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Psychological Comorbidities in Autism Spectrum Disorders

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Highlights

- Substantial overlapping occurs between autism spectrum disorders (ASDs) and psychological disorders.
- Mood disorders, anxiety disorders and ADHD, are among the psychological disorders most frequently related with ASD.
- Symptom presentation is similar whether ASD occurs alone or with other conditions.
- Numerous assessments after initial diagnosis of ASD are commonly required.
- The majority of the ASDs patients had poor QoL.

Abstract/Summary

Autism Spectrum Disorder (ASDs) is characterized by impairment in behavior, communication and social interaction. Thus, accurate identification, regular behavioral and other non-medical interventions would improve the diagnosis, management, and treatment of this condition.

In this chapter, we investigate the importance of diagnosing and identifying co-morbid psychiatric disorders that occur with ASD as these conditions can often complicate the treatment, and failure to recognize them can result in deficits that can persist into adolescence and adulthood. In addition, we explore the impact of a comprehensive psychological intervention in ASD patients with co-morbid psychiatric disorders with the ultimate goal of improving overall quality of life.

Keywords: Autism spectrum disorders, Psychiatric co-morbidities, Cognitive behavior therapy, Psychological interventions

Introduction

Central autism features like behavior, social and communication impairments are well-documented lifetime functional deficits (American Psychiatric Association, 2013).

The role of psychology in ASDs is classically to provide a comprehensive roadmap to evaluate patients' weaknesses and strengths, and provide a guide for treatment in these areas. Subsequent recommendations are based on afflicted patients' cognitive, behavioral, emotional and, academic or vocational needs. The overall aim is to improve functioning by identifying and adjusting maladaptive behaviors associated with the diagnosis; as well as, helping patients and their families succeed at key transition points such as starting school, entering adolescence and moving into adulthood (Weitlauf et al., 2014).

Each individual with ASD is unique and has a range of strengths and challenges. Some ASD individuals are able to succeed in their traditional schools, hold jobs and perform functions of daily living with varying levels of support. Others have substantial intellectual impairments, need to be integrated into special schools and need extensive support and assistance throughout their lives.

The reality of this disorder as a wide spectrum of symptom severity throws into light the importance of a dynamic and holistic approach to diagnosis as well treatment.

Diagnostic criteria of ASD

One of the biggest changes in the DSM 5 (American Psychiatric Association, 2013) was to introduce ASD. Previously, in the DSM IV (American Psychiatric Association, 1994), autistic symptoms were categorized into four groups: autistic disorder, Asperger's disorder, childhood disintegrative disorder, or the broader diagnosis of pervasive developmental disorder not otherwise specified. The main reason for this shift in diagnostic criteria was to limit the inconsistency in diagnosis across medical centers and practitioners; ultimately creating a comprehensive unified structure for assessing autism that would allow for greater efficacy in developing treatment plans (APA, 2013). Table 1 highlights the DSM 5 diagnostic criteria for ASD (APA, 2013).

Table 1- DSM 5 diagnostic criteria for ASD

A. Persistent deficits in social communication and social interaction across multiple contexts, as manifested by the following, currently or by history (examples are illustrative, not exhaustive, see text):
Deficits in social-emotional reciprocity, ranging, for example, from abnormal social approach and failure of normal back-and-forth conversation; to reduced sharing of interests, emotions, or affect; to failure to initiate or respond to social interactions.
Deficits in nonverbal communicative behaviors used for social interaction, ranging, for example, from poorly integrated verbal and nonverbal communication; to abnormalities in eye contact and body language or deficits in understanding and use of gestures; to a total lack of facial expressions and nonverbal communication.
Deficits in developing, maintaining, and understanding relationships, ranging, for example, from difficulties adjusting behavior to suit various social contexts; to difficulties in sharing imaginative play or in making friends; to absence of interest in peers.
B. Restricted, repetitive patterns of behavior, interests, or activities, as manifested by at least two of the following, currently or by history (examples are illustrative, not exhaustive; see text):
Stereotyped or repetitive motor movements, use of objects, or speech (e.g., simple motor stereotypies, lining up toys or flipping objects, echolalia, idiosyncratic phrases).
Insistence on sameness, inflexible adherence to routines, or ritualized patterns or verbal nonverbal behavior (e.g., extreme distress at small changes, difficulties with transitions, rigid thinking patterns, greeting rituals, need to take same route or eat food every day).
Highly restricted, fixated interests that are abnormal in intensity or focus (e.g, strong attachment to or preoccupation with unusual objects, excessively circumscribed or perseverative interest).
Hyper- or hyporeactivity to sensory input or unusual interests in sensory aspects of the environment (e.g., apparent indifference to pain/temperature, adverse response to specific sounds or textures, excessive smelling or touching of objects, visual fascination with lights or movement).
C. Symptoms must be present in the early developmental period (but may not become fully manifest until social demands exceed limited capacities or may be masked by learned strategies in later life).
D. Symptoms cause clinically significant impairment in social, occupational, or other important areas of current functioning.
E. These disturbances are not better explained by intellectual disability (intellectual developmental disorder) or global developmental delay. Intellectual disability and autism spectrum disorder frequently co-occur; to make comorbid diagnoses of autism spectrum disorder and intellectual disability, social communication should be below that expected for general developmental level.

For diagnostic clusters A and B, it is necessary to specify severity of symptoms based on social communication impairments and restricted, repetitive patterns of behavior into 3 levels (requiring support, requiring substantial support, requiring very substantial support). Considering the effect on the treatment plan, practitioners should also specify if:

- With or without accompanying intellectual impairment
- With or without accompanying language impairment
- Associated with a known medical or genetic condition or environmental factor
- Associated with another neurodevelopmental, mental, or behavioral disorder
- With catatonia

Comorbid psychological conditions in ASDs

While the DSM 5 goes to some length to standardize the method for assessing impairments or medical and neurodevelopmental disorders that co-occur with autism, it fails to do the same for psychological co-morbidities. In fact, the DSM 5 remains dependent on categorical definitions of psychological disorders, rather than dimensional classifications (Frenz, 2016).

The limitation in the DSM 5 to standardize assessment of co-morbidities generates a major gap in the ability to create an effective treatment plan that adequately meets the individual needs of each patient, and subsequently improve function. A burgeoning area of research has attempted to document the importance of identifying co-morbidities in ASD. In a twin study in Sweden, Lundstrom (2013) found that half of 272 ASD patients had 4 or more co-existing disorders and that only 4% did not have a comorbid diagnosis. Talisa (2015) found that some neuropsychiatric and behavioral conditions are related to anxiety, and not autism; indicating that failure to diagnose this would result in an inability to adequately improve function. Practitioners should become attuned to spotting signs for existing comorbidities like: a severe and incapacitating problem behavior, worsening of symptoms or abrupt changes from baseline, and not responding to treatment as expected. Should these issues arise, a thorough assessment of psychological co-morbidities should be undertaken using standardized assessment tools like:

- Young Mania Rating Scale (YMRS)
- Inventory of Depressive Symptomatology (IDS)
- Structured Clinical Interview for DSM IV for personality disorders (SCID-II)
- Structured Clinical Interview for DSM IV Childhood Diagnoses (Kid SCID)

Psychological conditions that commonly occur with ASDs are diverse, comprising of mood disorders (depression and bipolar), anxiety disorders, obsessive-compulsive disorder, attention-deficit/ hyperactivity disorder (ADHD). These conditions were found to be biologically based, and situation-induced. In the following sections, each of these disorders will be discussed but will be preceded by their DSM-5 diagnostic criteria.

Depression and bipolar disorder

In the DSM IV depressive disorders and bipolar disorders were grouped under the category of ‘mood disorders’, however in the DSM 5 these were reclassified into separate categories. Despite this, the diagnostic criteria for major depressive disorder (MDD) and bipolar I and II have remained more or less the same and changes were mostly conceptual in nature. Tables 2 – 4 outline the DSM 5 diagnostic criteria for MDD, bipolar disorder I and II, respectively.

Table 2 – DSM 5 criteria for Major Depressive Disorder

Major Depressive Disorder
The individual must experience five or more symptoms during the same 2-week period and at least one of the symptoms should be either (1) depressed mood or (2) loss of interest or pleasure.
1. Depressed mood most of the day, nearly every day.
2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day.
3. Significant weight loss when not dieting or weight gain, or decrease or increase in appetite nearly every day.
4. A slowing down of thought and a reduction of physical movement (observable by others, not merely subjective feelings of restlessness or being slowed down).
5. Fatigue or loss of energy nearly every day.
6. Feelings of worthlessness or excessive or inappropriate guilt nearly every day.
7. Diminished ability to think or concentrate, or indecisiveness, nearly every day.
8. Recurrent thoughts of death, recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide

Table 3 – DSM 5 criteria for Bipolar Disorder I

Bipolar Disorder I
A. Characterized by the occurrence of 1 or more manic or mixed episodes (the manic episode may have been preceded by and may be followed by hypomanic or major depressive episodes, but these are not required for diagnosis)
B. Distinct period of abnormally and persistently elevated, expansive, or irritable mood, and increased goal-directed activity or energy lasting ≥ 1 week (any duration if hospitalized), present most of the day, nearly every day
C. During the mood disturbance and increased energy or activity, at least 3 (or 4 if irritable mood only) of the following: <ul style="list-style-type: none"> – Inflated self-esteem or grandiosity – Decreased need for sleep – Pressured speech – Racing thoughts or flight of ideas – Distractibility – Increased activity – Excess pleasurable or risky activity.
D. Marked impairment not due to a substance or medical condition. In addition, these symptoms: <ul style="list-style-type: none"> A. Do not meet criteria for a mixed episode B. Cause functional impairment, necessitate hospitalization, or there are psychotic features C. Are not related to substance misuse D. Are not due to a general medical condition E. Are not caused by somatic antidepressant therapy.

Table 4 – DSM 5 criteria for Bipolar Disorder II

Bipolar Disorder II	
A.	Never had a full manic episode; at least 1 hypomanic episode and at least 1 major depressive episode
B.	Distinct period of abnormally and persistently elevated, expansive, or irritable mood, and increased goal-directed activity or energy lasting ≥ 4 but < 7 days, and clearly different from usual non-depressed mood, present most of the day, nearly every day
C.	During the hypomanic episode, at least 3 (or 4 if irritable mood only) of the following: <ul style="list-style-type: none"> – Inflated self-esteem or grandiosity – Decreased need for sleep – Pressured speech – Racing thoughts or flight of ideas – Distractibility – Increased activity – Excess pleasurable or risky activity.
D.	Episode is unequivocal change in functioning, uncharacteristic of person, and observable by others
E.	Not severe enough to cause marked impairment, not due to substance or medical condition, and no psychosis (if present, then this is mania by definition)
F.	During the major depressive episode, at least 5 of the following symptoms are present during the same 2-week period, and represent a change from previous functioning. At least one of the symptoms is either depressed mood or loss of interest or pleasure: <ul style="list-style-type: none"> – Depressed mood most of the day, nearly every day – Markedly diminished interest or pleasure, nearly every day – Significant weight loss when not dieting or weight gain, or decrease or increase in appetite, nearly every day – Insomnia or hypersomnia, nearly every day – Psychomotor agitation or retardation, nearly every day – Fatigue or loss of energy, nearly every day – Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional), nearly every day – Diminished ability to think or concentrate, or indecisiveness, nearly every day – Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation with or without a specific plan.
G.	In addition, these depressive symptoms: <ul style="list-style-type: none"> – Cause functional impairment (e.g., social, occupational) – Are not better explained by substance misuse, medication side effects, or other psychiatric or somatic medical conditions.

Postorino, Vicari and Mazzone (2016) reported the prevalence of co-occurrence of mood disorders (such as bipolar and depression) in ASDs to be between 1.4 % to 70 %. (Lainhart & Folstein, 1994; Wozniak et al., 1997; Ghaziuddin & Greden, 1998; Green et al. 2000; Kim et al., 2000; Barnhill & Smith, 2001; Stahlberg et al., 2004; Brereton et al., 2006; Hedley & Young, 2006; Leyfer et al., 2006; De Bruin et al., 2007; Vickerstaff et al., 2007; Munesue et al., 2008; Simonoff et al., 2008;

2012; Sterling et al., 2008; Williamson et al., 2008; Hofvander et al., 2009; Whitehouse et al., 2009; Mattila et al., 2010; Lugnegård et al., 2011; Mazefsky et al., 2011; Rosenberg et al., 2011; Amr et al., 2012; Joshi et al., 2013; Mazzone et al., 2013; Pouw et al., 2013; Strang et al., 2012; Cassidy et al., 2014; Gotham et al., 2014; Henry et al., 2014). The previous studies used different criteria and different assessment tools, both self-report and clinician administered, which can greatly alter the diagnosis, especially when taking into account the capabilities of the child (Chandrasekhar & Sikich, 2015). The wide variance of this prevalence highlights the importance of a single standardized diagnostic method and assessment for psychiatric disorders.

There is evidence to support that mood disorders are associated with greater adaptability in ASD. Several studies found that symptoms of depression and mania are directly correlated with higher levels of functioning and adaptation, more insight or self-awareness of own impairments, and a higher cognitive level of functioning (Sterling, 2008; Ghaziuddin, 2002). Similarly, Vickerstaff *et al.* (2007) found that there are significant associations between self-perception of social competence and depressive symptoms. In addition, high-functioning autism (HFA) patients were found to be predominantly afflicted with mood disorders (Ghaziuddin and Greden 1998; Kim et al., 2000; Mazzone et al., 2013; Munesue et al., 2008; Stewart et al., 2006; Vickerstaff et al., 2007; Whitehouse et al., 2009; Joshi et al., 2013). These rates of comorbid mood disorders were found to be even higher in adolescent and adult HFA patients (Cassidy et al. 2014; Hofvander et al., 2009; Lugnegård et al., 2011; Stahlberg et al., 2004; Sterling et al., 2008).

Conversely, other reports indicate that with more severe symptoms of autism, patients are more vulnerable to stressors, as well as to the development of depression (Pearson, 2006; Ghaziuddin, 1995). This is compounded further by Mazurek's (2010) findings that poorer quality of friendship is correlated with higher levels of anxiety and depression indicating the importance for protective factors to general stressors. Depression-induced regression was found to be noticeably present mainly in low functioning autism patients who are characterized by loss of language, social withdrawal, loss of eye contact, moodiness, tantrums, fearfulness, obsessiveness, stereotypies, hyperactivity, and occasionally self-injurious behaviors (Ghaziuddin et al., 2002; Myers & Winters, 2002).

Age was also found to be a significant predictor of comorbid depression as symptoms were found to increase with age; with emotional age being a more reliable predictor of the development of depression than chronological age (Vickerstaff, 2007). Several studies also showed that the age of onset of co-occurrence of depression is predominantly around pre-adolescence and adolescence. This could be attributed to the transition period of ASD patients becoming more conscious of their own social skills as well as awareness of lower self-perceived social competence (Ghaziuddin et al. 2002; Mazzone et al. 2012; Williamson et al., 2008; Brereton et al., 2006; Ghaziuddin et al., 2002; Vickerstaff et al., 2007).

The diagnosis of depression is substantially based on self-report of feelings and how those feelings impact daily functioning; this is often difficult to obtain in the ASD population due to inherent impairments in social interaction and verbal communication.

From a clinical point of view, the diagnosis of depression in ASD remains a challenge. Despite characteristic symptoms being recognized, such as depressed mood, irritability, anhedonia, sleep or appetite disturbances, cognitive problems like impaired concentration, indecision, feelings of hopelessness, morbid thoughts, and somatic complaints. Other symptoms are often neglected in observation of ASD patients like 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 (Magnuson, 2011). The failure to identify these symptoms as depression and assuming them as an extension of the ASD diagnosis can lead to loss of the patient's ability to learn new skills that might greatly improve their ability to live with ASD and may lead to missing suitable interventions that could deal with these problems.

Anxiety Disorders

Anxiety disorders in the DSM 5 include: separation anxiety disorder, selective mutism, specific phobia, social phobia, panic disorder, agoraphobia, and generalized anxiety disorder (GAD). The common symptoms across each of these diagnoses is best explained by the diagnostic criteria for GAD in table 5.

Table 5 – DSM 5 diagnostic criteria for Generalized Anxiety Disorder

Generalized Anxiety Disorder
A. The presence of excessive anxiety and worry about a variety of topics, events, or activities. Worry occurs more often than not for at least 6 months and is clearly excessive.
B. The worry is experienced as very challenging to control. The worry in both adults and children may easily shift from one topic to another.
C. The anxiety and worry are accompanied with at least three of the following physical or cognitive symptoms. (In children, only one symptom is necessary for a diagnosis of GAD): <ul style="list-style-type: none">– Edginess or restlessness– Tiring easily; more fatigued than usual– Impaired concentration or feeling as though the mind goes blank– Irritability (which may or may not be observable to others)– Increased muscle aches or soreness– Difficulty sleeping (due to trouble falling asleep or staying asleep, restlessness at night, or unsatisfying sleep)

Due to the nature of ASD heavily impairing social and communication skills, school-age children and adolescents are often commonly afflicted with anxiety-related concerns (Ghaziuddin 2002). Simonoff et al (2008) supported this further with findings showing that 41.9% of 112 ASD children aged from 10 -14 years met the criteria for at least one anxiety disorder.

Reported prevalence of anxiety in ASD varies widely, with estimates ranging from 13.6 to 84.1 % (Bellini 2004; Bradley et al. 2004; Kim et al. 2000 ; Muris et al. 1998 ; Lidstone et al. 2014). A recent systematic review obtained from 31 studies (van Steensel et al., 2011) identified that clinically significant levels of anxiety were present in 39.6% of a pooled sample of 2,121 individuals under the age of 18 with ASD. Although findings are inconsistent, the most frequent anxiety disorders in ASD appear to be specific phobias, generalized anxiety disorder, separation anxiety disorder, and social phobia; with social anxiety being the most prevalent in ASDs (29.2%) (Muris et al., 1998; Evans et al., 2005; Gadow et al., 2005; Weisbrot et al., 2005; de Bruin et al., 2007; Gillot & Standen, 2007; Sukhodolsky et al., 2008).

While Sukhodolsky et al. (2008) similarly found that 43% of 171 ASD children aged from 5 – 14 years met the criteria for at least one anxiety disorder. They also reported that increased anxiety was associated with higher IQ, as well as with less ASD severity, which could be attributed to more self-awareness of social dysfunction.

ASD children presented with a distinctive set of fears when compared to chronological- and mental- age matched peers, reporting more frequent situation phobias and medical fears, but less often related to fears of being harmed or injured (Evans et al., 2005)

In conclusion, anxiety seems to be more common in ASD than in both the general population and several clinical groups, with probably up to 40% of ASDs patients presenting with at least one anxiety subtype.

Obsessive-Compulsive Disorder

Obsessive-compulsive disorder (OCD) is characterized by recurrent disturbing thoughts or images, and repetitive behaviors. In the DSM IV, OCD was previously categorized as an anxiety disorder however in the DSM 5 it was reclassified as a distinct disorder due to the focus on the behavioral component. Table 6 describes the DSM 5 criteria for diagnosing OCD.

Table 6 – DSM 5 diagnostic criteria for Obsessive Compulsive Disorder

Obsessive Compulsive Disorder (OCD)
<p>A. Presence of obsessions, compulsions, or both:</p> <ul style="list-style-type: none">– Obsessions are defined by (1) and (2):<ol style="list-style-type: none">1. Recurrent and persistent thoughts, urges, or impulses that are experienced, at some time during the disturbance, as intrusive and unwanted, and that in most individuals cause marked anxiety or distress.2. The individual attempts to ignore or suppress such thoughts, urges, or images, or to neutralize them with some other thought or action (i.e., by performing a compulsion).– Compulsions are defined by (1) and (2):<ol style="list-style-type: none">1. Repetitive behaviors (e.g., hand washing, ordering, checking) or mental acts (e.g., praying, counting, repeating words silently) that the individual feels driven to perform in response to an obsession or according to rules that must be applied rigidly.2. The behaviors or mental acts are aimed at preventing or reducing anxiety or distress, or preventing some dreaded event or situation; however, these behaviors or mental acts are not connected in a realistic way with what they are designed to neutralize or prevent, or are clearly excessive.
<p>B. The obsessions or compulsions are time-consuming (e.g., take more than 1 hour per day) or cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.</p>
<p>C. The obsessive-compulsive symptoms are not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition.</p>
<p>D. The disturbance is not better explained by the symptoms of another mental disorder (e.g., excessive worries, as in generalized anxiety disorder; preoccupation with appearance, as in body dysmorphic disorder; difficulty discarding or parting with possessions, as in hoarding disorder; hair pulling, as in trichotillomania [hair-pulling disorder]; skin picking, as in excoriation [skin-picking] disorder; stereotypies, as in stereotypic movement disorder; ritualized eating behavior, as in eating disorders; preoccupation with substances or gambling, as in substance-related and addictive disorders; preoccupation with having an illness, as in illness anxiety disorder; sexual urges or fantasies, as in paraphilic disorders; impulses, as in disruptive, impulse-control, and conduct disorders; guilty ruminations, as in major depressive disorder; thought insertion or delusional preoccupations, as in schizophrenia spectrum and other psychotic disorders; or repetitive patterns of behavior, as in autism spectrum disorder).</p>

OCD often begins in childhood and adolescence; several studies show an increased incidence of OCD in the ASD population, as well as increased ASD among those diagnosed with OCD (Kumar, 2012; West, 2009). Postorino *et al.* (2017) reported prevalence of OCD in ASD cases ranged between 2.6% and 37.2%.

It can be difficult to determine an OCD diagnosis in an autistic child as there are overlapping rituals common in both diagnoses such as repetitive behavior and rigid adherence to routines (Lugnegard, Hallerback & Gillberg, 2011; South, Ozonoff & McMahon, 2005; Mack *et al.*, 2010). However, the compulsions are characterized by their distressing effect on the individual and anxiety peaks as a result of the attempt to resist carrying out the compulsive behavior. Rituals of autistic patients, on the other hand, are not characterized by any preceding anxiety or distress and are often a rewarding and pleasant experience for the child.

Ruta *et al.* (2010) summarized the differences between children who have received a diagnosis for OCD only, ASD only, and those with a co-morbidity of OCD and ASD. They found that OCD groups and ASD groups reported different types of obsessive behaviors, with OCD children reporting higher frequencies of aggressive obsessions and checking compulsions, while ASD children displaying higher frequencies of saving/hoarding behaviours. However, they found that groups with co-morbid diagnoses, ASD with OCD or Tourette syndrome, had comparable levels of symptom severity and impairment.

Anholt *et al.* (2010) reported that adults with OCD show increased frequency of ADHD and autism symptoms and speculated common etiological factors to ASD, ADHD and OCD.

Attention-Deficit / Hyperactivity Disorder

Attention-Deficit / Hyperactivity Disorder (ADHD) is characterized by symptoms of inattention, hyperactivity, and impulsivity across multiple settings. Table 7 specifies the diagnostic criteria for ADHD according to the DSM 5.

Table 7 – DSM 5 diagnostic criteria for Attention-Deficit/Hyperactivity Disorder

Attention-Deficit/ Hyperactivity Disorder (ADHD)
<p>A. Persistent pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development, as characterized by (1) and/or (2):</p> <ol style="list-style-type: none">1. Inattention: Six (or more) of the following symptoms have persisted for at least 6 months to a degree that is inconsistent with developmental level and that negatively impacts directly on social and academic/occupational activities.<ul style="list-style-type: none">– Often fails to give close attention to details or makes careless mistakes in schoolwork, at work, or during other activities (e.g., overlooks or misses details, work is inaccurate).– Often has difficulty sustaining attention in tasks or play activities (e.g., has difficulty remaining focused during lectures, conversations, or lengthy reading).– Often does not seem to listen when spoken to directly (e.g., mind seems elsewhere, even in the absence of any obvious distraction).– Often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (e.g., starts tasks but quickly loses focus and is easily sidetracked).– Often has difficulty organizing tasks and activities (e.g., difficulty managing sequential tasks; difficulty keeping materials and belongings in order; messy, disorganized work; has poor time management; fails to meet deadlines).– Often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort (e.g., schoolwork or homework; for older adolescents and adults, preparing reports, completing forms, reviewing lengthy papers).– Often loses things necessary for tasks or activities (e.g., school materials, pencils, books, tools, wallets, keys, paperwork, eyeglasses, mobile telephones).– Is often easily distracted by extraneous stimuli (for older adolescents and adults, may include unrelated thoughts).– Is often forgetful in daily activities (e.g., doing chores, running errands; for older adolescents and adults, returning calls, paying bills, keeping appointments).2. Hyperactivity and impulsivity: Six (or more) of the following symptoms have persisted for at least 6 months to a degree that is inconsistent with developmental level and that negatively impacts directly on social and academic/occupational activities.<ul style="list-style-type: none">– Often fidgets with or taps hands or feet or squirms in seat.– Often leaves seat in situations when remaining seated is expected (e.g., leaves his or her place in the classroom, in the office or other workplace, or in other situations that require remaining in place).– Often runs about or climbs in situations where it is inappropriate. (Note: In adolescents or adults, may be limited to feeling restless.)– Often unable to play or engage in leisure activities quietly.– Is often “on the go,” acting as if “driven by a motor” (e.g., is unable to be or uncomfortable being still for extended time, as in restaurants, meetings; may be experienced by others as being restless or difficult to keep up with).– Often talks excessively.– Often blurts out an answer before a question has been completed (e.g., completes people’s sentences; cannot wait for turn in conversation).– Often has difficulty waiting his or her turn (e.g., while waiting in line).– Often interrupts or intrudes on others (e.g., butts into conversations, games, or activities; may start using other people’s things without asking or receiving permission; for adolescents and adults, may intrude into or take over what others are doing).

- B. Several inattentive or hyperactive-impulsive symptoms were present prior to age 12 years.
- C. Several inattentive or hyperactive-impulsive symptoms are present in two or more settings (e.g., at home, school, or work; with friends or relatives; in other activities).
- D. There is clear evidence that the symptoms interfere with, or reduce the quality of, social, academic, or occupational functioning.
- E. The symptoms do not occur exclusively during the course of schizophrenia or another psychotic disorder and are not better explained by another mental disorder (e.g., mood disorder, anxiety disorder, dissociative disorder, personality disorder, substance intoxication or withdrawal).

So far, no meta-analyses have been conducted on the prevalence of ADHD in ASDs. However, ADHD was found to co-occur in as many as 30 - 80% of ASD cases, while the presence of ASD is estimated to be between 20 to 50% of ADHD children (Rommelse et al., 2010; van der Meer, Oerlemans & van Steijn, 2012; Mahajan, Bernal & Panzer, 2012; Grzadzinski et al., 2011)

For instance, van der Meer et al. (2012) conducted a study in three groups of patients (1. ADHD plus ASD; 2. predominant ASD plus ADHD; and 3. ADHD only) and found a significantly slower identification of facial emotions in the ASD plus ADHD, and ADHD plus ASD groups when compared with ADHD-alone. Significant differences were also found in visual spatial attention, verbal attention, and working memory amongst the groups but no significant differences in inhibition and cognitive flexibility was noticed (van der Meer et al., 2012). The ADHD plus ASD and ADHD-alone groups performed significantly worse in detail-focused processing (van der Meer et al., 2012).

Personality disorders (PD)

In the DSM 5, the ten PD outlined in the DSM IV were retained and they are: paranoid personality disorder, schizoid personality disorder, schizotypal personality disorder, antisocial personality disorder, borderline personality disorder, histrionic personality, narcissistic personality disorder, avoidant personality disorder, dependent personality disorder, and obsessive-compulsive personality disorder.

However, much like autism and as opposed to schizophrenia or post-traumatic stress disorder, personality disorders are not categorical and do exist on a continuum. For this reason, the DSM 5 has put forward proposed changes for further study in a separate section. The proposed model would evaluate impairments in personality functioning, and assess five broad areas of

pathological personality traits. This model includes only six PD as evidenced by research: antisocial, avoidant, borderline, narcissistic, obsessive-compulsive, and schizotypal.

In this vein, distinct PD are not as commonly found to be diagnosed as co-morbidities of ASD. However, certain traits like aggression, and self-injurious behavior that are symptomatic of PD like borderline personality disorder and antisocial personality disorder were prevalent ASD comorbidities (Kanne & Mazurek, 2010; Wallace et al., 2012). While there is a correlation between aggression, self-injurious behavior, and ASD; we cannot infer a causal relationship. In fact, it is difficult to determine whether these variables affect each other distinctly or if they are manifestations of the same problem. However, as it is not possible to diagnose any PD before the age of 18, as the personality is still forming, problematic traits and behaviors should be monitored using functional analysis to identify factors that might perpetuate or reinforce the trait or behavior (Belardinelli, Raza & Taneli, 2016).

Interventional Models

Children with ASD generally require a combination of therapies and interventions to address their individual constellation of symptoms. Approaches can be broadly categorized according to conceptual models; however, there is no uniformly agreed upon classification system. The availability of programs varies by region; access to interventions may affect the choice of programming. A systematic review found insufficient evidence to suggest that any interventional model is superior to another (Magoline, 2012). However, there is moderate evidence that greater intensity (in hours per week) and greater duration (in months) of treatment lead to better outcomes (Linstead et al., 2017).

Table 8 summarizes five interventions commonly used to treat ASD and the strengths of each therapy.

1 Table 8 – Summary of interventional models for ASD

<i>Intervention</i>	<i>Description</i>	<i>Type</i>	<i>Objective</i>	<i>Strengths</i>
Developmental Behavioral interventions	<p>This therapy is applied in the client’s natural setting or in a structured environment, and includes behavioral modification, structured teaching, and is relationship-based. Generally, it works by reinforcing productive behaviors and discouraging maladaptive behaviors.</p> <p>Examples of developmental behavioral interventions include: [insert names]</p>	Behavioral and developmental therapy	Focuses on using a variety of behavioral strategies to teach necessary skills relevant to the development stage	<ul style="list-style-type: none"> – Targets specific domains (e.g., social, language, cognitive) – May occur in various settings (e.g., naturalistic versus structured) – Involves the parents, particularly when interventions are provided in the home
Treatment and Education of Autistic and Related Handicapped Children (TEACCH)	The TEACCH method uses Structured Teaching to help individuals overcome areas of weakness.	Generalist (does not identify with one developmental discipline)	The goal is to modify the environment and to improve skills.	<ul style="list-style-type: none"> – Understands culture of autism – Uses an individualized person and family-centered plan – Organizes the physical environment – Uses a predictable sequence of activities – Utilizes visual schedules and visually structured activities – Implements routines with flexibility – Structured work/activity systems
Occupational therapy	Occupational therapy is often used to address deficits in adaptive functioning and fine motor skills that affect academic and everyday functioning.	Occupational	To enhance functioning inhibited by a specific deficit and to encourage self-sufficiency.	<p>In young children with ASD, occupational therapy focuses on enhancing:</p> <ul style="list-style-type: none"> – sensory processing, sensorimotor and social-behavioral performance

				<ul style="list-style-type: none"> - self-care (e.g., dressing, hygiene), - participation in play. <p>In older children, the focus of occupational therapy may include:</p> <ul style="list-style-type: none"> - social and behavioral performance - transition to work and independence in the community.
CBT (self management)	CBT focuses on replacing negative or ineffective patterns of thought and behavior with structured strategies that are effective in improving mood and adaptive functioning.	Cognitive-behavioral therapy	To help those with ASD learn to independently regulate their own behaviors and act appropriately in a variety of home, school, and community-based situations.	<p>Those with ASD are taught to:</p> <ul style="list-style-type: none"> - discriminate between appropriate and inappropriate behaviors, - accurately monitor and record their own behaviors, - reward themselves for behaving appropriately - eventually take on greater responsibility in their own self-care

3 **Treating psychological co-morbidities in ASD**

4 Once a diagnosis of a co-morbidity has been ascertained, an individualized treatment plan that
5 compliments the interventions he or she is already receiving needs to be determined.

6 Comprehensive integrative models address multiple domains of function. For example, the Early
7 Start Denver Model (ESDM) uses a combination of behavioral programming and developmental-
8 and relationship-based approaches and includes parents as therapists. These types of
9 comprehensive therapies are often beneficial with co-morbid psychiatric disorders and tend to
10 directly and indirectly target symptoms that often complicate the treatment of ASD. A randomized
11 trial comparing the ESDM program with interventions commonly available in the community
12 demonstrated significant language, cognitive, and adaptive functioning gains in 48 toddlers over a
13 two-year period (Touzet et al., 2017). The Agency for Healthcare Research and Quality (AHRQ)
14 published a systematic review (2014) suggesting the utility of parent training for improving
15 behavioral outcomes in general and of adding parent training to medication interventions for
16 children with challenging behaviors. However, the studies were small, relied on parent report, and
17 used varying intervention models.

18 Nevertheless, the National Autism Center's National Standards Reports (2015) considers targeted
19 behavioral interventions to be the general standard of treatment. Historically, behavioral
20 interventions have also been found to be beneficial. A systematic review of 251 studies conducted
21 between 1980 and 1996 of targeted behavioral interventions found that focal behavioral
22 interventions consistently result in positive behavioral outcomes across a wide range of targets,
23 including aberrant behaviors (e.g., self-injury, aggression), language skills, daily living skills,
24 social skills, etc. (Matson et al., 1996).

25 On the other hand, a 2014 systematic review of studies published after 2000 suggested the efficacy
26 of CBT interventions in reducing anxiety symptoms in individuals with ASD and IQ scores above
27 70 (Weitlauf et al, 2014). Moreover, a systematic review published by the US
28 Massachusetts National Standards projects, classified CBT as an established intervention for
29 children and adolescents (National Autism Center, 2015). Similarly, a meta-analysis of 12 studies
30 for anxiety co-morbidity involving 511 youth with high functioning ASD found statistically
31 significant pooled treatment effect for CBT with significant IQ heterogeneity (Ung, 2015).

32 A systematic review (Kose, Fox & Storch, 2018) evaluating the efficacy of CBT on ASD and OCD
33 co-morbidities found that although CBT with various modifications has been shown to be
34 beneficial, the research includes small populations and a variety of nonstandard modifications; the
35 lack of standardization in applying CBT limits the generalizability of the findings. Nevertheless,
36 all the studies did show at least some treatment gains despite the variation in age and severity of
37 diagnosis. The methods involved in the studies, while varied, generally included: mapping,
38 cognitive restructuring, fear hierarchy development, [exposure and response prevention], and
39 relapse prevention.

40 With a co-morbid diagnosis of ASD and ADHD, non-pharmacological treatments found to be
41 moderately effective include: dietary interventions (restricted elimination diets, artificial food
42 color exclusions, and free fatty acid supplementation), behavioral interventions, cognitive training,
43 and neurofeedback (Daley et al., 2014).

44 It is likely that comorbid emotional or behavioral problems would influence outcomes of social
45 skills interventions. In a study observing the effect of a social skills training program, it was
46 reported that social skills improved for children with ASD, and children with ASD and comorbid
47 anxiety, but that there was no improvement among children with ASD and comorbid ADHD,
48 highlighting the importance of individualizing treatment plans for different co-morbid diagnoses
49 (Antshel et al., 2011).

50 **Quality of Life (QoL)**

51 In the simplest terms, QoL is defined as: inner subjective personal satisfaction across 4 basic
52 domains; physical, emotional, social and vocational (Frisch, 2006). QoL interventions from a
53 positive psychology point of view, aim at promoting a life satisfaction in which humans identify,
54 pursue, and fulfill their most cherished goals, desires and wishes across all valued areas of life
55 (Toghyani et al., 2011). In the context of ASD, QoL Clinical Practice (QoLCP) normalizes the life of
56 patients and their families so that it does not fall below a predetermined cutoff threshold (Morsi
57 et al., 2016).

58 With this definition, QoL Clinical Practice could be a precise patient and family centered care
 59 method for measuring improvement, monitoring ASD symptoms, optimizing interventions and
 60 personalizing medico-social care amongst individuals with ASD.

- 61 – **Key features in ASD conventional QoLCP:**
- 62 – **CASIO Rubric**

63 QoL provides a rubric model for life satisfaction (Change in Circumstances, Attitude, Standards,
 64 Importance, and Other aspects; CASIO) as a blueprint for positive psychological intervention. The
 65 model presented in Figure 1 offers a strategy for management of 16 areas of life over 8
 66 therapeutic sessions (Frisch, 2006, Toghyani et al., 2011). The program (illustrated in Table 9)
 67 starts with introducing clinical participants and each session consists of reviews, discussions and
 68 assigning of homework steps.

69 Figure 1: CASIO model for life satisfaction



70

71 Table 9 – CASIO 8 session program for improving QoL

Session 1		Session 5	
Introduce participants			
Review	Goals QoL interventions and rationale	Review	CASIO model in Values Homework
Discuss	16 areas of life satisfaction Difficult areas	Discuss	Relationships and its role in life satisfaction
Homework	Think how to improve QoL	Homework	Everyday life skills: Enhance relationships using writing a letter and basket of eggs techniques (Frisch, 2006)

<u>Session 2</u>		<u>Session 6</u>	
Review	QoL progress. Homework	Review	CASIO model in relationships. Homework
Discuss	Role of self-esteem in happiness increasing and present skills in these areas	Discuss	The role of play and leisure in increasing happiness
Homework	Everyday life skills: Improve strengths and gratitude through BAT (Blessings, Accomplishments, Talents and Traits) technique (Frisch, 2006)	Homework	Everyday life skills: Increase play and family recreation time (Frisch, 2006)

<u>Session 3</u>		<u>Session 7</u>	
Review	CASIO model in self-esteem. Homework	Review	CASIO model of Play. Homework
Discuss	Health topics and concerns	Discuss	Learning and skills
Homework	Everyday life skills: Report on frequent health concerns using Trigger, Actions and Consequences (TAC) technique (Frisch, 2006)	Homework	Everyday life skills: Boost learning satisfaction using problem solving technique (Frisch, 2006)

<u>Session 4</u>		<u>Session 8</u>	
Review	CASIO model in health concerns. Homework.	Review	CASIO model of learning. Homework. All treatment sessions.
Discuss	Goals and important values	Discuss	Transition to being own QoL therapist and using relapse prevention techniques
Homework	Everyday life skills: Tweak goals and values using Daily Action Plan (DAP) and Life Script techniques (Frisch, 2006)	Homework	Further study and work in QoL

72 **Constructive Mode Activation for ASD Co-morbidities**

73 The QoLCP also provides patients access to constructive cognitive creation of life satisfaction and
74 happiness through the above CASIO model. Individual differences in relation to life satisfaction is
75 accommodated via recognition of interaction between external life conditions and patients' own
76 circumstances, personal values attached to life goals, and personal standards for reaching goals

77 in 16 areas of life (Toghyani et al., 2011). Table 10 highlights definitions of the 16 areas of life
 78 focused on in QoLCP.

79 Table 10 – 16 areas of life for QoLCP; *adapted with minimal modifications from Frisch, 2006*

1. Health is being physically fit, not sick, and without pain or disability.
2. Self-Esteem means liking and respecting yourself in light of your strengths and weaknesses, successes and failures, and ability to handle problems.
3. Goals-and-Values ± Spiritual Life: are beliefs about what matters most in life and how you should live, both now and in the future.
4. Money (or Standard of Living) is made of the money you earn, the things you own (like a car or furniture), and believing that you will have the money and things that you need in the future.
5. Work means your career or how you spend most of your time.
6. Play (or Recreation) means what you do in your free time to relax, have fun, or improve yourself. This could include watching movies, visiting friends, or pursuing a hobby like sports or gardening.
7. Learning means gaining new skills or information about things that interest you. Learning can come from reading books or taking classes on subjects like history, car repair, or using a computer.
8. Creativity is using your imagination to come up with new and clever ways to solve every day problems or to pursue a hobby like painting, photography, or needlework. This can include decorating your home, playing the guitar, or finding a new way to solve a problem at work.
9. Helping (Social Service and Civic Action) means helping others (not just friends or relatives) in need or helping to make your community a better place to live.
10. Love (or Love Relationship) is a very close romantic relationship with another person. Love usually includes sexual feelings and feeling loved, cared for, and understood.
11. Friends (or Friendships) are people (not relatives) you know well and care about who have interests and opinions like yours.
12. Children includes a measure of how you get along with your child (or children). Think of how you get along as you care for, visit, or play with your child (or children).
13. Relatives means how you get along with your parents, grandparents, brothers, sisters, aunts, uncles, and in-laws.
14. Home is where you live. It is your house or apartment and the yard around it.
15. Neighborhood is the area around your home.
16. Community is the whole city, town, or rural area where you live (not just your neighborhood). Community includes how nice the area looks, the amount of crime, and how well you like the people. It also includes places to go for fun like parks, concerts, sporting events, and restaurants.

81 – **Innovative key features of ASD QoLCP**

82 As the QoL of autistic patients and their families is lower than for the general population
83 (Mason et al., 2018), it requires innovative practice in addition to these 2 conventional key
84 features. The traditional QoL / psychological diagnosis of autistic patients and associated co-
85 morbidity involve medical and psychological history taking, mental state examination and
86 psychological screening. The end result of such process is a subjective diagnosis of the case and
87 the difficulties that families might be going through as a result of the disorder. Recently, these
88 subjective projections of health care practitioners are being challenged and pursuing objective
89 non biased assessment tools are being pursued (Morsi et al., 2018). This represents a key
90 requirement in personalizing QoL management of patients and families and optimizing their
91 well-being in several domains of the 16 areas of life of the CASIO model.

92 – **Assessment of QoL in ASD patients**

93 If the assessment is carried out by a QoL practitioner who is not a physician, he or she interacts
94 with the primary physician to get a medical report and a green light to carry out the QoL
95 interventions (Frisch, 2006). However, if a physician is carrying out the intervention, then QoL
96 assessment followed by a psychiatric ASD assessment should be performed starting with a
97 comprehensive history taking, and physical and mental state examination. Screening tools are
98 then applied as a baseline and a follow up investigation.

99 – **Screening tools for adults:**

100 The Research Autism of the National Autistic Society of UK validated the use of Autism Specific
101 QoL survey (ASQoL) to be used alongside the World Health Organization Quality of Life – Brief
102 (WHOQoL-BREF) and World Health Organization Quality of Life (WHOQoL) disabilities modules.
103 It is used with adults to evaluate a total ASQoL score (8 items), and a score for the global item
104 (item 9) about ‘autistic identity’ (McConachie et al., 2018).

105 – **Screening tools for children and adolescents**

106 The most commonly used instruments are the QoL battery of Varni (Varni et al., 2007, Varni et
107 al., 2001). The battery contains the Pediatric Quality of Life Inventory™ (PedsQL) and other
108 instruments to assess a wide variety of domains related to QoL, family satisfaction, and burden
109 of diseases (Ikeda et al., 2014).

110 In conclusion, ASD patients experience a specific and unique form of QoL, the normalization of
111 which is an endpoint medical care and requires a multi-disciplinary team effort that includes a
112 QoL therapist. This normalization takes place for ASD and all its associated co-morbidities
113 through the conventional and innovative QoLCP key features and it encompasses all aspects of
114 patient's life and his / her family.

115 **Pharmacotherapy**

116 While non-pharmacological treatments have been shown to be effective in treating co-morbidities
117 of ASD; a valid treatment option is medication. Pharmacotherapy should be considered when
118 symptoms of co-morbidities are extremely severe (e.g., depression or OCD), if there is severe
119 functional impairment secondary to disruptive behavior or if there is no response to behavioral
120 interventions. Moreover, as patients with ASD often undergo several hours of weekly interventions
121 to improve general functioning, it can be overwhelming to recommend further interventions for
122 their co-morbidities.

123 Interventions should be guided by evidence and appropriate treatment guidelines (West, Waldrop
124 & Brunssen, 2009). Below is a summary of medications found to be effective in treating co-
125 morbidities in ASD:

- 126 – **Depression:** The efficacy of selective serotonin reuptake inhibitor (SSRIs) and serotonin
127 norepinephrine reuptake inhibitor (SNRIs) in the treatment of depression and ASD has not
128 been sufficiently validated through randomized controlled trials; nonetheless, empirical
129 data support their use as indicated in neurotypical children (Posey, Erickson, Stigler, &
130 McDougale, 2006).
- 131 – **Anxiety:** The treatment of anxiety in children with ASD and neurotypical children is
132 similar. A multimodal approach is recommended, including modified cognitive behavioral

133 therapy, with some evidence that supports its efficacy in high functioning ASD.
134 Pharmacological data in this population is limited (Vasa, Carroll, & Nozzolillo, 2014).
135 Behavioral interventions should also be considered to address sensory and special
136 education needs (White, Oswald, Ollendick, Scahill, 2009).

137 – **OCD:** Similarities between OCD and the repetitive behaviors of ASD led researchers to
138 investigate the use of SSRIs in the autism core domain (West, 2009). In a randomized
139 placebo-control crossover study of 44 children with ASD, SSRI (fluoxetine) was found to
140 be beneficial in reducing repetitive behaviors in ASDs patients. The strength of evidence
141 for the effect of other SSRIs (e.g., citalopram and escitalopram) is insufficient
142 (McPheeters, Warren & Sathe, 2011). The evidence indicating that medication is effective
143 in treating similar symptoms common in both OCD and ASD.

144 – **ADHD:** Medications could be considered in the treatment of ADHD in the context of ASD
145 (Bramson, Ravan & Wright, 2005; Ji & Findling, 2015). Methylphenidate (Ritalin) is the
146 most commonly used drug and is effective in reducing symptoms of inattention and
147 hyperactivity in children with ASD, although response rates may be lower than for children
148 with typical ADHD. Randomized control trials suggest less benefit and more side effects
149 for ADHD plus ASD compared with ADHD alone (Research Units on Pediatric
150 Psychopharmacology Autism Network, 2005). Methylphenidate was found to significantly
151 improve joint attention and emotional self-regulation as well as improvement in
152 hyperactive and impulsive behaviors. However, the results on the efficacy of
153 amphetamines are less conclusive. Alpha-2 adrenergic agonists were also effective when
154 dealing with ADHD/ASD comorbidities and were found to significantly improve
155 behavioral symptoms in 62 children when compared with a placebo. Alternatively,
156 norepinephrine reuptake inhibitor (NERI) namely, atomoxetine was found in two
157 randomized controlled trials to improve ADHD symptoms.

158 – **Aggression:** Haloperidol, a typical neuroleptic, is commonly used to treat severe
159 aggression in autistic children however these have been found to significantly impair
160 movement in recipients (Miral et al., 2008). In addition risperidone was found to reduce
161 irritability, aggression, self-injurious behaviors, and severe tantrums in ASD (Huffman,
162 Sutcliffe, Tanner & Feldman, 2011; MCPheeters, Warren & Sathe, 2011; McVoy &
163 Findling, 2009) For younger ASD cases aged between 6 to 17 years, aripiprazole is

164 recommended to treat aggression and in a longitudinal study both risperidone and
165 aripiprazole were found to adequately treat aggression and irritability in ASD patients,
166 especially when combined with Parent Training in behavioral management (Arnold, Aman
167 & Li, 2012).

168

169 **Conclusions and future directions**

170 Psychological comorbidities are relatively recently recognized phenomena in ASD. Although, the
171 majority of ASD have at least one comorbid psychological disorder.

172 The high level of comorbidities could be attributed to similar or associated risk factors, i.e., the
173 occurrence of one disorder increases the risk of another disorder. In addition, limitations could
174 include misdiagnosis and inadequacy of the diagnostic systems to reflect the factual nature of
175 psychiatric disorders that co-occur with an ASD diagnosis.

176 These comorbid conditions persist from childhood to adolescence to adulthood and are
177 associated with more impaired social functioning (Chang, Quan, & Wood, 2012; Simonoff et al.,
178 2013).

179 The current understanding of the processes that contribute to the high rates of comorbidities in
180 ASD remains incomplete; furthermore, there has been nearly no research on interventions
181 involving comorbid presentations in ASD with other psychological and psychiatric disorders.

182 Thus, research studies in this field is highly needed that may provide important clues about the
183 underlying mechanisms, and potential risk and protective factors involved in ASD.

184 Targeting two comprehensive modules of processes likely involved in high rates of comorbidities
185 in ASD may be mainly useful. The first class is central developmental processes directly linked to
186 the etiology of ASD, while the second module includes wider, transdiagnostic risk processes. It is
187 possible that as developing social neural systems increasingly advance from 'normal' trajectories
188 in ASD children, other processes related to mental health may be affected as well.

189 In this vein, we can consider core processes such as social detachment and atypical social
190 information processing in the possible pathogenesis of comorbid conditions. As an actual
191 example, decreased hedonic responses to the social-emotional bids of others may be involved in
192 the development of oppositional problems or aggression.

193 The second class is transdiagnostic processes that are not necessarily causally linked to ASD core
194 impairments.

195 Rather, they are 'fundamental' in the sense that they are central to many forms of
196 psychopathology. There are many transdiagnostic processes, such as attentional avoidance,
197 persistent negative affect, and rumination. Poor emotion regulation, for example, is a

198 transdiagnostic process that has been linked theoretically to the high rates of anxiety disorders
199 seen in people with ASD (Mazefsky et al., 2013; White, Schry, Miyazaki, Ollendick, & Scahill,
200 2014). These processes occur over the course of development and thus it will be important for
201 future research to consider the longitudinal course of comorbidity and the possibility of
202 sequential comorbidities over the course of a lifetime (Rutter, Kim Cohen, & Maughan, 2006).

203

204 The early identification and treatment of the psychological comorbidities are useful for symptom
205 relief, quality of life and daily adaptive functioning.

206 However, it is also similarly important that comorbid conditions do not take clinical attention
207 away from core/primary ASD symptoms in need of intervention.

208

209 Previous studies on ASD and their comorbidities used different criteria and assessment tools
210 completed by different informants (e.g., parents, teachers, practitioners/clinicians or self-report),
211 resulting in different diagnoses and comorbidity results. Thus, further research and efforts should
212 concentrate on comprehensive standardized diagnostic methods and assessments for ASD and
213 psychiatric and psychological comorbidities. Furthermore, some ASD impairments overlap with
214 some of the features of comorbid disorders, making it difficult to differentiate between them. For
215 example, OCD diagnosis and ASD impairments have overlapping rituals in common. These
216 include repetitive behaviour and rigid adherence to routines. However, whilst OCD compulsions
217 are characterized by distress and anxiety, similar rituals of autistic patients are often a rewarding
218 and pleasant experience for the child and free of such anxiety and distress. Thus, assessment tools
219 should have the ability to distinguish clearly between pure ASD and ASD and its comorbidities.
220 In some cases, it may be difficult to extract information for self-reports from ASD patients (e.g.
221 self-report of feelings and how those feelings impact daily functioning) due to inherent
222 impairments in social interaction and verbal communication. This can result in a diagnosis being
223 missed and the patient not receiving helpful interventions.

224 Cognitive Behavioural Therapy (CBT) has been shown to be effective in treating ASD and some
225 of its comorbidities, however, research was limited. These limitations included small population
226 size, a lack of standardization in applying CBT, and the neglect of ASD comorbidities and/or

227 different outcomes for different comorbidities of ASD (e.g., improvement in some but not for
228 others). This highlights the importance of individualizing treatment plans for different co-morbid
229 diagnoses.

230 In conclusion, improved comprehensive assessment diagnostic tools taking into account various
231 comorbidities and how they relate to ASD are needed. Once accurate diagnoses have been made,
232 better individualized and comprehensive interventions should be constructed to yield optimum
233 outcomes for patients.

234

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