REVIEW PAPER

Comorbid Psychopathology in Autism Spectrum Disorder

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Abstract Matson and Nebel-Schwalm (Research in Developmental Disabilities 28(4) 341-352, 2007) conducted an overview of comorbid psychopathology with autism spectrum disorder (ASD) in children. The purpose of the current paper is to expand on Matson and Nebel-Schwalm (Research in Developmental Disabilities 28(4) 341-352, 2007) by discussing the relationship between comorbid psychopathology in ASD and other variables. The current paper will include research across the lifespan, from babies and toddlers to children, adolescents, and adults. Topics explored are the prevalence of comorbid psychological disorders, the importance of studying comorbid psychopathology, as well as the measures used to assess comorbid psychopathology in ASD. Research on the relationships between comorbid psychopathology in ASD and parental and sibling stress and well-being, developmental regression, language and communication, adaptive behavior, social skills, autism severity, challenging behavior, gastrointestinal symptoms, sleep problems, epilepsy, sensory issues, and quality of life is also discussed. Age-related variations in comorbid psychopathology are also examined. Finally, recommendations for treatment are given as well as areas where future research is needed.

Keywords Autism spectrum disorders · Comorbidity · Comorbid psychopathology · Treatment

This research was conducted by the first and second authors under the supervision of the third author.

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Introduction

Comorbid psychopathology is defined as the occurrence of two or more forms of psychopathology in the same person (Matson and Nebel-Schwalm 2007). Comorbid psychopathology includes mood disorders, anxiety disorders, conduct and oppositional defiant disorders, attention deficit/hyperactivity disorder (AD/HD), and other psychological disorders such as schizophrenia. Mood disorders include depression and bipolar disorder. Anxiety disorders include generalized anxiety disorder, phobias, panic disorder, obsessive compulsive disorder (OCD), posttraumatic stress disorder, and social anxiety disorder. While Matson and Nebel-Schwalm (2007) conducted a literature review on comorbid psychopathology with autism spectrum disorder in children, the current paper aims to expand on this. Comorbid psychopathology research discussed will include adolescents and adults as well as babies, toddlers, and children. The aim of this paper is to explore the relationship between comorbid psychopathology and other variables such as parental and sibling stress and well-being, developmental regression, language and communication, adaptive behavior, social skills, autism severity, challenging behavior, gastrointestinal symptoms, sleep problems, epilepsy, sensory issues, and quality of life.

Overview

Matson and Nebel-Schwalm (2007) conducted a thorough review on comorbid psychopathology in children with autism spectrum disorder (ASD). The authors discussed the different types of comorbid psychopathology, such as mood disorders, phobias, OCD, anxiety, obsessions, and psychosis. The review discussed the difficulties in diagnosing comorbid psychopathology due to the waxing and waning and change in symptoms and the wide range of the core symptoms of ASD.

The authors commented on the need for identification of comorbidity by multiple investigators and the need for development of scaling methods to assess comorbidity. They also discussed the need for differential diagnosis studies. Differential diagnosis studies would involve comparing groups who are diagnosed with specific psychological disorders to individuals with ASD, using the same assessment tools. That way, the similarities and differences between ASD and other psychiatric conditions may be determined. Determining which is the primary disorder and which is the secondary disorder is also an issue that needs to be addressed, for prioritizing intervention goals, determining required resources, and in terms of long-term prognosis (Matson and Nebel-Schwalm 2007).

Anxiety appears to be a common comorbid condition in individuals with ASD. MacNeil et al. (2009) conducted a comprehensive review on anxiety with children and adolescents with ASD. The authors discussed the assessment of anxiety disorders in children and adolescents with ASD using clinical interviews, anxiety rating scales, direct observation, and physiological measures. They recommended that assessment of anxiety is multimodal, with multiple informants, and uses appropriate instrumentation. The review also evaluated the literature on anxiety in children and adolescents with ASD. Their review concluded a number of key points. First, children and adolescents with ASD experience a high level of anxiety symptoms. Second, children and adolescents with anxiety show greater levels of anxiety than those in community populations. Third, anxiety levels appear to be comparable to clinically anxious populations. Fourth, children and adolescents with anxiety show higher levels than those with conduct disorders or individuals with language impairments. Finally, children with Asperger's syndrome and pervasive developmental disorder-not otherwise specified (PDD-NOS) may exhibit more anxiety symptoms than those with autistic disorder.

Matson and Goldin (2013) reported that the majority of research on comorbid psychopathology in ASD is on AD/HD, general psychopathology, and anxiety. Most of the studies only dealt with one comorbidity (199 studies out of a total of 261 studies). The authors commented on the need for research investigating the effects of multiple comorbid conditions and how they interact with one another.

Previous research has examined the prevalence and assessment of comorbid psychopathology, yet little research has been conducted examining the effect that comorbid psychopathology has on outcome variables. It is hypothesized that a diagnosis of a comorbid psychological disorder in ASD would have a knock on effect on an individual's overall outcome and level of functioning. An aim of the current paper is to explore the relationship between comorbid psychopathology and outcome variables, such as challenging behavior, adaptive behavior, language and communication, and quality of life.

Comorbid Psychopathology and ASD

Prevalence

Grondhuis and Aman (2012) commented that variations in assessment tools can produce differing prevalence rates of anxiety. When researchers and clinicians use different assessment tools to assess comorbid psychopathology symptoms and diagnose psychiatric disorders, there can be a wide range of prevalence found for different psychiatric disorders. Grondhuis and Aman (2012) discussed the research conducted by White et al. (2009) who found prevalence rates of anxiety ranging from 11 to 84 % in children with ASD in their literature review. Intellectual disability needs to be considered, as intellectual disability is a common comorbidity in ASD. Research has been conducted including those with ASD, but with and without intellectual disabilities. This allows us to determine whether it is the intellectual disability or ASD that is the bigger risk factor for comorbid psychopathology. Caamaño et al. (2013) investigated psychopathology in children and adolescents with ASD, but without intellectual disabilities. The researchers also compared those with ASD to control participants without ASD. Significant differences were found for the following between those with and without ASD: depressive disorder, anxiety separation disorder, agoraphobia and specific phobias, OCD, and AD/HD. There was a significant difference between those with ASD and those without in the prevalence of anxiety, where 76 % of those with ASD presented with anxiety symptoms compared to 36 % of the controls. It was found that 56 % of those in the ASD group had attention problems, while only 4 % of the control group presented with these problems. Irritability and anger and recurring thoughts of death were significantly more frequent in the ASD group than in those without ASD.

Hess et al. (2010) compared children and adolescents with ASD to typically developing children and adolescents. Inclusion criteria for the study were individuals with ASD but without intellectual disability. It was found that children and adolescents with ASD endorsed a higher number of psychiatric symptoms compared to same aged typically developing peers. The factors of worry/depressed, undereating, overeating, avoidant behavior, and repetitive behavior were significantly different between those with and without ASD. However, conduct behavior and tantrum behavior were not significantly different among those with and without ASD.

Helverschou and Martinsen (2011) investigated anxiety in adults with ASD and an intellectual disability (ID). Nearly 40 % of those with ASD and ID had anxiety symptoms. The researchers found that anxiety can be recognized in those with ASD and ID by similar symptoms to those without ASD and ID. However, signs of physiological arousal seem to be more difficult to recognize in individuals with ASD by informants.



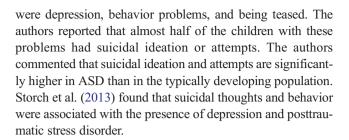
Gjevik et al. (2011) found that 72 % of children and adolescent with ASD were diagnosed with at least one comorbid disorder. Anxiety disorders were the most prevalent at 41 %, followed by AD/HD at 31 %. Tureck et al. (2013) compared children with ASD to those with anxiety disorders and to typically developing children. Children with ASD showed higher rates of comorbid symptoms than children with anxiety disorders. Those with ASD and those with anxiety disorders evinced higher rates of comorbid symptoms than typically developing children without additional diagnoses. The researchers found high rates of worry/depressed behavior and avoidant behavior, which would support the high prevalence of anxiety disorders in children with ASD. Children with anxiety disorders had higher rates of tantrum behaviors, repetitive behaviors, worry/depressed behaviors, and avoidant behaviors than control participants.

Amr et al. (2012) found that 63 % of children with ASD were diagnosed with at least one comorbid disorder, with the most prevalent being anxiety disorders at 58.3 %. This was followed by AD/HD at 31.6 %, conduct disorders at 23.3 %, and major depressive disorder at 13.3 %. Of all the anxiety disorders, obsessive compulsive disorder was the most prevalent with 55 % of those with an anxiety disorder presenting with it. Wakabayshi et al. (2012) investigated whether the traits of autism spectrum overlapped with schizophrenia or OCD in the typically developing young adults. Their results suggested that there is a relationship between the autism spectrum and some schizophrenic traits such as "excessive social anxiety" and "no close friends." The study also found similarity between autism spectrum and obsessive compulsive traits, in particular "impaired control of mental activities."

Importance of Studying Comorbid Psychopathology

Storch et al. (2012) reported that peer victimization may be associated with anxiety and depressive symptoms and loneliness in children with ASD and comorbid anxiety. They reported that total levels of peer victimization were strongly related to symptoms of panic and moderately related to symptoms of depression. Adams et al. (2013) found that adolescent reports of peer victimization were associated with internalizing symptoms. The authors also found that parental report of peer victimization was not associated with internalizing symptoms. Adams et al. (2013) commented that the experience of peer victimization may help to explain the high rates of internalizing behaviors in adolescents with ASD. Rosbrook and Whittingham (2010) found social problem-solving ability and past teasing experiences to be significant mediators between traits of autism and anxiety symptoms. The authors commented on the need for interventions focused on improving problem-solving skills and reducing bullying experiences.

Mayes et al. (2013) found that the comorbid psychological disorders that highly predicted suicidal ideation or attempts



Assessment

In 1996, Tsai (1996) commented on the lack of a reliable and valid alternative diagnostic instrument to be applied to those with ASD who are lower functioning or nonverbal. Since then, there have been large advances in the field of comorbid psychopathology, but a lot more needs to be done in terms of assessment. While a variety of measures exist to assess comorbid psychopathology in the general population, it is important that when conducting research in individuals with ASD, the assessment tools used have been designed and validated for use with ASD. Grondhuis and Aman (2012) conducted a comprehensive literature review on anxiety assessment measures. The authors discussed the overlap of symptoms of ASD and anxiety and how communication and cognitive deficits can restrict the assessment of anxiety symptoms. The same is true with many psychiatric disorders; when an individual cannot communicate and describe their covert thoughts and feelings, it may be difficult to receive a diagnosis of a comorbid psychiatric condition.

In support, Helverschou et al. (2011) discussed how communication difficulties in ASD may mean that individuals with communication difficulties may be less likely to receive a diagnosis of depression. The authors commented that "while verbally intact patients may be reliably diagnosed with a comorbid mood condition, clinicians may be reluctant to diagnose mood disorders in individuals with greater communication impairment" (p. 64). The authors discussed how due to the challenges in assessing mood disorders in individuals with ASD, "treatment may be delayed for years despite frequent medical evaluations and visits" (p. 64). Therefore, both researchers and clinicians need to determine what the most effective way of assessing a comorbid psychiatric condition is if an individual cannot self-report their symptoms due to communication difficulties. Gronhuis and Aman (2012) commented that anxiety could be assessed using physical measures, such as heart rate, skin conductance, muscle tension, or brain activation. This is an area where future research is needed, as physiological measures can tell us a lot about anxiety and other comorbid conditions through the use of objective measurement.

In their review of anxiety assessment measure, Grondhuis and Aman (2012) discussed various assessment measures that can be used in individuals with ASD to assess anxiety



symptoms. The researchers included a combination of self-report and caregiver-report measures. Three of the 10 anxiety assessments were empirically derived and validated for children and adolescents with ASD. These included The Baby and Infant Screen for Children with aUtIsm Traits (BISCUIT), Part II (Matson et al. 2007), the Autism Spectrum Disorders Comorbidity-Child Version (ASD-CC) (Matson and González 2007), and Autism Comorbidity Interview-Present and Lifetime Version (ACI-PL) (Leyfer et al. 2006). Of the 10 assessment tools discussed, Grondhuis and Aman (2012) could "not conclude yet that any of these instruments does an adequate job of assessing anxiety in youth with ASDs" (p. 1362).

The assessment tools designed and validated for children and adolescents with ASD will now be discussed. These tools aim to discriminate between the core symptoms of ASD and comorbid psychopathology symptoms. The BISCUIT, Part II (Matson et al. 2007) is a comorbid psychopathology measure for infants aged 17 to 37 months. It consists of 57 items. Five subscales have been identified for the BISCUIT, Part 2 (Matson et al. 2011). These are avoidance behavior, eating/sleeping problems, tantrum/conduct behavior, anxiety/repetitive behavior, and inattention/impulsivity. Matson et al. (2009b) established cutoffs for the subscales, ranging from no/minimal impairment to moderate impairment and severe impairment. Matson et al. (2009c) reported that the BISCUIT, Part II has an internal consistency coefficient of 0.96.

Matson and Tureck (2012) conducted a review on the current status of the BISCUIT (parts 1, 2, and 3). The authors commented that the psychometric properties of the BISCUIT have been well established. The authors commented on how comorbid conditions are present at a very young age. This highlights the importance of assessing comorbid psychopathology at as young an age as possible, in order to implement early intervention and treatment. Matson and Tureck (2012) also commented on how little information there is on psychopathology in very young children, but that the BISCUIT has provided useful insights in this young age group.

Tools have been validated for use with children also. The ASD-CC (Matson and González 2007) is an assessment of comorbid psychopathology measure for children and adolescents aged 2 to 18 years, and it consists of 39 items. Moderate test–retest reliability (k=0.51) and inter-rater reliability (k=0.46) have been observed (Matson and Dempsey 2008). Internal reliability has been shown to be very good (α =0.91) (Matson and Wilkins 2008). Thorson and Matson (2012) established cutoff scores for each of the subscales, ranging from no/minimal impairment, moderate impairment, and severe impairment.

The ACI-PL (Leyfer et al. 2006) is a modified instrument, derived from The Kiddie Schedule for Affective Disorders and Schizophrenia (Chambers et al 1985). The tool is a semistructured interview and is administered to informants

by trained professionals. The researchers examined reliability and validity for the modified scale. Underwood et al. (2011) summarized the psychometric qualities of the ACI-PL. Interrater reliability (*k*) ranged from 0.7 to 0.8. Test–retest reliability ranged from 0.61 to 0.75. Sensitivity was 100 %, and the range of specificity across different diagnoses was 83–94 %. Mazefsky et al. (2011) found that results of self-report measures in adolescents with high functioning autism did not correspond to parental report using the ACI-PL. The authors recommended that caution should be exercised in the interpretation of self-report measures.

Measures designed for individuals with ASD are available across the lifespan. Measures are available to assess comorbid psychopathology in adults with ASD also. The Autism Spectrum Disorders-Comorbidity for Adults (Matson et al. 2006) consists of 37 items, including 5 subscales: anxiety/repetitive behaviors, conduct problems, irritability/behavioral excesses, attention/hyperactivity/impulsivity, and depressive symptoms. Inter-rater reliability ranged from 0.30 to 0.77, with an average kappa for all the items of 0.43, and test-retest reliability was an overall average kappa of 0.59 (Matson and Boisjoli 2008). Matson and Boisjoli (2008) found overall internal consistency to be 0.91.

The Psychopathology in Autism Checklist (PAC) (Helverschou et al. 2009) is another measure of comorbid psychopathology for adults with ASD. It consists of 42 items and includes 5 subscales. The subscales are as follows: psychosis, depression, anxiety disorders, OCD, and general adjustment problems. Results from the pilot study (Helverschou et al. 2009) indicated acceptable psychometric properties. Internal consistency was acceptable for all subscales, including psychosis (α =0.89), depression (α =0.85), anxiety disorder (α =0.78), OCD (α =0.88), and general adjustment problems (α =0.88). Inter-rater agreement was computed by Cohen's kappa and was as follows: psychosis (k=0.51), depression (k=0.67), anxiety disorder (k=0.58), OCD (k=0.53), and general adjustment problems (k=0.66). The PAC was found to discriminate between adults with autism and ID, with and without psychiatric disorders. It was also found to partially discriminate between individuals diagnosed with different psychiatric disorders, especially psychosis and OCD.

Relationships Between Comorbid Psychopathology in ASD and Other Variables

Parental and Sibling Stress and Well-being

Comorbid psychopathology in children with ASD can have an impact on caregiver well-being. Meltzer (2011) found that mothers who reported more child behavior problems also reported more depressive symptoms for themselves. Also, fathers who reported more child behavior problems also



reported more depressive symptoms. Parents of children with ASD and comorbid symptoms are not the only ones affected with psychological symptoms. Shivers et al. (2013) investigated sibling well-being. Parental history of anxiety and sibling (with ASD) behavior problems predicted sibling anxiety.

Developmental Regression

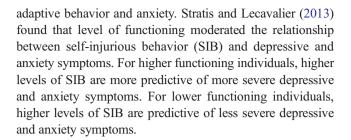
Rosenberg et al. (2011) examined parent report of community psychiatric comorbid diagnoses in children with ASD. The research found that lack of autistic regression was associated with increased risk of psychiatric comorbidity. Therefore, those who had not regressed had an increased risk of having a comorbid psychiatric diagnosis. For children who regressed, this regression was associated with a lower risk of any comorbidity, any mood disorder, and AD/HD or attention deficit disorder. The relationship between regression and comorbid psychopathology is one that needs to be further explored in research.

Language and Communication

Grondhuis and Aman (2012) commented on how language and cognitive functioning impact the prevalence of anxiety disorders in ASD. The authors commented that while those with better language skills and greater cognitive functioning are reported has having more anxiety symptoms, there are other factors to consider. First, lower functioning children may not have the insight to understand or express emotions that they are feeling. Second, children themselves may be poor raters of their symptoms. Finally, lack of communication may be a barrier to parental reports of symptoms. Blakeley-Smith et al. (2012) compared children and parent agreement of anxiety. Moderate to strong agreement was found on several domains. More advanced verbal ability was associated with better agreement on separation, school avoidance, and total anxiety. It was also found that higher metacognitive skills were associated with better agreement on social anxiety. Gjevik et al. (2011) found no association between comorbid psychiatric disorder and intellectual level or receptive language ability. Witner and Lecavalier (2010) found that nonverbal children with ASD were more likely to show symptoms of oppositional defiant disorder (ODD).

Adaptive Behavior

Rieske et al. (2013) found that adaptive developmental quotient was significantly related to total anxiety scores in babies and infants. However, adaptive developmental quotient only accounted for 8 % of the variance in total anxiety scores. Surprisingly, it was found that as adaptive behaviors increased, anxiety also increased. The authors commented on the importance of future research on the relationship between



Social Skills

Chang et al. (2012) found that a greater severity of social anxiety disorder was associated with a higher level of social functioning deficits in children with ASD. Higher levels of social anxiety disorder predicted lower assertive and responsible social skills. Mayes et al. (2011b) found that anxiety and depression were highly correlated with social problems in children with ASD. Pouw et al. (2013) investigated emotion regulation, social functioning, and depression in boys with ASD. Poor social functioning was found to be associated with more symptoms of depression. Waters and Healy (2012) found that comorbid psychopathology had a negative impact on social skills in children and adolescents with ASD and self-injurious behavior.

Kanai et al. (2011) found that with adults with Asperger's syndrome had higher total scores of social anxiety and also had higher scores on the subscales of "fear of anxiety" and avoidance. Matson et al. (2009a) found that psychopathology symptoms, in particular impulse and mania, were associated with negative social behaviors and positive verbal and nonverbal social skills in adults with ASD and intellectual disability. Rosbrook and Whittingham (2010) found that social problem-solving ability was a significant mediator in the relationships between autistic traits and anxiety and depressive symptoms of adults in the general population. However, social competence was not a significant mediator in the relationship between autistic traits and depressive symptoms. Hillier et al. (2011) investigated the effectiveness of a social skills and vocational training program in young adults with ASD. It was found that participating in the intervention significantly reduced feelings of depression and anxiety in the adolescents and young adults with ASD. Though it did not reach significance, peer relationships also improved after intervention.

Autism Severity

Rieske et al. (2013) investigated the effect of autism symptomatology on anxiety symptoms in infants and toddlers. Autism symptomatology accounted for over 50 % of the variance in total anxiety scores. Autism symptomatology also moderated the relationship between cognitive developmental quotient and adaptive developmental quotient with anxiety.



While autism symptomatology was found to be a statistically significant moderator, the authors commented that it does not have a clinically significant moderating effect on the relationship between cognitive and adaptive abilities with anxiety. Mayes et al. (2011b) found that anxiety and depression increased with autism severity. Increasing autism severity was found to be the single best predictor of anxiety and depression.

Mayes et al. (2011a) reported that more children with high functioning autism had symptoms of anxiety, depression, and irritability than children with low functioning autism. It was found that 54 % of children with high functioning autism and 42 % with low functioning autism had depressive symptoms. It was reported that 79 % of those with high functioning autism and 67 % of those with low functioning autism presented with anxiety, and 88 % of those with high functioning autism had symptoms of irritability, while 84 % of those with low functioning autism presented with irritability symptoms. The following symptoms were exhibited more in children with low functioning autism than high functioning autism: crying, self-harm, clingy, and explosive. In their review of depression in autism, Ghaziuddin et al. (2002) commented on the differences in symptoms of depression between those with high functioning autism and low functioning autism.

Rosenberg et al. (2011) found that diagnoses of PDD-NOS and Asperger's syndrome (AS) were associated with increased prevalence of any and every type of psychiatric disorder, when compared to autistic disorder. The researchers commented that this may be because those with PDD-NOS and AS may present with more typical symptoms of disorders which may be more readily recognized. Mattila et al. (2010) investigated psychiatric comorbidity in children and adolescents with AS and high functioning autism. It was found that 74 % of participants presented with a current psychiatric disorder. Those who had ODD, major depressive disorder, and anxiety disorders indicated significantly lower levels of functioning.

Ketelaars et al. (2008) examined comorbid psychopathology in adults with mild ASD compared to adults not diagnosed with ASD. Very little differences were found between those with ASD and those without, and psychiatric disorders seemed to be equally prevalent within the two groups. Strang et al. (2012) did not find that increased IQ or fewer autism symptoms were related to more emotional symptoms in children with ASD. The researchers did not find higher IQ or fewer autism symptoms in those with depression or anxiety symptoms. The authors reported an increased risk of depression and anxiety symptoms in children and adolescents with ASD and no intellectual disability, regardless of age, IQ, or autism symptoms.

Challenging Behavior

Mayes et al. (2011b) found small correlations between anxiety and depression and behavior problems. They found the relationship to be weak between anxiety and depression and externalizing problems. Pugliese et al. (2013) compared children with high functioning ASD to children with social anxiety disorder (SAD) and to children with ODD/conduct disorder (CD). Children with high functioning ASD had similar levels of fears of humiliation and rejection to those with SAD. They also exhibited similar levels of aggression to those with ODD/CD. The relationship between fears of humiliation and rejection and aggression was explored. Those with high functioning ASD and high or low levels of fears of humiliation and rejection exhibited the highest levels of aggression. Those with moderate levels of anxiety exhibited the lowest aggression. The authors commented that managing social anxiety at a moderate level may reduce aggressive behavior in children with high functioning ASD. For those who had lower levels of social anxiety and low levels of social awareness, the authors commented on the need for treatment to increase social awareness and motivation for peer relationships. Waters and Healy found that frequency and severity of self-injurious behavior and comorbid psychopathology combined had a negative impact on social skills in children and adolescents with ASD.

Stratis and Lecavalier (2013) investigated the relationship between repetitive behavior and psychiatric symptoms in children and adolescents with ASD. Anxiety symptoms were positively associated with the presence of ritualistic and sameness behavior. ADHD symptoms were positively associated with stereotypic behavior. Restricted interests were a negative predictor of depression. Therefore, the researchers suggested that restrictive interests may be a protective factor in the development of depression in those with ASD. Ritualistic and sameness behavior is predictive of anxiety, depression, and ODD.

Rodgers et al. (2012) found that children with ASD and high anxiety had more repetitive behaviors than those without anxiety. Higher levels of insistence on sameness/circumcised interests were associated with higher levels of anxiety in the anxiety group. However, in the non-anxious group, anxiety was associated with sensory motor repetitive behaviors. Zandt et al. (2007) compared children with ASD to children with OCD. Children with OCD showed more compulsions and obsessions than children with ASD, while the type of compulsions and obsessions tended to be less sophisticated in children with ASD than those with OCD.

Gastrointestinal Symptoms

In typically developing children, Shelby et al. (2013) found that functional abdominal pain (FAP) in childhood was associated with high risk of anxiety disorders in adolescence and young adulthood. During follow-up in adolescence and young adulthood, 51 % of those with a childhood history of FAP met criteria for an anxiety disorder during their lifetime and 30 % currently met criteria for an anxiety disorder. Lifetime risk of



depressive disorder was significantly higher in those with FAP than control participants.

Mazurek et al. (2013) found that children with ASD which presented with each type of gastrointestinal symptom had significantly higher rates of anxiety. The following gastrointestinal symptoms were included: chronic constipation, chronic diarrhea, chronic abdominal pain, chronic bloating, and chronic nausea. A relationship was found between the number of gastrointestinal symptoms and anxiety also. Those with no chronic gastrointestinal problems had significantly lower anxiety scores than those with only one gastrointestinal problem, those with two problems, or those with three or more problems.

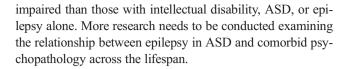
In their review of gastrointestinal symptoms in ASD, Mannion and Leader (2014a) discussed the relationship between comorbid psychopathology and gastrointestinal symptoms. In their analysis of predictors of comorbid psychopathology, Mannion and Leader (2013) found that gastrointestinal symptoms predicted comorbid psychopathology in children with ASD. Nausea, abdominal pain, and constipation individually predicted conduct behavior. Nausea also predicted worry/depressed behavior and avoidant behavior. Diarrhea predicted tantrum behavior.

Sleep Problems

Research is needed on the relationship between comorbid psychopathology and sleep problems in ASD. If a link is established between comorbid psychopathology and sleep problems, this has implications for treatment outcomes. The treatment of comorbid psychopathology may have an impact on sleep problems. Alternatively, the treatment of sleep problems may mean a reduction in comorbid psychopathology symptoms. This is an area where much more research is needed. Mayes et al. (2011b) found small correlations between anxiety and depression and sleep disturbance. The authors reported that it does not appear that sleep problems are further exacerbated by symptoms of anxiety and depression. Mannion et al. (2013) found that avoidant behavior and under-eating predicted sleep problems. In their review of sleep problems in ASD, Mannion and Leader (2014b) discuss the relationship between sleep problems and comorbid psychopathology.

Epilepsy

There is little research examining the relationship between comorbid psychopathology and epilepsy in ASD. Smith and Matson (2010) divided adults into groups of four, including (1) intellectual disability, (2) ASD, (3) epilepsy, and (4) combined ASD and epilepsy. They were compared in their endorsement of symptoms of comorbid psychopathology. Those with comorbid epilepsy and ASD were significantly more



Sensory Issues

Mazurek et al. (2013) examined the relationship between sensory over-reactivity and anxiety in children with ASD. Mazurek et al. (2013) found that sensory over-responsivity and anxiety were highly associated. The researchers found that there were higher levels of anxiety among children who have greater levels of reactivity to various sensory stimuli. Both anxiety and sensory over-responsivity significantly predicted gastrointestinal symptoms. The authors concluded that anxiety, sensory over-responsivity, and gastrointestinal problems are possibly interrelated phenomenon for children with ASD.

Quality of Life

Kuhlthau et al. (2010) found that health-related quality of life was related to internalizing and externalizing problems in children with ASD. There were stronger correlations found between quality of life and internalizing behaviors. García-Villamisar et al. (2013) investigated the quality of life in adults with ASD and intellectual disability. The presence of symptoms of ASD and behavior problems is related to lower ratings of quality of life. The authors commented on the need to explore comorbid psychopathology as a potential mediating variable contributing to the relationship between challenging behaviors and autism symptoms in future research. The authors also commented on the need for future research to focus on designing programs that enhance quality of life and the importance of evaluating the effects of such programs on internalizing and externalizing behaviors and ASD psychopathology.

Age-Related Variations in Comorbid Psychopathology

Fodstad et al. (2010) found that there was an increasing trend of comorbid behaviors as age increased in toddlers with ASD. Mayes et al. (2011b) found that levels of depression and anxiety increased with increasing age. The researchers found that 88 % of adolescents with low functioning autism and 89 % of adolescents with high functioning autism had anxiety. It was also found that 58 % of adolescents with low functioning autism and 72 % of adolescents with high functioning autism had depression. Vasa et al. (2013) found that the percentage of children with clinical anxiety increased with age. The authors reported that over 40 % of adolescents experienced clinical anxiety. In contrast, Strang et al. (2012) found that emotional difficulties did not increase with age.



Davis et al. (2011) found that anxiety rises from toddlerhood to childhood, decreases from childhood to young adulthood, and again increases from young adulthood into older adulthood.

Recommendations for Treatment

In their review of depression in autism, Ghaziuddin et al. (2002) discussed the suitable forms of treatment for individuals with ASD and depression. The authors also commented on the need to examine the efficacy of treatment, such as medication and psychotherapy. The authors also commented on the improvement in quality of life that can be provided by treatment for both the individual with ASD and for those around them. Hillier et al. (2011) implemented social and vocational skills training to decrease depression and anxiety among young adults. More research is needed on similar interventions to treat comorbid psychopathology symptoms, including anxiety and depression and expanding to other psychological disorders.

Medication

Coury et al. (2012) examined the rates of psychotropic medication use in children and adolescents with ASD. It was reported that 80 % of those with a diagnosis of AD/HD, bipolar disorder, OCD, depression, or anxiety were on more than one psychotropic medication. Only 15 % of children with no comorbid psychiatric disorder were taking psychotropic medication. The researchers found strong relationships between medication use and parent reports of other psychiatric conditions.

Tsakanikos et al. (2011) compared gender differences in comorbid psychopathology and clinical management in adults with ASD. While personality disorder and schizophrenia were more common among males and dementia was more common among females, there were also differences in clinical management. Males were more likely to be prescribed a combination of medications, while females were more likely to receive sedation. It was reported that 60 % of participants had no diagnosable psychiatric disorder. The authors commented that females may be more likely to receive sedation due to behavior problems.

Cognitive-Behavioral Therapy

Moree and Davis (2010) conducted a thorough literature review on cognitive-behavioral therapy (CBT) for anxiety in children with ASD. The review included general recommendations for using CBT with children with ASD and also included four modification trends where CBT is modified for use with children with ASD. First, disorder-specific

hierarchies are important to consider. This can be done by not only focusing on the comorbid disorder but also by creating a broad hierarchy that includes disorder-specific problems too, such as social skills training, communication training, and reduction of challenging behavior. Second, concrete visual tactics can be used. Third, child-specific interests can be included. Finally, parent involvement can be combined to promote generalization.

Future Research

Tsai (1996) commented on the need for a great deal of work to be done. It was suggested that future research should employ a randomized double-blind placebo-controlled crossover design, as well as using multicenters and uniformed diagnostic criteria to study adolescents and adults with ASD. There is still a great deal of research that needs to be done in the future, despite it being over 17 years since Tsai's article was written.

MacNeil et al. (2009) recommended five key avenues for future research examining anxiety in children and adolescents with ASD. First, research should distinguish comorbid anxiety from the core symptoms and ASD. The prevalence of anxiety in low functioning youths should be examined. Second, developmental issues should be examined. Research should examine age-related differences in onset; course and symptom presentation should be conducted. Third, new instruments to measure anxiety in ASD are needed. These should be validated on ASD samples. Fourth, physiological assessments of anxiety should be made. Fifth, more research is needed comparing those with ASD to other clinical groups.

Research needs to be conducted on comorbid psychopathology across the lifespan. Longitudinal studies are needed to understand how comorbid psychopathology changes over time. Vasa et al. (2013) commented on the high cost of conducting longitudinal studies and recommended that it may be more realistic to examine anxiety across transitional periods, such as preschool to school age and school age to adolescence. Ghaziuddin et al. (2002) commented on the need to examine the impact of depression on long-term outcomes in individuals with ASD. The authors also commented on the need to conduct research in individuals who have marked communication deficits.

Ghaziuddin et al. (2002) commented on how other medical disorders may contribute to depression. Hollway et al. (2013) commented on how anxiety and depression need to be better understood in terms of their relationship to sleep disturbance. Research is needed to investigate the relationship between comorbid psychopathology and other comorbidities such as sleep problems and gastrointestinal symptoms.



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