ASD alone was excluded, as some ADHD symptoms were deemed universally present in ASD. The authors offered clinical descriptions through Conner's Parent Rating Scale (CPRS) and the Social Communication Questionnaire (SCQ) as well as through the study of cognitive functioning profiles. Symptoms such as poor social skills, emotional dysregulation, and oppositional behavior were found in both diagnoses, but these may be qualitatively distinguishing. There are descriptive similarities and differences from a cognitive perspective. The authors described significantly slower identification of facial emotions in the ASD plus ADHD, and ADHD plus ASD groups, compared with ADHD-alone. No significant differences were found in inhibition and cognitive flexibility. Small, but significant differences were found in visual spatial attention, verbal attention, and working memory. The ADHD plus ASD and ADHD-alone groups performed significantly worse in detail-focused processing. Mahajan et al. [42] found comorbidity of ADHD in 41 to 78% of children with ASD. These findings support the comorbid diagnosis of ADHD and ASD, disallowed in the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), but implemented in the fifth edition (DSM-5).

Clinicians in Northern Europe have conceptualized an entity known as "Deficit of attention, motor control and perception" (DAMP), which represents a combination of ADHD with motor-perceptual and coordination problems. Studies from these countries found a significant incidence of autistic features in this population where almost half of children with severe DAMP and autistic features met full criteria for Asperger syndrome [43].

It is important to optimize educational and behavioral interventions. Neuropsychological and psycho-educational testing may be necessary in order to design an individualized educational plan.

Medications should be considered in the treatment of ADHD in the context of ASD [25, 44]. Methylphenidate is effective in reducing symptoms of inattention and hyperactivity in children with ASD, although response rates may be lower than for children with typical ADHD. In a crossover trial, approximately 50% of children with ASD response to methylphenidate with a dose-dependent effect size from 0.20 to 0.54. Randomized control trials suggest less benefit and more side effects for ADHD plus ASD compared with ADHD alone [45].

In a secondary analysis of RUPP Autism Network data, a significant positive effect of methylphenidate was also seen on joint attention and emotional self-regulation [46]. For extended release preparations, parents and teachers reported improvement in hyperactivity and impulsivity, but only parents saw gains for inattention [47].

Studies on amphetamines in the treatment of attention / hyperactivity symptoms in ASD are lacking. It is unclear if results from trials of methylphenidate can generalize to amphetamines [48].

Alpha-2 adrenergic agonists are also used to manage ADHD symptoms in ASD [49, 50]. In a multicenter randomized trial comparing extended release guanfacine with placebo in 62 children with ASD, hyperactivity, impulsiveness and distractibility; guanfacine was effective in reducing behavioral symptoms [51]. A

small crossover trial with clonidine suggests decreased irritability, hyperactivity and oppositional behavior [52].

There is evidence to support treatment with the atypical antipsychotics risperidone and aripiprazole in cases of ADHD with aggression, agitation and irritability, or for safety concerns related to increased accident risk due to impulsivity [42].

Two randomized controlled trials compared the use of atomoxetine in ASD with ADHD and placebo, reporting 21% and 48% improvement, respectively, in ADHD rating scale scores [53, 54].

Tics and Tourette Syndrome

Tourette Syndrome (TS) is a highly heritable neuropsychiatric disorder characterized by motor and vocal tics, the prevalence of which varies from 0.4% to 3.8% [55]. A wide range of frequency has been found for the co-occurrence of autism, tics and TS. The heterogeneity may be related to difficulties differentiating tics from the stereotypies of autism. Kano et al. [56] pointed out several distinguishing characteristics: tics are usually single and random, involve the face, neck and shoulders, seem to react to an inner state of tension, fluctuate, and are temporarily suppressible. In contrast, stereotypies are more frequently rhythmic, involve the whole body, hands, or fingers; are less subject to influence by the environment, and are seen in association with sensory deficits. Tics in ASD were found more frequently in AS and higher intellectual functioning children [57].

A clinical sample of children and adolescents with ASD (n = 105) included a subgroup with comorbid ASD and tics (n = 24). Among individuals with ASD, 22% had tic disorders: 11% with TS and 11% with chronic motor tics. All had various degrees of cognitive impairment. An association between the level of mental retardation and tic severity was described [58].

Several medicines have been studied for the treatment of tics and TS in ASD. Some studies support the use of topiramate [59]. Risperidone and aripiprazole were useful for the treatment of stereotypies associated with autism [60]. One randomized controlled trial of fluvoxamine showed decrease in repetitive behaviors and aggression, although it would need replication [61].

There is not enough evidence to support the efficacy of stimulants and selective serotonin reuptake inhibitors (SSRIs) for the treatment of repetitive behaviors [62].

Depression

The reported prevalence of depression in ASD varies widely from 0.9 to 10% [5, 10]. Multiple reports support that rates of depression are directly correlated with higher level of functioning and adaptation, more insight or self-awareness of own impairments, and higher cognitive level of functioning [14, 63]. A high degree of vigilance and regular screening would improve the diagnosis and treatment of this burden. The diagnosis of depression is substantially based on self-report of feelings and how those feelings impact daily functioning, many times difficulty to obtain in the ASD population due to inherent impairments in social interaction and verbal communication. Vickerstaf and colleagues [64], among studied variables, found significant association between self-perception of social competence and depressive symptoms. Others report children with more severe symptoms of autism were more vulnerable to stressors, as well as to the development of depression [47, 65]. Peer approval was found to be a predictor for depression among youth with Asperger syndrome [66] and poorer quality of friendship correlated with higher levels of anxiety and depression [67]. A number of comorbid psychiatric disorders, including depression, predicted antipsychotic treatment [68].

Emotion dysregulation and hypersensitivity or overtly overwhelming reaction to daily stressors has been postulated to have an impact on mood problems in ASD [69]. Victimization in the educational setting, i.e., being bullied, as well as family conflict are correlated with depression [70].

The presentation of depression might vary in different contexts. It is, therefore recommended that information is obtained from observers in various settings. Parents reported less internalizing symptoms compared with youth and teachers [71]. Reports of depression increase with age. It is proposed that emotional age is more likely than chronological age to influence the development of depression [64].

From a clinical perspective, the diagnosis of depression in ASD remains a challenge. Despite characteristic symptoms such as depressed mood, irritability, anhedonia, sleep or appetite disturbances, cognitive problems like impaired concentration, indecision, feelings of hopelessness, morbid thoughts, and somatic complaints, the following should also be considered in ASD: aggression, mood lability, hyperactivity, decreased self-care, decreased level of functioning, regression, changes in core symptoms, increased compulsions, self-injurious behavior, catatonia, and overall changes in adaptive functioning [69].

The efficacy of SSRIs and serotonin norepinephrine reuptake inhibitors (SNRIs) in the treatment of depression and ASD has not been sufficiently validated through randomized controlled trials; nonetheless, empirical data support their use as indicated in neurotypical children [72].

Anxiety

In the clinical setting, anxiety-related concerns are among the most common presenting problems for school-age children and adolescents with ASD [63]. Simonoff et al. [10] studied a sample of 112 children with ASD between 10 and 14 years of age and found 41.9% met criteria for at least one anxiety disorder. Social anxiety disorder was most prevalent (29.2%). Similar results were replicated by Sukhodolsky et al. [73] who studied a population of 171 children with ASD, ages 5 to 14 years, finding at least one anxiety disorder in 43%. Increased anxiety is associated with lower IQ, as well as with less ASD severity, attributed to more self-awareness of social dysfunction [74].

ASD children presented with a different set of phobias and fears, compared to chronological- and mental-age matched peers, reporting more frequent situation phobias and medical fears, but less often related to harm / injury fears [75]. A review of literature reveals wide variability in prevalence that might

be confounded by level of functioning, specific ASD diagnosis, intellectual abilities, and age, among others. A gold standard tool to accurately capture anxiety symptoms in ASD is lacking. Even though the developmental progression of anxiety symptoms is similar to neurotypical children, several peculiarities should be kept in mind. For example, due to limited insight, ASD children may not report fears or worries, acting out behaviorally, instead [76].

The treatment of anxiety in children with ASD and neurotypical children is similar. A multimodal approach is recommended, including modified cognitive behavioral therapy, with some evidence that supports its efficacy in high functioning ASD. Pharmacological data in this population is limited [77]. One must also consider behavioral interventions to address sensory and special education needs [78].

Mania

7% prevalence for Bipolar disorder with psychotic features is reported among ASD, attributed to an unspecified vulnerability for mood disorder comorbidity, without specific family genetic load [13]. In contrast, other authors who have studied family histories of individuals with autism found a high incidence of major affective disorders — especially bipolar disorder.

A specific ASD / Bipolar phenotype has also been hypothesized, with vulnerability to develop bipolar disorder in adolescence or early adulthood [79]. As for any other comorbidity, early recognition and treatment may have significant impact on the patient's functioning. Munesue et al. [80] found a 16% comorbidity rate for mood disorders in his sample of HFA and AS, with 75 % of those, having bipolar disorder. ASD may share common vulnerability genes with bipolar spectrum disorders.

Mood symptoms in children with ASD and other disabilities may be overlooked due to masking of symptoms by ASD core manifestations. A change from baseline, such as obsessiveness, stereotypies, self-injurious behavior, hyperactivity, sleep disturbances, as well as increase in silliness, distractibility, poor judgment, intrusiveness, excessive laughing, pressured speech, and agitation may indicate symptoms of mania.

More rigorous studies are needed to support the use for mood stabilizers in ASD; nonetheless multiple agents have been empirically used, such as atypical antipsychotics, lithium and lamotrigine. Divalproex sodium has been demonstrated to be efficient in decreasing irritability, aggression, social relatedness and mood lability [81].

Eating Disorders

Problems with eating are particularly common in ASD, which may present as refusal of particular textures of food, pica, hoarding, overeating, anorexia, complete food refusal or excessive ordering of food in the plate [43]. Shmaya and colleagues [82] compared 3 to 6 year-old children with ASD, to their typically developing siblings, and to a typically developing age- and gender-matched control groups. Children with ASD had a higher Z-score for weight and BMI despite nutritional deficiencies due to feeding problems.

Janet Treasure et al. have emphasized the importance of autistic traits in anorexia nervosa [83]. Those with anorexia nervosa find it difficult to change self-set rules, see the world in close-up detail, as if looking through a zoom lens, and risk getting constantly lost in the details. Christopher Gillberg and colleagues found 23% of female patients with severe eating disorders had symptoms of the autism spectrum [43].

Psychosis and Catatonia

It is well accepted that autism is a disorder separate from early psychosis or early schizophrenia, in contrast to the view held well into the 1970s. Nevertheless, a variety of presentation combine symptoms of autism with psychotic symptoms, as well as catatonia and may possibly point to common etiopathogenesis [84].

Psychotic symptoms in ASD have been more frequently related to mood disorders, than to schizophrenia. Negative symptoms, such as flat affect and attention problems, were found more frequently in adults with ASD. The presence of frank hallucinations and delusions are likely indicative of comorbid Schizophrenia. Prevalence of AS in first-episode psychosis is considerably higher than in the general population [85].

Catatonia can manifest as paucity of movements, mutism, catalepsy and waxy flexibility, as well as episodes of excitement, restlessness, agitation and bizarre behavior [86]. It can co-occur with other psychiatric disorders, such as schizophrenia, depression, bipolar disorder, and with other medical conditions. Catatonia is reported in 12 to 17% of cases; with age at presentation between 10 to 19 years [87]. Overlapping symptoms can make the differential diagnosis challenging. Mutism, echolalia, stereotypic speech and repetitive behavior, posturing, grimacing, rigidity, mannerisms, and purposeless agitation, are some symptoms that are shared.

A number of clinical tools and guidelines exist to help raise suspicion for a catatonia diagnosis when there is marked deterioration in movement, and decrease of self-care and practical skills.

Trends in Pharmacological Treatment and Future Considerations

Pharmacological treatment can bring significant improvement in functioning and decrease overall child impairment, particularly when the severity of symptoms does not permit the child to participate in therapy or when behavioral intervention alone fails. Considering the clinical heterogeneity, medicine treatments should be individualized and integrated into a comprehensive, multimodal approach. Most studies target symptom clusters, given the challenges of diagnosing comorbid disorders in individuals with ASD. There remains a need to compare treatment efficacy for comorbidity in both neurotypical and ASD groups [88].

Selective pharmacological interventions on specific neurobiological pathways may improve clinical features apparently related to dysfunctional neurochemical signaling systems [89]. For example, GABAergic signaling mediates autism related stereotypies in animal models [90] and excessive NMDA receptor stimulation may potentially be involved in the course of the disorder [91].

Open label studies of memantine have demonstrated some improvement in language and behavior [38]. A double-blind study with amantadine has shown improvement in hyperactivity and inappropriate language [92].

N-acetylcysteine may have significant effects on irritability based on the Aberrant Behavior Checklist (ABC-1) [93] and oxytocin may promote social behavior [94] and emotion recognition [95]. D-cycloserine may improve social withdrawal [96]. Arbaclofen may be involved in social relatedness [56]. There is no evidence to support the efficacy of naltrexone and secretin for the treatment of autism core symptoms [9].

Sleep problems, reported in 43% to 83% of children with ASD [97], can be targeted with melatonin [98], anti-histamines, alpha-2 agonists, and zolpidem [99].

Future research is needed on screening tools and diagnostic questionnaires in order to improve validity and power to discriminate overlapping core and comorbid symptoms. In order to establish clinical efficacy, the results of smaller studies need to be replicated in rigorously designed large scale, long-term studies. Studies need to be inclusive of behavioral, educational, and vocational interventions, as well as consider adaptive social skills, with hopes of helping individuals with ASD develop their maximum potential and facilitate transition to adulthood [61].

Conclusion

Comorbidity in ASD is frequently associated with severe impairment. Recognition and treatment of specific syndromes is highly encouraged, in order to improve general functioning and alleviate symptoms. The presence of a comorbid condition should be considered when there are changes from baseline functioning or with new onset symptoms when no other medical or environmental cause is found. Assessment of comorbid condition requires skills and expertise with the ASD population. A comprehensive approach, including information from several sources, specific diagnostic tools adjusted to the ASD population, and emerging interventions may contribute to successful diagnosis and treatment.

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