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Comorbidity in autism spectrum disorder: A literature review.

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Abstract

Comorbidity is defined as the co-occurrence of two or more disorders in the same person (Matson & Nebel-Schwalm, 2007). The current study provides a review of the literature on comorbidity, in relation to comorbid psychiatric and medical disorders in babies and infants, children, adults and across the lifespan. We also examine comorbid conditions such as attention deficit/hyperactivity disorder (AD/HD), epilepsy, gastrointestinal symptoms, sleep problems, feeding problems and toileting problems in individuals with autism spectrum disorder.

Keywords: Comorbidity, Autism Spectrum Disorder, Attention deficit/hyperactivity disorder (AD/HD), Epilepsy, Sleep problems, Gastrointestinal symptoms.

Comorbidity in autism spectrum disorder

Comorbidity is defined as the co-occurrence of two or more disorders in the same person (Matson & Nebel-Schwalm, 2007). A comorbid condition is a second order diagnosis which offers core symptoms that differ from the first disorder. Comorbidity in the assessment of autism spectrum disorder (ASD) is a topic that has infrequently been addressed (Matson & Nebel-Schwalm, 2007). One of the main difficulties in diagnosing comorbid psychopathology is the lack of diagnostic instruments designed to screen for these disorders in individuals with ASD. Instruments are only recently being developed, piloted and tested for reliability and validity. Instruments designed for assessing comorbid psychopathology in adults with ASD include the Psychopathology in Autism Checklist (PAC) (Hellerschou, Bakken & Martinsen, 2009) and the Autism Spectrum Disorders-Comorbidity for Adults (ASD-CA) (Matson, Terlonge & González, 2006).

Instruments designed to screen for comorbid psychopathology in children are a more recent development than the instruments designed for adults. Comorbid disorders often are more difficult to diagnose at a younger age. The Baby and Infant Screen for Children with aUtism Traits (BISCUIT), Part II (Matson, Boisjoli & Wilkins, 2007) was developed to screen for comorbid psychopathology in infants aged 16-37 months and has been psychometrically validated (Matson, Fodstad, Mahan & Sevin, 2009). The Autism Spectrum Disorders Comorbidity-Child Version (ASD-CC) (Matson & González, 2007) is another instrument used to diagnose comorbid psychopathology in children. Leyfer, Folstein, Bacalman, Davis, Dinh, Morgan et al., (2006) modified the existing instrument The Kiddie Schedule for Affective Disorders and Schizophrenia for use with children and adolescents with ASD. The modified instrument, the Autism Comorbidity Interview-Present and Lifetime Version (ACI-PL) was used to research prevalence rates of specific disorders.

Comorbid psychiatric and medical conditions

Babies and infants

While there is now a great emphasis on the early diagnosis of ASD and the provision of early intensive behavioral intervention programs, there is a lack of research regarding comorbid conditions in very young children. The Baby and Infant Screen for Children with aUtism Traits (BISCUIT), Part II (Matson et al., 2007) is an instrument developed to screen for comorbid psychopathology, and has been used in all of the following studies. Fodstad, Rojahn and Matson (2010) divided participants into the ASD group and atypically developing group. They then divided participants by age groups into 12-18 months, 19-24 months, 25-31 months and 32-39 months. The authors found that those with ASD had more severe comorbid symptoms than atypically developing toddlers. Younger children had fewer problems, and there was an increasing trend as the older age groups displayed the most severe problems across all classes of behaviors.

Kozlowski, Matson, Belva and Rieske (2012) compared feeding and sleeping issues using items on the BISCUIT Part II, in children with Autistic disorder, Pervasive Developmental Disorder-Not otherwise specified (PDD-NOS) and atypically developing children without an ASD. Children with Autistic disorder presented with significantly more feeding and sleeping problems than children with PDD-NOS or atypically developing children. Those with PDD-NOS presented with more feeding and sleeping issues than atypically developing children. When developmental functioning is controlled for, there was a difference between groups in terms of feeding and sleeping issues.

Infants with autistic disorder had higher avoidance and anxiety scores than infants with PDD-NOS or atypically developing infants (Davis, Fodstad, Jenkins, Hess, Moree, Dempsey et al., 2010). Davis, Moree, Dempsey, Hess, Jenkins, Fodstad and Matson (2012) found that as communication scores increased, so did anxiety scores in children with autistic disorder. The authors discussed the importance communication plays in terms of anxiety.

Infants and toddlers with ASD need to understand from others what they should be anxious of, and through this lack of understanding, they may be likely to be overly anxious. The authors also commented on the likelihood that children with lower communication ability may be unable to accurately communicate any anxiety experienced, thus appearing that they experience lower levels of anxiety overall. Additionally, females were found to have significantly higher communication scores.

Matson and Tureck (2012) conducted a literature review about the current status of BISCUIT-Parts 1, 2 and 3. While Part 2 is used to determine comorbid psychopathology, Part 1 is used as a diagnostic tool for ASD, and Part 3 is a measure of challenging behavior. The article gives an overview of all the research conducted using the BISCUIT as well as research that is currently underway, such as a 15 nation study using the BISCUIT.

---Insert Table 1 about here---

Children

Investigation of co-occurrences of medical and psychiatric conditions, such as sleep disorders, epilepsy, food intolerance, gastrointestinal dysfunction, mood disorder, aggressive and self-injurious behaviors were examined in a study (Ming, Brimacombe, Chaaban, Zimmerman-Bier & Wagner, 2008). Sleep disorders were found to be associated with gastrointestinal dysfunction and with mood disorders (Ming et al., 2008). No association was found between epilepsy and any of the co-occurring conditions. Individuals with a pervasive developmental disorder (PDD) diagnosis were more likely to have a medical disorder, while participants with Asperger syndrome were more likely to have psychiatric comorbidities (Ming et al., 2008).

Hess, Matson and Dixon (2010) used the Autism Spectrum Disorder Comorbidity-Child Version (ASD-CC) (Matson & González, 2007) to compare symptoms in children and

adolescents with and without autism spectrum disorder. Differences lay between children and adolescents with autism spectrum disorder and typically developing children in symptoms of worry/depressed behavior, under-eating, avoidant behavior and repetitive behavior. There was no significant difference between the two groups in conduct and tantrum behaviors. Matson, Fodstad & Dempsey (2009) used the under and over eating subscale of the ASD-CC to investigate feeding difficulties among four groups; autism, pervasive developmental disorder-not otherwise specified (PDD-NOS), atypically developing children and typically developing children. Individuals with autism and PDD-NOS had higher rates of feeding difficulties than typically or atypically developing children.

Davis, Moree, Dempsey, Reuther, Fodstad, Hess et al. (2011) compared anxiety symptoms and communication scores among children with autistic disorder (AD), Pervasive Developmental Disorder-Not Otherwise Specified (PDD-NOS) and those with no diagnosis. Anxiety decreased as communication deficits increased for those with AD compared to those with PDD-NOS or no diagnosis. In contrast, anxiety increased as communication deficits increased, compared to those with no diagnosis. The authors interpreted the findings of lower anxiety scores as communication deficits increased in AD in two ways. Firstly, those with AS may reflect a severe presentation overall across areas of functioning and a decreased ability to be anxious. Secondly, increased communication deficits may impair children from being able to express symptoms of anxiety, as they are currently defined in the ASD-CC.

Mannion, Leader and Healy (2013) also used the ASD-CC to investigate comorbid psychopathology in children and adolescents with ASD. The mean ASD-CC subscale scores were all no/minimal impairment. Mannion et al. (2013) found that 46.1% of children and adolescents had a comorbid disorder. When intellectual disability was included, this number rose to 78.7%. It was found that 15.7% of individuals presented with an anxiety disorder.

The ASD-CC subscales of avoidant behavior and under-eating were found to be significant predictors of sleep problems in those with ASD.

Joshi, Petty, Wozniak, Henin, Fried, Galdo et al. (2010) used the Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS-E) (Orvaschel, 1994; Orvaschel and Puig-Antch, 1987). Compared to an age-matched and sex-matched control group, youth with ASD suffered from a significantly higher number of comorbid conditions than youth without ASD. Ninety five percent of those with ASD had three or more comorbid psychiatric diagnoses, while 74% had five or more comorbid disorders. Those with ASD had more anxiety disorders, including specific phobia and agoraphobia, than controls. Those without ASD were more likely to have substance use disorders than those with ASD. Leyfer et al., (2006) modified the K-SADS-E to create the Autism Comorbidity Interview-Present and Lifetime Version (ACI-PL).

Leyfer et al., (2006) found specific phobia to be the most common comorbid diagnosis among children with ASD, followed by obsessive compulsive disorder (OCD). While 37% of children with autism had a diagnosis of OCD in Leyfer et al.'s study, only 8% of children had a diagnosis in Simonoff, Pickles, Charman, Chandler, Loucas and Baird's (2008) study. Simonoff et al. (2008) used the Child and Adolescent Psychiatric Assessment, and found social anxiety disorder to be the most common, followed by attention deficit/hyperactivity disorder (AD/HD), and oppositional defiant disorder (ODD). They also found that 70% of children had at least one comorbid disorder and 41% had two or more. The presence of epilepsy was a risk factor for a psychiatric disorder.

Strang, Kenworthy, Daniolos, Case, Wills, Martin et al. (2012) used the Child Behavior Checklist to examine anxiety and depression symptoms in children with ASD. Fifty-six percent of individuals were in the clinical range of anxiety symptoms, while 24%

were in the borderline range for depression. In contrast to previous research, higher IQ or fewer ASD symptoms did not predict anxiety and depression symptoms in ASD. In support, Amr, Raddad, El-Mehesh, Bakr, Sallam and Amin (2012) found that children with comorbid psychiatric disorders had significantly lower IQ than those without comorbid psychiatric disorders. Sixty-three percent of children were diagnosed with at least one comorbid psychiatric disorder, which is supported by previous literature (Simonoff et al., 2008).

---Insert Table 2. about here---

Adults

While a number of studies have used structured clinical interviews to diagnose psychiatric disorders in adults with ASD (Lugnegard, Unenge Hallerback & Gillberg, 2011; McCarthy, Hemmings, Kravariti, Dworynksi, Holt, Bouras et al., 2010; Hofvander, Delorme, Chaste, Nydén, Wentz, Ståhlberg et al., 2009), others used measures especially designed for ASD (e.g. the Psychopathology in Autism Checklist, PAC; Helverschou et al., 2009; Autism Spectrum Disorders-Comorbidity for Adults, ASD-CA; Matson et al., 2006), and intellectual disability (e.g. Diagnostic Assessment for the Severely Handicapped-revised, DASH-II; Matson, 1995a).

The Autism Spectrum Disorders-Comorbidity for Adults (ASD-CA) (Matson et al., 2006) is a 37 item scale, which includes five subscales: Anxiety/repetitive behaviors; Conduct problems; Irritability/ Behavioral excesses; Attention/Hyperactivity/Impulsivity and Depressive symptoms. The scale's reliability was established by Matson & Boisjoli (2008). LoVullo & Matson (2009) developed cut-off scores for the subscales of the ASD-CA. They compared the frequency of symptoms across three groups; individuals with intellectual disability (ID), individuals with ID and ASD, and individuals with ID, ASD and additional psychopathology.

The ID and ASD group scored significantly higher than the ID group on most subscales, except for conduct problems. It was suspected that individuals with ID, ASD and additional psychopathology would score highest, however this was not the case. The authors suggested that this may be due to the differences between the groups in terms of usage of psychotropic medication. Over 71% of the ID, ASD and additional psychopathology group were on psychotropic medication, compared to 15.8% of those in the ID and ASD group. The authors commented on the overall suppressive effect on behavior that psychotropic medication can have (LoVullo & Matson, 2009).

The Psychopathology in Autism Checklist (PAC) (Hellerschou et al., 2009) is a 42 item scale, with five subscales; Psychosis, Depression; Anxiety disorders; Obsessive Compulsive Disorder (OCD) and General Adjustment Problems. Hellerschou et al. (2009) piloted the scale, tested its reliability and found acceptable psychometric properties. It was found that the scale discriminated between adults with autism and ID with and without psychiatric disorders, and partially between individuals diagnosed with different psychiatric disorders.

Bakken, Hellerschou, Eilertsen, Heggelund, Myrbakk and Martinsen, (2010) used the PAC to assess the prevalence of psychiatric disorders in individuals with intellectual disability only and those with a combination of ID and autism. Over fifty-three percent of those with autism and ID combined had high psychiatric disorders scores and severe general adjustment problems, compared to 17.4% of the ID only group. Anxiety symptoms were present in 64% of those who had a psychiatric disorder and autism and ID, compared to 52% in those who had a psychiatric disorder and ID. The majority of individuals in both groups had more than one psychiatric disorder.

Bradley, Summers, Wood and Bryson (2004) used the Diagnostic Assessment for the Severely Handicapped-revised (DASH-II) (Matson, 1995a), and compared individuals with

severe intellectual disability with and without ASD. Individuals with ASD showed four times more psychiatric comorbidity than those without ASD. Those with ASD showed significantly more anxiety, mood disorders, sleep disorders and organic syndromes than those without ASD. La Malfa, Lassi, Salvini, Giganti, Bertelli and Albertini (2007) also used the DASH-II (Matson, 1995). Participants were compared in terms of whether screened positive for a Pervasive developmental disorders (PDD) or not, and if they were in the 'clinical significance' or 'no clinical diagnosis' groups, based on their scores on the DASH-II. PDD was correlated with an increased presence of psychiatric disorders. A relationship was also observed between PDD and mood, mania and depression.

Hermans, van der Pas and Evenhuis (2011) conducted a literature review of instruments assessing anxiety in adults with intellectual disability. Self-report measures, informant-report measures and diagnostic instruments were reviewed. The most promising self-report instrument was the Glasgow Anxiety Scale for people with an Intellectual Disability (GAS-ID) (Mindham & Espie, 2003), while the Anxiety, Depression and Mood Scale (ADAMS) (Methot & Morin, 2004) is the most promising informant-report measure. Hermans et al. (2011) included the PAC in their review, and found the pilot study to be of good methodological quality, while the anxiety subscale of the PAC had moderate reliability but did not differentiate between different psychiatric diagnoses.

A number of studies used structured clinical interviews. Lugnegard et al., (2011) examined psychiatric comorbidity in individuals with Asperger syndrome, and found that 70% of individuals had at least one episode of major depression, while 50% had suffered from recurrent depressive disorders. Fifty six percent of individuals had an anxiety disorder. Hofvander et al. (2009) compared the frequency of psychiatric disorders among three groups; individuals with Autistic disorder, those with Asperger syndrome and those with pervasive developmental disorder-not otherwise specified (PDD-NOS). Forty-three percent of

individuals were diagnosed with attention deficit/hyperactivity disorder (AD/HD). Fourteen percent had a diagnosis of dyslexia. The most common comorbid condition was mood disorder, with 53% of individuals having a diagnosis, followed by anxiety disorder, whereby 50% had a diagnosis. One third of individuals had been treated with an antidepressant at least once in their lives. The frequency of comorbid diagnoses did not differ between the ASD subgroups or between males and females.

McCarthy et al. (2010) used interviews also, but they additionally examined the association between challenging behavior and comorbid psychopathology. They compared those with ID and ASD, and those with ID only. There were significant differences in comorbid psychopathology between those with and without ASD. Those with ASD and challenging behavior were not more likely to receive a psychiatric diagnosis than those with ASD without challenging behavior. However, those with ASD and challenging behavior were less likely to receive a diagnosis of schizophrenia. The authors suggested that the presence of challenging behavior in an individual with ASD may make the diagnosis of psychotic symptoms more difficult. There was no association between challenging behavior when age, level of ID and gender was controlled for. A diagnosis of ASD predicted challenging behavior, but a diagnosis of a psychiatric disorder did not.

Morgan, Roy and Chance (2003) collected data using medical records and psychiatric case notes. Thirty-five percent of those with autism had another comorbid psychiatric condition. The most common psychiatric diagnosis was depression, whereby 20% had a diagnosis. Eleven percent of individuals with ASD had a diagnosis of bipolar affective disorder, while 5% had a diagnosis of schizophrenia. Thirty four percent of individuals had a diagnosis of epilepsy, while 6% had a diagnosis of hypothyroidism. Similar to LoVullo and Matson (2009), a high percentage (50%) of individuals were on at least one psychotropic

medication. Forty percent of those on neuroleptics did not have an additional psychiatric diagnosis.

Munesue, Ono, Mutoh, Shimoda, Nakatani and Kikuchi (2008) assessed individuals with ASD for mood disorders in an outpatient clinic. Thirty-six percent of individuals were diagnosed with mood disorder. In those with mood disorders, bipolar disorder accounted for 75% of the cases. None of the individuals with autistic disorder had mood disorders. The majority (75%) of those with mood disorders had a diagnosis of Asperger syndrome.

Lifespan

Davis, Hess, Moree, Fodstad, Dempsey, Jenkins and Matson (2011) examined the developmental trajectory of anxiety symptoms across the lifespan in individuals with ASD. The study examined anxiety in toddlers, children, young adults and older adults, using three different measures; the BISCUIT Part 2 (Matson et al., 2007), ASD-CC (Matson & González, 2007), and the ASD-CA (Matson et al., 2006). Anxiety rose from toddler-hood, peaked in childhood, decreased through young adulthood and began to rise again in older aged individuals. Future research should examine how other comorbid symptoms change throughout the lifespan.

---Insert Table 3 about here---

Attention deficit/hyperactivity disorder (AD/HD)

The prevalence of Attention-deficit/hyperactivity disorder (AD/HD) in those with ASD has ranged from 14-78% (Gargaro, Rinehart, Bradshaw, Tonge & Sheppard, 2011). In a recent study, Mannion et al. (2013) found that 18% of children and adolescents with autism spectrum disorder also had a comorbid diagnosis of AD/HD. Mannion et al. (2013) also examined predictors of sleep problems and found that AD/HD was not a significant predictor of sleep problems in children and adolescents with autism spectrum disorder. In their

literature review, Gargaro et al. (2011) provided evidence of the current status of neuroimaging research in autism and ASD. The authors also focused on the theoretical models and neuropsychology of the two disorders as well as treatment strategies. They commented on the importance of considering the social outcome of treatment, as children with autism and AD/HD comorbidity are at increased risk of bullying when compared to children with either autism or AD/HD alone (Montes & Halterman, 2007; Gargaro et al., 2011).

As afore mentioned, Simonoff et al. (2008) found AD/HD to be the second most common comorbid condition in their sample. Keen and Ward (2004) compared the prevalence of ASD and comorbidity in 1997 and 2001. In that time, there was a significant increase in the number of children with ASD AD/HD, from 5.2% to 13.7% (Keen & Ward, 2004). Skokauskas and Gallagher (2012) compared children with ASD to those without. The authors found that almost half (44.78%) of the ASD group met criteria for clinically significant attention deficit/hyperactivity disorder. Borderline clinically significant difficulties were found for the AD/HD subscale for 47% of children with ASD (Skokauskas & Gallagher, 2012).

Goldstein and Schwebach (2004) conducted a retrospective chart review study on children with a diagnosis of either pervasive developmental disorders (PDDs) or AD/HD. It was found that 26% of those with PDDs met DSM-IV criteria for the combined type of AD/HD, while 33% met criteria for the Inattentive type of AD/HD. Forty-one percent of those with PDDs did not have a comorbid diagnosis of AD/HD. Those with PDDs and the combined type of AD/HD did not significantly demonstrate more impairment in daily life functioning than those with a PDD only. However, these children with a comorbid diagnosis were rated by parents and teachers as experiencing more daily living difficulties than those with a PDD alone.

Mayes, Calhoun, Mayes and Molitoris (2012) conducted a study to determine what symptoms overlap in ASD and AD/HD and what symptoms are distinct. Mayes et al. (2012) compared children with high functioning autism, low functioning autism, AD/HD combined type and AD/HD inattentive type. The authors also compared the scores to typically developing children whose results had been used in a previous study. The study found that while autism is distinct from AD/HD but the core symptoms of attention deficit, hyperactivity and impulsivity are part of autism. The authors state that autism and AD/HD are “neurobiological disorders with similar underlying neuropsychological deficits” (p.283).

Sinzig, Morsch, Bruning, Schmidt and Lehmkuhl (2008) compared children with ASD and comorbid AD/HD symptoms to children with ASD, but without AD/HD symptoms, and to children with AD/HD and typically developing children. They exhibited executive functioning skills such as inhibition, flexibility, working memory and planning. Children with comorbid AD/HD symptoms showed more problems in inhibitory performance when compared to children with ASD alone. The ASD and comorbid AD/HD group showed similarities to the AD/HD only group with regard to inhibitory performance, but not in working memory deficits. The study also found that individuals with ASD and comorbid AD/HD have more of a speed problem than a comprehension problem in planning, working memory of flexibility tasks.

Nydén, Niklasson, Stahlberg, Anckarsater, Wentz, Rastam and Gillberg (2010) compared adults with ASD to those with AD/HD and those with ASD and comorbid AD/HD. The authors compared groups in terms of intellectual ability, learning and memory, attention/executive function and theory of mind function. As supported by Mayes et al. (2012), there appeared to be an overlap between the three diagnostic categories. There is also distinction between the three groups, as the neurocognitive problems experienced by the ASD and comorbid AD/HD group were not just a summary of the ASD and AD/HD groups. The

authors commented that children with neuropsychiatric developmental disorders should be re-examined as adults as ‘criteria for diagnosis may not be fulfilled and the neurocognitive functions may have changed over time’ (p.1667).

---Insert Table 4 about here---

Epilepsy

The prevalence of epilepsy among all children is estimated at 2-3% compared to some 30% in autism (Tuchman & Rapin, 2002). Variability in prevalence rates has been attributed to the heterogeneity of samples with respect to age, sex, comorbidity, subtype of pervasive developmental disorder (PDD) or intellectual disability (ID) (Amiet, Gourfinkel-An, Bouzamondo, Tordjman, Baulac, Lechat, et al., 2008). In a retrospective review of electroencephalography (EEG) data and review of medical record charts, 40% of children referred were diagnosed with epilepsy (Gabis, Pomeroy & Andriola, 2005). However, this is not surprising as epilepsy symptoms were present in many of the children, where half presented with convulsions. Mannion et al. (2013) found that 10.1% of children and adolescents with ASD had a comorbid diagnosis of epilepsy. The authors found that epilepsy was not a significant predictor of sleep problems in those with ASD.

Amiet et al. (2008) conducted a meta-analysis of epilepsy in autism. The authors investigated the relationships between epilepsy and intellectual disability (ID), and epilepsy and gender in individuals with autism. It was found that 21.4% of individuals with an intellectual disability had epilepsy, while 8% of those without an intellectual disability had epilepsy. Epilepsy in autism was found to be associated with intellectual disability. The authors found that the more severe the intellectual disability, the more prevalent epilepsy was. The risk for epilepsy was found to be significantly higher for females (Amiet et al., 2008).

Bolton, Carcani-Rathwell, Hutton, Goode, Howlin and Rutter (2011) followed up 150 participants that were diagnosed with ASD in childhood, when they were 21 years of age. They found that 22% of individuals with ASD had epilepsy. More than half of those with epilepsy had seizures occurring weekly or less frequently. The average age of onset of confirmed epilepsy was 13.3 years, and for the majority of participants, seizures first began after the age of 10 years. In support of Amiet et al. (2008), Bolton et al. (2011) found that females were significantly more likely to develop epilepsy, where 30% of female participants developed epilepsy, compared to 18% of male participants. Males had a higher age of onset of seizures than females, and they did not differ in their level of intellectual disability or verbal abilities. Epilepsy was significantly more common in those with a lower overall language ability, where 45% of those with epilepsy had a very limited language ability, compared to 25% of those without epilepsy.

Turk, Bax, Williams, Amin, Eriksson and Gillberg (2009) compared children with ASD who had epilepsy, with those who did not have a diagnosis of epilepsy. A diagnosis of ASD and epilepsy was found to be associated with a later age at diagnosis of autism. The authors suggest that either ASD develops later or diagnostic overshadowing occurred. Having ASD and epilepsy was found to be associated with greater numbers and severities of gross and fine motor problems, incontinence, social impairments and challenging behaviors. Those with ASD and epilepsy showed delayed daily living skills. Those with ASD and epilepsy engaged in staring behavior, where they were found to stare longer and harder than those with ASD only. The ASD only group displayed more brief glances as a means of eye contact and experienced more abnormal fascination with objects than the ASD and epilepsy group.

Seizures are more frequent when intellectual disability is associated with ASD and when neurological signs are evident (Canitano, 2007). Individuals with autism and additional

neurological impairment, such as cerebral palsy are at a higher risk for seizures (Steffenburg, Steffenburg & Gillberg, 2003). A much lower rate of epilepsy, of approximately 6% has been reported in children with autism without additional neurological disorders (Pavone, Incorpora, Fiumara, Parano, Trifiletti, & Ruggieri, 2004). Tuchman, Rapin and Shinnar (1991) also found that type of language dysfunction was a risk factor for seizures, with the highest percentage of seizures occurring in children with the most severe deficits in receptive language. De-Long and Heinz (1997) and Rapin, Mattis, Rowan and Golden (1977) hypothesised that the association of severe receptive language disorders with epilepsy and with autism implicates temporal-lobe dysfunction (Tuchman & Rapin, 2002).

Matson, Neal, Hess, Mahan and Fodstad (2010) investigated adaptive behavior, personal-social behavior, communication, motor and cognitive skills in toddlers who were atypically developing compared to those with ASD, and also compared those with and without seizures. Toddlers with seizure disorders exhibited greater impairments across all domains of functioning when compared to those without seizure disorders. While there was not a significant interaction found between diagnostic group, the general trend showed that those with ASD and seizures exhibited the greatest impairments, followed by those with ASD alone, atypically developing children without seizures and finally, atypically developing children without seizures.

As with many other comorbid disorders, there is a lack of research in the area of adults with autism and comorbid epilepsy. Smith and Matson (2010a, 2010b, 2010c) focused on adults with epilepsy and the relationships between epilepsy, challenging behavior, comorbid psychopathology and social skills in three papers. In all three papers, the authors compared four groups: 1) Intellectual disability, 2) Epilepsy, 3) ASD and 4) ASD and epilepsy combined. The first, Smith and Matson (2010a) investigated challenging behavior. It was found that those with comorbid ASD and epilepsy were more impaired than the other

groups. Specifically, those with epilepsy and ID showed significantly higher disruptive behavior scores than those with ID only group, ASD only group and epilepsy only group.

The second, Smith and Matson (2010b) investigated comorbid psychopathology, Smith and Matson (2010b) compared ASD-CA scores among four groups; those with ID alone, those with epilepsy alone, those with ASD alone and those with ASD and epilepsy combined. Those with ASD and a comorbid condition (e.g. epilepsy) were more impaired in terms of psychopathology than those with ID, epilepsy or ASD on its own. The ASD and epilepsy group showed higher scores on irritability/behavioral excesses, attention/hyperactivity and depressive symptoms than the ID alone group. Those with combined ASD and epilepsy scored higher on the anxiety/repetitive behavior subscale and on the attention/hyperactivity subscale than those with epilepsy alone.

The third, Smith and Matson (2010c) investigated social skills deficits. Individuals with ID and comorbid ASD and epilepsy were significantly more impaired in social skills than those with ID alone, or those with ASD or epilepsy. Having multiple disorders increased the odds of having diminished social skills. For the positive verbal subscale of the Matson Evaluation of Social Skills for Individuals with sEvere Retardation (MESSIER; Matson, 1995b) individuals with ASD and epilepsy combined were more impaired but epilepsy contributed more to the effect than ASD alone.

Matson and Neal (2009) conducted a literature review about seizures and epilepsy in ASD. The authors examined the prevalence, nosology and etiology. They also looked at the relationship between seizures and epilepsy and regression in ASD. The authors noted that much of the research on regression and epilepsy is correlational and that a causal link between the two has yet to be established. They also commented on the need for clinicians to

be aware of the high co-occurrence between seizures and ASD during assessment and intervention.

---Insert Table 5 about here---

Gastrointestinal symptoms

The published literature is inconsistent regarding the prevalence of gastrointestinal problems in individuals with ASD (Wang, Tancredi & Thomas, 2011). The reported prevalence of gastrointestinal problems in children with ASD has ranged from 9% to 91% (Coury, Ashwood, Fasano, Fuchs, Geraghty, Kaul et al., 2012; Ming, Brimacombe, Chaaban, Zimmerman-Bier & Wagner, 2008; Black, Kaye & Jick, 2002; Fombonne & Chakrabarti, 2001; Ibrahim, Voigt, Katusic, Weaver & Barbaresi, 2009; Molloy & Manning-Courtney, 2003; Mouridsen, Rich & Isager, 2010; Nikolov, Bearss, Lettinga, Erickson, Rodowski, Aman et al., 2009; Taylor, Miller, Lingam, Andrews, Simmons & Stowe, 2002; Valicenti-McDermott et al., 2008; Horvath & Perman, 2002; Wang, Tancredi & Thomas, 2011; Parracho, Bingham, Gibson & McCartney, 2005; Smith, Farnworth, Wright & Allgar, 2009). It has been questioned if gastrointestinal symptoms are more common in those with autism spectrum disorder than in the general population. Kuddo & Nelson (2003) commented on the lack of research using appropriate controls in their review.

Ibrahim et al., (2009) compared children with autism and gastrointestinal symptoms to matched control participants. No significant association found between autism and gastrointestinal symptoms. However, significant differences were found between those with autism and control participants in relation to constipation and feeding issues/ food selectivity. Children with autism had a higher incidence of constipation and feeding issues. The authors suggested that these issues may have a behavioral etiology. Insistence on sameness in children with autism may lead them to demand stereotyped diets, which may result in an

adequate intake of fibre, which in turn can lead to constipation (Ibrahim et al., 2009). Use of psychotropic medication may also lead to feeding issues, as side-effects of medications may include appetite suppression or increased appetite (Ibrahim et al., 2009).

Black et al. (2002) found that only 9% of children with autism had gastrointestinal symptoms prior to diagnosis, similar to controls. Wang et al. (2011) compared gastrointestinal symptoms in children with autism to their typically developing siblings. It was found that there were significantly more gastrointestinal symptoms in children with ASD (42%) compared to their typically developing siblings (12%). The two most common gastrointestinal problems in children with ASD were constipation and chronic diarrhea. The researchers divided autism severity into three groups; Full Autism, Almost Autism and Spectrum. Increased autism symptom severity was associated with higher odds of gastrointestinal problems (Wang et al., 2011). In contrast, Molloy & Manning-Courtney (2003) found that frequency of gastrointestinal symptoms did not vary by age, gender, race or severity of autism. In support of this, Nikolov et al. (2009) also found that those with gastrointestinal problems were no different from those without gastrointestinal problems in autism symptom severity, demographic characteristics or measures of adaptive functioning. Nikolov et al. (2009) found that when compared to children without gastrointestinal problems, those with gastrointestinal problems showed greater symptom severity on measures of irritability, anxiety and social withdrawal. With regards to irritability, those with current gastrointestinal symptoms had lower irritability scores than those with a history of gastrointestinal symptoms.

Similar to the lack of instruments available for measuring comorbid psychopathology in individuals with ASD, there is an absence of instruments to measure gastrointestinal symptoms in those with ASD. Molloy and Manning-Courtney (2003) used medical record reviews to determine if participants in their study had gastrointestinal symptoms. Nikolov et

al. (2009) similarly reviewed medical records, as well as using a Side Effects Review Form (Research Units of Pediatric Psychopharmacology, RUPP). Valicenti-McDermott et al. (2008) derived The Gastrointestinal Questionnaire from an existing questionnaire, designed for typically developing children. The Autism Treatment Network developed the the Gastrointestinal Symptom Inventory (Autism Treatment Network, 2005), which is a parental-report questionnaire.

Mazurek, Vasa, Kalb, Kanne, Rosenberg, Keefer et al. (2013) used the Gastrointestinal Symptom Inventory (Autism Treatment Network, 2005) to study the relationships between chronic GI symptoms, anxiety and sensory over-responsivity. There was a strong association between anxiety and sensory over-responsivity, with higher levels of anxiety among children who have greater levels of reactivity to various sensory stimuli. Children with chronic GI symptoms evidenced higher levels of both anxiety and sensory over-responsivity. Increasing numbers of chronic GI symptoms were associated with higher levels of anxiety and sensory over-responsivity.

Mannion et al. (2013) also used the Gastrointestinal Symptom Inventory (Autism Treatment Network, 2005) to determine the frequency of GI symptoms in children and adolescents with ASD. The authors found that 79.3% of individuals had at least one gastrointestinal symptom within the last 3 months. The most common gastrointestinal symptom was abdominal pain, where 51.7% of individuals presented with it, followed by constipation where 49.4% presented with the symptom. Total number of GI symptoms was found to be a significant predictor of sleep problems. Specifically, abdominal pain predicted sleep anxiety.

The Questionnaire on Pediatric Gastrointestinal Symptoms-Rome III Version (QPGS-RIII) is an adaptation and abbreviation of the Questionnaire on Pediatric Gastrointestinal

Symptoms (QPGS) (Walker, Caplan-Dover & Rasquin-Weber, 2000). The 71 item parental-report questionnaire assesses symptom criteria for pediatric functional gastrointestinal disorders and additional gastrointestinal symptoms. Gorrindo, Williams, Lee, Walker, McGrew and Levitt (2012) used the QPGS-RIII as well as clinical evaluations by pediatric gastroenterologists. Agreement between parental-report gastrointestinal symptoms and physician diagnosis was high (92.1%). The study divided participants into three groups; those with ASD and gastrointestinal symptoms, those with ASD and no gastrointestinal symptoms and those with gastrointestinal symptoms only. Gastrointestinal symptoms in ASD were not associated with diet or medication usage. Constipation was the most common gastrointestinal symptom, with 85% of those with ASD and gastrointestinal symptoms presenting with it. Odds of constipation were associated with younger age, increased social impairment and lack of expressive language.

Valicenti-McDermott et al. (2008) investigated the relationship between gastrointestinal symptoms and language regression. It was found that 68% of children with ASD were reported to have one or more lifetime gastrointestinal symptoms. Children with language regression had more gastrointestinal problems (84%) than those without language regression (61%). An association was observed between children with language regression, a family history of autoimmune disease and gastrointestinal symptoms. Molloy & Manning-Courtney (2003) found that a history of regression was present in 23.4% of children with ASD. In contrast to Valicenti-McDermott et al. (2008), Molloy & Manning-Courtney (2003) found that regression was not significantly associated with gastrointestinal symptoms. Hansen, Ozonoff, Krakowiak, Angkustsiri, Jones, Deprey et al. (2008) used two definitions of regression: 1) loss of both language and social skills, and 2) loss of either language or social skills. No significant differences were found between the children with or without regression in terms of gastrointestinal symptoms, history of seizures or sleep problems.

Buie, Fuchs III, Furuta, Kooros, Levy, Lewis, Wershil and Winter (2010b) published an article which provides guidelines for evaluation and treatment of common gastrointestinal problems for health care practitioners. As many practitioners may not be aware of the high co-occurrence of GI symptoms in those with ASD, this is an extremely important article for health care practitioners. Buie, Campbell, Fuchs III, Furuta, Levy, VandeWater et al, (2010a) conducted a literature review of gastrointestinal symptoms in ASD, and provided a list of consensus statements, including a key statement: 'Individuals with ASDs who present with gastrointestinal symptoms warrant a thorough evaluation, as would be undertaken for individuals without ASDs who have the same symptoms and signs'. The authors also included a table of vocal and motor behaviors and changes in overall state. Vocal and motor behaviors that may be markers of abdominal pain or discomfort in individuals with ASD include behaviors like frequent clearing of throat and facial grimacing. Changes in overall state may include sleep disturbances, increased irritability and non-compliance with demands. The authors recommend that a functional behavior assessment would be useful in interpreting these behaviors. The article also includes a concise table of key take-away messages. One of the messages is that the communication impairments characteristic of ASD may lead to unusual presentations of gastrointestinal disorders including sleep disturbances and problem behaviors.

---Insert Table 6 about here---

Sleep problems

Johnson (1996) reported that 34% to 80% of children with an intellectual disability (ID) have a sleep problem (Richdale, Francis, Gavidia-Payne & Cotton, 2000). Rzepecka, McKenzie, McClure and Murphy (2011) found that 77.2% of children with ASD had sleep problems. They investigated the relationship between sleep problems, anxiety and challenging behavior. Medication usage, sleep problems and anxiety accounted for 42% of

the variance in challenging behavior, with sleep problems being the strongest predictor. It can also be noted that children on medication scored higher on sleep problems, anxiety and challenging behavior.

Mannion et al. (2013) found that 80.9% of children and adolescents with ASD presented with sleep problems. The study also investigated predictors of sleep problems. Total number of gastrointestinal symptoms predicted sleep, as did the ASD-CC subscales of under-eating and avoidant behavior. The types of sleep problems predicted by these variables were sleep anxiety, parasomnias and daytime sleepiness. Specifically, abdominal pain predicted sleep anxiety.

Many studies have investigated the relationship between sleep and problem behavior. Goldman, McGrew, Johnson, Richdale, Clemons and Malow (2011) compared children with ASD who were good sleepers to poor sleepers. It was found that poor sleepers had a higher percentage of behavioral problems than good sleepers. Over 75% of poor sleepers had problems with attention span and social interactions. Poor sleepers displayed more stereotypy, hyperactivity and anxiety, as well as having more sensory and eating issues. A poor sleeper had a high risk of exhibiting self-injurious behavior, even when age was adjusted for. A poor sleeper had a 20.4% higher likelihood of self-injurious behavior than a good sleeper. Younger children who were poor sleepers were more likely to have language problems, aggression, hyperactivity and poor eating habits than older poor sleepers.

Mayes and Calhoun (2009) found that sleep problems were not related to age, IQ, gender, race, parent occupation, neuropsychological functioning and learning ability. Sleep problems increased with severity of autistic symptoms and with severity of parent reported symptoms, such as oppositional behavior, aggression, explosiveness, attention deficit, impulsivity, hyperactivity, anxiety, depression and mood variability. Autism severity was the single most powerful predictor of sleep problems and explained 20% of the variance. The

most powerful combined predictors of sleep disturbances were autism severity, hyperactivity, mood variability and aggression, explaining 31% of the variance.

Children in the pervasive developmental disorders (PDDs) group are more likely to fall asleep later at night, have longer sleep latencies, sleep less at night, and spend a significant period of time awake during the night, when compared to controls (Patzold, Richdale & Tonge, 1998). Children in the PDD group displayed significantly more energetic and more difficult daytime behavior, compared to a control group (Patzold et al., 1998). Richdale et al. (2000) used a control group in their study of children with intellectual disability (ID), where 13% of those with an ID had a diagnosis of autism also. Sleep problems were associated with both the intensity and frequency of family stress, and the presence of problem behavior (Richdale et al., 2000). Children with intellectual disability and severe sleep problems showed more severe levels of daytime problem behavior, such as aggression, non-compliance and hyperactivity (Didden, Korzilius, van Aperlo, van Overloop, & de Vries, 2002). In a single-subject study, sleep deprivation was found to increase escape-maintained self-injurious behavior in a child with intellectual disability (O' Reilly & Lancioni, 2000).

Research has compared sleep problems in children with ASD, attention deficit/hyperactivity disorder (AD/HD), epilepsy and typically developing children (Tsai, Chiang, Lee, Gau, Lee, Fan, et al., 2012). While children with ASD and AD/HD exhibited more sleep problems than children with epilepsy, current or lifetime sleep problems did not differ between children with ASD and children with AD/HD, or between children with epilepsy and typically developing children (Tsai et al., 2012). Schreck, Mulick and Smith (2004) conducted a study where information was retrieved from a database of parent reported sleep problems; therefore all participants had sleep problems. Fewer hours of sleep per night predicted overall autism severity scores and social skills deficits, while stereotypic behavior

was predicted by fewer hours of sleep per night and screaming during the night. Increased sensitivity to environmental stimuli in the bedroom and screaming at night predicted communication problems. Therefore, it is of extreme importance to identify and treat sleep problems, as they may influence the effectiveness of daily interventions (Schreck et al., 2004).

---Insert Table 7 about here---

Feeding problems

Children with autism were found to have significantly more feeding problems and eat a significantly narrower range of foods than children without autism (Schreck, Williams & Smith, 2004). Matson and Kuhn (2001) developed the Screening Tool of Feeding Problems (STEP) to identify feeding problems in adults with an intellectual disability. Fodstad and Matson (2008) compared feeding problems in those with intellectual disabilities with and without autism. Individuals with ASD and intellectual disability displayed more behaviorally-based feeding issues like food selectivity and refusal related behaviors than those with intellectual disability alone. The ASD and intellectual disability group had more severe feeding and mealtime problems than the intellectual disability alone group (Fodstad & Matson, 2008).

Seiverling, Hendy and Williams (2011) modified the STEP for use with children, calling it the STEP-CHILD. The authors then compared children with autism to children with special needs and to children with no special needs. Stealing food was more common in children with autism than those with and without special needs. Emond, Emmett, Steer and Golding (2010) conducted a longitudinal study on feeding symptoms in children with ASD. Children with ASD demonstrated feeding difficulties from infancy and had a less varied diet at 15 months of age than controls. However, energy intake or growth was not impaired. The infants with ASD were described as 'slow feeders' at 6 months old. The authors suggested

that effective behavioral strategies need to address the neophobia and sensory sensitivities e.g. colour, taste, texture, for children with ASD.

Bandini, Anderson, Curtin, Cermak, Evans, Scampini et al. (2010) compared food selectivity between children with ASD and typically developing children. Children with ASD exhibited more food refusal and had a more limited food repertoire than typically developing children. Sharp, Jaquess and Lukens (2013) completed a multi-method assessment battery involving standardized mealtime observation, a food preference inventory and the Brief Autism Mealtime Behavior Inventory (BAMBI) (Lukens & Linscheid, 2008). Food selectivity on the BAMBI were negatively associated with a child's acceptance of bites and positively associated with disruptions during the presentation of foods during a structured mealtime observation. There was no relationship between ASD symptom severity and feeding problems. Neither was there a relationship between growth parameters and feeding problems.

Nadon, Feldman, Dunn and Gisel (2011) examined the relationship between sensory processing problems and the number of eating problems in children with ASD, and found there was an association between both. A significant association was found between visual and auditory sensitivity and the number of eating problems in children with ASD. The relationship between sensory processing and feeding problems needs to be further examined in the future. For practitioners interested in the treatment of feeding disorders, Matson and Fodstad (2009) conducted an excellent review of the treatment of food selectivity and other feeding problems in children with ASD.

---Insert Table 8 about here---

Toileting problems

Toileting is a critical skill necessary for independent living, and incontinence is a significant quality of life barrier for individuals with autism (Kroeger & Sorensen-Burnworth, 2009). Kroeger and Sorensen-Burnworth (2009) conducted a very thorough literature review about toilet training individuals with autism and other developmental disabilities. They examined teaching strategies such as graduated guidance, reinforcement-based training, scheduled sittings, elimination schedules, punishment procedures, hydration, manipulation of stimulus control, night time training for diurnal continence and priming and video modelling.

Dalrymple and Ruble (1992) found that lower cognition and lower verbal levels were significantly correlated with age of accomplishment of bowel and urine training in individuals with autism. In their survey of toileting issues, the authors found that twenty-two percent of individuals still wet at night time, with their ages ranging from nine to 32 years. Five percent of the sample with a mean age of 23.8 years were not trained for urine, bowel or during the night. About 30% of the individuals with autism had fears associated with toileting, whereby verbal individuals had the most. The most common toileting problems were urinating in places other than the toilet, constipation, stuffing up toilets, continually flushing and smearing feces.

Matson, Dempsey and Fodstad (2010) developed the Profile of Toileting Issues (POTI) questionnaire for individuals with an intellectual disability between the ages of 4 through adulthood. Matson, Neal, Hess and Kozlowski (2011) examined the reliability of the POTI and found it have good internal consistency ($\alpha=.83$). Belva, Matson, Barker, Shoemaker and Mahan (2011) used the POTI questionnaire to investigate toileting issues in individuals with intellectual disability, ranging from 23 to 72 years. They found that lower adaptive functioning was associated with greater toileting problems. Matson, Horovitz and Sipes (2011) used the POTI questionnaire in 153 adults with intellectual disability, and found that the most frequently endorsed problems were toileting accidents during the day and night.

Significant differences on total POTI score were found based on verbal ability, ambulatory ability, fiber or laxative use and level of intellectual disability. Therefore, those who were non-verbal, non-ambulatory, using fiber or laxatives and with a profound intellectual disability had higher total scores on the POTI.

Matson and LoVullo (2009) conducted a literature review on encopresis, soiling and constipation in children and adults with developmental disabilities. The authors note that etiology, prevalence, assessment and treatment of encopresis, soiling and constipation have received very little attention, and suggest that future attention and efforts by researchers are warranted. There is a lack of research on toileting problems in developmental disabilities, and this is especially true in the case of autism spectrum disorders. Much more research is needed to examine the prevalence of toileting problems in individuals with ASD, and to investigate other variables that may be associated with toileting problems, such as communication and challenging behavior.

---Insert Table 9 about here---

Conclusion

It is important that there is an understanding of the types of comorbid disorders that affect those with ASD among both practitioners and researchers. In order to implement the most effective intervention plans for those with ASD, comorbid conditions should be considered. Comorbidity in ASD is an area where much more research is required.

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Table 1.

Summary of comorbid psychopathology in babies/infants with ASD articles.

Study	Research Question	Age of participants	Number of participants	Measures used	Outcome
Davis, Fodstad, Jenkins, Hess, Moree, Dempsey et al., (2010).	To compare anxiety and avoidant behavior between infants/ toddlers with autistic disorder, PDD-NOS and atypically developing children.	17-37 months	513	Baby and Infant Scale for Children with aUtism Traits (BISCUIT) (Part II) (Matson, Boisjoli, & Wilkins, 2007).	Infants with Autistic Disorder had higher anxiety and avoidant behavior scores than those with PDD-NOS and atypically developing children.
Davis, Moree, Dempsey, Hess, Jenkins, Fodstad & Matson (2011).	To determine whether deficits in communication skills have an effect on the expression of anxiety in	15-36 months.	735	BISCUIT (Part II).	As communication increased, so did anxiety in children with ASD compared

infants and toddlers.

to typically

developing children.

Fodstad, Rojahn & Matson (2010).	To compare comorbid psychopathology in toddlers with ASD and atypically developing children, and across age ranges.	12-39 months.	ASD: 109 Atypical controls: 160	BISCUIT (Part II)	Those with ASD had more severe comorbid symptoms than atypical controls, with there being an increasing trend of comorbid symptoms as age increased.
Kozlowski, Matson, Belva & Rieske (2012).	To compare feeding and sleeping difficulties between infants/toddlers with autistic disorder, PDD-NOS and atypically	17-37 months.	1747	BISCUIT (Part II)	Children with Autistic disorder had more feeding and sleeping difficulties than

developing children.

children with PDD-
NOS or atypically
developing
children.

Table 2.

Summary of comorbid psychopathology in children with ASD articles.

Study	Research Question	Age of participants	Number of participants	Measures used	Outcome
Amr, Raddad, El-Mehesh, Bakr, Sallam & Amin (2012).	To estimate the prevalence of comorbid psychiatric disorders in children with ASD in 3 Arab countries.	6-11 years.	60	Semi-structured clinical interview for children and adolescents (SCICA) (McConaughy & Achenbach, 1994).	Children with ASD and comorbid psychiatric disorders were found to have significantly lower IQ than those with ASD but without comorbid psychiatric disorders.
Davis, Moree, Dempsey, Reuther, Fodstad, Hess et al. (2011).	Compared anxiety scores and communication deficits in children with Pervasive Developmental Disorder-Not Otherwise Specified	2-14 years.	99	Autism Spectrum Disorders-Comorbidity for Children (ASD-CC) (Matson & González, 2007). Diagnostic checklist	Anxiety decreased as communication deficits increased for those with Autistic Disorder (AD),

(PDD-NOS), children with Autistic Disorder (AD) and those with no diagnosis.

from the Diagnostic and Statistical Manual-Fourth Edition-Text Revision (DSM-IV-TR) (APA, 2000), and the International Classification of Diseases, Tenth Edition (ICD-10) (World Health Organization, 1992). compared to those with Pervasive Developmental Disorder-Not Otherwise Specified (PDD-NOS), or those with no diagnosis.

Hess, Matson & Dixon (2010).

Examining symptom endorsements in children and adolescents with ASD compared to typically developing children and adolescents. ASD group: 14-16 years. Control group: 4-14 years. 65 72

Autism Spectrum Disorder Comorbidity-Child Version (ASD-CC) (Matson & González, 2007). Differences between worry/depressed behavior, under-eating, over-eating, avoidant behavior and repetitive behavior.

Joshi, Petty,

Compared a 3-17 years. ASD group: 217

Schedule for Affective Youth with ASD have

Comorbidity in autism spectrum disorder

Wozniak, Henin, Fried, Galdo et al., (2010).	psychiatrically referred population with ASD to controls.		Control group: 217	Disorders and Schizophrenia for School-Age Children (K-SADS-E) (Orvaschel and Puig-Antch, 1987).	high levels of psychiatric comorbidity than those without ASD.
Leyfer, Folstein, Bacalman, Davis, Dinh, Morgan et al., (2006).	Piloted modified instrument, the Autism Comorbidity Interview- Present and Lifetime Version (ACI-PL)	5-17 years.	109	Autism Comorbidity Interview-Present and Lifetime Version (ACI-PL).	Specific phobia was the most common comorbid disorder.
Mannion, Leader & Healy (2013)	Investigated frequency of comorbid psychopathology, sleep problems, gastrointestinal symptoms and epilepsy. Also investigated	3-16 years.	89	ASD-CC	It was found that 46.1% of individuals had a comorbid disorder, with this number rising to 78.7% if intellectual

	predictors of sleep problems.				disability is included.
Matson, Fodstad & Dempsey (2009).	Comparing feeding problems among with autism, PDD-NOS, atypically developing children and typically developing children.	3-16 years.	279	ASD-CC	Those with autism and PDD-NOS had more issues than atypically developing and typically developing children.
Ming, Brimacombe, Chaaban, Zimmerman-Bier & Wagner (2008).	Investigating concurrent clinical disorders in ASD.	2-18 years.	160	Retrospective analysis of a clinical practice database.	Individuals with Asperger's syndrome are more likely to have a psychiatric condition, while those with PDD are more likely to have a medical condition.
Simonoff, Pickles, Charman, Chandler,	Analysed risk factors of psychiatric disorders	10-14 years.	112	Child and Adolescent Psychiatric Assessment.	Seventy percent of children with ASD

Loucas & Baird (2008).
in children with ASD.

had at least one
comorbid disorder.

Strang, Kenworthy, Daniolos, Case, Wills, Martin et al. (2012).
Investigating depression and anxiety symptoms in children with ASD.
6-18 years. 95

Child Behavior
Checklist (CBCL).

IQ and autism severity
is not associated with
depression/anxiety
symptoms.

Table 3.

Summary of comorbid psychopathology in adults with ASD and throughout the lifespan articles.

Study	Research Question	Age of participants	Number of participants	Measures used	Outcome
Bakken, Helverschou, Eilertsen, Heggelund, Myrbakk & Martinsen (2010).	Compared psychopathology in those with ASD, and those with ASD and intellectual disability (ID).	14-72 years.	194 (62 in autism group and 132 in ID group).	Psychopathology in Autism Checklist (PAC) (Helverschou, Bakken & Martinsen, 2008).	53.2% of those with ASD+ID had high psychiatric disorder scores, and severe general adjustment scores, while 17.4% of the ID only group had high scores.
Bradley,	Comparing psychiatric	14-20 years.	12	Diagnostic	Individuals with

Comorbidity in autism spectrum disorder

Summers, Wood & Bryson (2004). and behavior disorders in individuals with severe ID with and without autism.

Assessment for the Severely Handicapped-II (DASH-II) (Matson, 1995a). ASD showed 4 times as much psychiatric comorbidity as those without ASD.

Davis, Hess, Moree, Fodstad, Dempsey, Jenkins & Matson (2011). Investigating anxiety symptoms across the lifespan in ASD. 18-36 months. 40 3-16 years. 34 20-48 years. 30 49-65 years. 27

Baby and Infant Screen for Children with Autism Traits (BISCUIT) (Part II) (Matson, Boisjoli & Wilkins, 2007). Autism Spectrum Disorders- Comorbidity- Anxiety rose from toddler-hood, peaked in childhood, decreased through young adulthood and rose again in older adulthood.

Comorbidity in autism spectrum disorder

Child Version

(ASD-CC)

Matson &

González, 2007).

Autism Spectrum

Disorders-

Comorbidity for

Adults (ASD-CA).

Matson, Terlonge

& González, 2006).

Psychopathology in

Autism Checklist

(PAC) (Hellerschou,

Bakken & Martinsen,

2008).

The scale has

acceptable

psychometric

properties,

and

discriminates

between

<p>Hellerschou, Bakken & Martinsen (2009).</p>	<p>Pilot study using the Psychopathology in Autism Checklist (PAC).</p>	<p>17-56 years.</p>	<p>35</p>
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Comorbidity in autism spectrum disorder

					adults with ASD and ID
					with and
					without
					psychiatric
					disorders.
Hofvander, Delorme, Chaste, Nydén, Wentz, Ståhlberg et al. (2009).	Investigated psychiatric problems in individuals with ASD and normal intelligence.	16-60 years.	122	Structured Clinical Interview for DSM-IV-Axis I Disorders (SCID-I) (First, 1997).	Lifetime psychiatric axis I comorbidity was very common, especially mood and anxiety disorders, as well as attention

Comorbidity in autism spectrum disorder

					deficit/ hyperactivity disorder (AD/ HD).
La Malfa, Lassi, Salvini, Giganti, Bertelli & Albertini (2007).	Compared those with pervasive developmental disorders (PDDs) to those without.	No age range given. Mean age: 38.4 years.	90	DASH-II	Pervasive developmental disorders were clearly correlated with increased presence of psychiatric disorders.
LoVullo & Matson (2009).	1) To calculate cut-off scores for subscales of the ASD-CA. 2) To compare the	No age range given. Mean ID group: 55 years. Mean ID+ASD group:	313	ASD-CA	ID+ASD group scored higher than the ID group on most

Comorbidity in autism spectrum disorder

	Frequency of symptoms among 3 groups: individuals with ID; individuals with ID+ASD and individuals with ID, ASD and additional psychopathology.	49 years. Mean ID+ASD+ psychopathology group: 48 years.			subscales, except for conduct problems.
Lugnegard, Unenge Hallerback & Gillberg (2011).	Investigated psychiatric comorbidity in young adults with Asperger Syndrome.	No age range given. Mean age: 27 years.	54	Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) (First & Gibbon, 2004).	Mood disorders and anxiety disorders are common in Asperger Syndrome.
Matson & Boisjoli	Developed ASD-CA and tested its reliability.	16-78 years.	169	ASD-CA.	The internal consistency of the scale was

Comorbidity in autism spectrum disorder

good, and well above the acceptable cut-off.

<p>McCarthy, Hemmings, Kravariti, Dworzynski, Holt, Bouras et al. (2010).</p>	<p>Investigated the relationship between challenging behavior and comorbid psychopathology in adults with ASD and ID, compared to adults with ID alone.</p>	<p>18-65 years.</p>	<p>686 (125 with ASD+ID; 562 with ID alone).</p>	<p>International Classification of Diseases-10 (ICD-10) clinical criteria using information gathered from interviews with key informants and the patients.</p>	<p>There was no association between comorbid psychopathology and challenging behavior, when level of ID, gender and age were controlled for.</p>
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Comorbidity in autism spectrum disorder

Morgan, Roy & Chance (2003).	Examined the prevalence rates of major psychiatric disorders in learning disabled adults with autism and analysed the use of medication.	No age range given.	164	Medical records and psychiatric case notes.	Thirty-five percent of those with ASD had a comorbid psychiatric disorder.
Munesue, Ono, Mutoh, Shimoda, Nakatani & Kikuchi (2008).	Investigated the frequency of mood disorders in individuals with ASD.	12+ years	44	Interviewing based on Diagnostic and Statistical Manual of Mental Disorders IV (DSM-IV) criteria of mood disorder.	Thirty-six percent of those with ASD had a mood disorder.

Table 4.

Summary of Attention deficit/hyperactivity (AD/HD) articles.

Study	Research Question	Age of participants	Number of participants	Measures used	Outcome
Goldstein & Schwabach (2004).	To determine if a sample of children with PDDs display symptoms sufficiently related to AD/HD to warrant a comorbid diagnosis of AD/HD. Furthermore, do children with PDDs and AD/HD symptoms demonstrate more impairment in daily living activities than those children with a	Mean age=8.5 years.	57	Retrospective chart review. Conners Parent and Teacher Rating Scales-Revised, Long Version (CPRS-R:L & CTRS-R:L; Conners, 1997).	26% of those with PDDs met criteria for the combined type of AD/HD, while 33% met criteria for the Inattentive type of AD/HD.

	PDD only.				
Mayes, Calhoun, Mayes & Molitoris (2012).	To determine the degree to which core ADHD and autistic symptoms overlap and are distinct.	2-16 years.	847 with autism 158 with AD/HD	Based on DSM-IV criteria, licenced PhD psychologists made the diagnosis.	AD/HD symptoms were common in autism.
Nydén, Niklasson, Stahlberg, Anckarsater, Wentz, Rastam & Gillberg (2010).	To assess which types of neuro-psychological deficits appear to be most commonly associated with ASD and AD/HD in adults. The effect of the combination of	18+ years.	161	DSM-IV criteria checklist.	The dysfunctions of the the ASD and comorbid AD/HD group cannot be seen as a summary of the dysfunction found in the ASD and ADHD groups.

	ASD with AD/HD was also studied.				
Sinzig, Morsch, Bruning, Schmidt & Lehmkuhl (2008).	To evaluate and compare executive functioning (EF) profiles in children with AD/HD and in children with ASD with and without comorbid ADHD.	6-18 years.	80	Examination by an experienced child and adolescent psychiatrist according to DSM-IV-TR criteria.	Those with ASD and comorbid AD/HD symptoms showed more problems in inhibitory performance than those with ASD alone.
Skokauskas & Gallagher (2012).	To examine patterns of comorbid psychiatric problems in children with	ASD group: Mean= 12.73 years. Control group: Mean=	134 (67 in each group).	Child Behavior Checklist 6-18 (CBCL/6-18)	Almost half (44.78%) of the ASD group met

Comorbidity in autism spectrum disorder

ASD and their parents
11.85 years.
compared to age-matched
controls and their parents.

(Achenbach &
Rescorla, 2001).
CBCL criteria
for clinically
significant
hyperactivity
disorder.

Table 5.

Summary of epilepsy articles.

Study	Research Question	Age of participants	Number of participants	Measures used	Outcome
Amiet, Gourfinkel-An, Bouzamondo, Tordjman, Baulac, Lechat et al. (2008).	To compare the prevalence of epilepsy in 1) those with and without intellectual disability, and 2) males and females with autism.	1-28 years.	2112	Meta-analysis study so variety of measures used in individual studies.	Epilepsy in autism is associated with intellectual disability and gender.
Bolton, Carcani-Rathwell, Hutton, Goode, Howlin & Rutter (2011).	To under-take a long-term follow-up study of individuals with autism in order to better characterise the features and correlates of epilepsy in individuals with autism.	26-56 years.	150	Clinical records. Semi-structured interview. Where possible, the authors sought reports of electro-encephalogram (EEG)	Epilepsy was associated with gender (female), intellectual disability and poorer verbal abilities.

Comorbidity in autism spectrum disorder investigations that had taken place.

Gabis, Pomeroy & Andriola (2005).	To address the incidence and electroencephalographic abnormalities in children with pervasive developmental disorders (PDDs).	1-14 years.	56	Retrospective review of EEG data and independent review of medical record charts.	Forty percent of children with autism were diagnosed with epilepsy.
Matson, Neal, Hess, Mahan & Fodstad (2010).	To examine the effect that seizure disorder has on symptom presentation in toddlers with ASD compared to atypically developing children.	18-24 months.	36(9 in each group).	Diagnoses of seizure disorders were previously determined by the children's primary care physician.	Those with seizures tended to be more impaired than those without.
Turk, Bax, Williams, Amin, Eriksson	To compare developmental and psychological functioning in two groups	7-17 years.	120 (60 in each group).	Epilepsy was previously diagnosed by a	Those with ASD and epilepsy showed more

& Gillberg
(2009). of children with ASD, one
with epilepsy and one without.

medical professional. motor
difficulties,
developmental
delays and
challenging
behaviors than
those with ASD
alone.

Smith & Matson
(2010a). Compared behavior problems 29-72 years. 100 (25 in
each group).
among 4 groups:
Group 1) ID
Group 2) Epilepsy
Group 3) ASD
Group 4) ASD+epilepsy

International League Against
Epilepsy (ILAE). Clinical description
of seizure activity. Available medical
information (e.g. family history, age
of onset, prior
Those with ASD
and a comorbid
condition (e.g.
epilepsy) were
more impaired
than those with
ID, ASD or
epilepsy.

Comorbidity in autism spectrum disorder
neurological trauma).

Smith & Matson (2010b).	Compared psychopathology scores among 4 groups: Group 1) ID Group 2) Epilepsy Group 3) ASD Group 4) ASD+ epilepsy	29-72 years.	100 (25 in each group).	International League Against Epilepsy (ILAE). Clinical description of seizure activity. Available medical information (e.g. family history, age of onset, prior neurological trauma).	Those with ASD and a comorbid condition (e.g. epilepsy) were more impaired than those with ID, ASD or epilepsy.
Smith & Matson (2010c).	Compared social skills scores among 4 groups: Group 1) ID Group 2) Epilepsy Group 3) ASD	29-72 years.	100 (25 in each group).	International League Against Epilepsy (ILAE). Clinical description of seizure activity.	Those with ASD and a comorbid condition (e.g. epilepsy) were more impaired

Group 4) ASD+ epilepsy

Comorbidity in autism spectrum disorder
Available medical information (e.g. family history, age of onset, prior neurological trauma) in social skills than those with ID, ASD or epilepsy.

Table 6.

Summary of gastrointestinal symptom (GI) articles.

Study	Research Question	Age of participants	Number of participants	Measures used	Outcome
Gorrindo, Williams, Lee, Walker, McGrew & Levitt (2012).	Compared 3 groups; ASD+GI symptoms, ASD+no GI symptoms and GI symptoms only.	5-17 years.	121	Clinical evaluation by pediatric gastroenterologists. Questionnaire on Pediatric Gastrointestinal Symptoms-Rome III Version (QPGS) (Walker, Caplan- Dover & Rasquin- Weber, 2000).	Constipation was the most common GI symptom in ASD. It was associated with younger age, increased social impairment and lack of expressive language.

Comorbidity in autism spectrum disorder

Hansen, Ozonoff, Krakowiak, Angkustsiri, Jones, Deprey et al. (2008).	Examined the prevalence of regressive autism and associated demographic, medical and developmental factors.	2 to 5 years.	333.	CHARGE Gastrointestinal history form. CHARGE Sleep history form.	No statistically significant differences were found between children with/without regression in terms of gastrointestinal symptoms, history of seizures or sleep problems.
Ibrahim, Voigt, Katusic, Weaver & Barbaresi (2009).	Compared children with ASD and GI symptoms to matched control	Up to 18 years.	363 (121 case participants and 2 controls per	Medical records.	No significant association found between

	participants.		case participant).		ASD and GI symptoms, except more children with ASD had constipation and feeding issues.
Mazurek, Vasa, Kalb, Kanne, Rosenberg, Keefer et al. (2013).	Investigating the relationship between gastrointestinal symptoms, anxiety and sensory over-responsivity.	2-17 years.	2973	GI symptom inventory questionnaire (Autism Treatment Network, 2005).	Children with each type of GI symptom had significantly higher rates of anxiety and sensory over-responsivity.
Molloy &	Investigated the prevalence	24-96 months.	137	Medical records.	Twenty-four

Comorbidity in autism spectrum disorder

Manning-Courtney (2003).
of GI symptoms in children with ASD.

percent of children had a history of at least one GI symptom. No association was found between GI symptoms and developmental regression.

Nikolov, Bearss, Lettinga, Erickson, Rodowski, Aman et al.
Evaluated GI symptoms in children with pervasive developmental disorders (PDDs).
5-17 years.
172.

Medical history. Side Effects Review Form (Research Units of Pediatric Psychopharmacology)
Those with GI symptoms were no different from those without GI symptoms in

(2009).

terms of

adaptive

functioning or

autism

symptom

severity. Those

with GI

symptoms

showed greater

irritability,

anxiety and

social

withdrawal,

and were less

likely to

respond to

treatment.

Comorbidity in autism spectrum disorder

Valicenti-McDermott, McVicar, Cohen, Wershil & Shinnar (2008).	Investigated GI symptoms and language regression.	1-18 years.	100	The Gastrointestinal Interview.	Children with language regression had more GI problems than those without language regression.
Wang, Tancredi & Thomas (2011).	Compared children with ASD to their siblings in relation to GI symptoms.	1-18 years.	752 (589 participants with ASD and 163 of their siblings in control group).	Structured medical history interview.	More GI symptoms in children with ASD than their typically developing siblings. Increased autism

Comorbidity in autism spectrum disorder

symptom

severity was

associated

with higher

odds of GI

problems.



Table 7.

Summary of sleep problems articles.

Study	Research Question	Age of participants	Number of participants	Measures used	Outcome
Goldman, McGrew, Johnson, Richdale, Clemons & Malow (2011).	Investigated the relationship between sleep problems and problem behavior in children with ASD.	2-18 years.	1784.	Children's Sleep Habits Questionnaire (CSHQ) (Owens, Nobile, McGuinn, & Spirito, 2000). Parental Concerns Questionnaire (PCQ) (McGrew, Malow, Henderson, Wang, Song & Stone (2007).	Poor sleepers had a higher percentage of behavioral problems than good sleepers.
Mayes &	Investigated	1-15 years.	477.	Pediatric Behavior	The strongest

Comorbidity in autism spectrum disorder

Calhoun (2009). variables related to sleep problems in children with ASD.

Scale (PBS) (Chervin, Hedger, Dillon & Pituch, 2000). predictors of sleep disturbance were autism severity, hyperactivity, mood variability and aggression.

Patzold, Richdale & Tonge(1998). Explored the relationship between sleep problems and daytime behavior.

3-14 years.

67 (31 children with ASD and 36 participants in control group).

Sleep Diary.

Children with ASD are likely to fall asleep later, have longer sleep latencies, sleep less at night and spend a significant period of time awake during the night, when compared to

Comorbidity in autism spectrum disorder

controls. Those with ASD displayed significantly more difficult daytime behavior than controls.

Richdale, Gavidia-Payne & Cotton (2000).	Examined stress, challenging behavior and sleep problems in children with intellectual disability (ID).	2-19 years.	77(52 with ID, 7 of which had ASD and 25 in control group).	Sleep Problems Questionnaire (Richdale, Cotton & Habit, 1999). Epworth Sleepiness Scale (ESS) (Johns, 1991). Apnoea and narcolepsy scales	Sleep problems were significantly associated with intensity and frequency of parental stress and the presence of problem behaviors.
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Comorbidity in autism spectrum disorder

(Douglass,
Bornstein,
Nino-Murcia,
Keenan, Miles,
Zarcone et al.,
1994).

Rzepecka, McKenzie, McClure & Murphy (2011).	Investigated the relationship between sleep, anxiety and challenging behavior in children with intellectual disability and/or ASD.	5-18 years.	187.	Children's Sleep Habits Questionnaire (CSHQ).	Medication, sleep problems and anxiety accounted for 42% of the variance in challenging behavior.
Schreck, Mulick & Smith (2004).	Investigated the relationship between sleep problems	5-12 years.	55.	Behavior Evaluation of Disorders of	Fewer hours of sleep per night predicted

Comorbidity in autism spectrum disorder

and symptoms of
autism.

Sleep (BEDS) overall autism
(Schreck 1997/
1998; Schreck,
Mulick & Rojahn,
2003). severity scores
and social
skills deficits.

Tsai, Chiang,
Lee, Gau, Lee,
Fan, Wu &
Chiu (2012).
Compared sleep
problems in those
with ASD,
AD/HD and
epilepsy.
6-17 years.
256.

Sleep Habits
Questionnaire
(SHQ) (Gau, 2006).
There was an
increased risk
of sleep
problems in
children with
ASD and
AD/HD than
typically
developing
children.

Table 8.

Summary of feeding problems articles.

Study	Research Question	Age of participants	Number of participants	Measures used	Outcome
Bandini, Anderson, Curtin, Cermak, Evans, Scampini et al. (2010).	To compare food selectivity in children with ASD and typically developing children.	3-11 years.	111	Modified version of Youth/Adolescent Food Frequency Questionnaire (YAQ) (Field, Camargo, Taylor, Berkey, Frazier, Gillman et al. (1999).	Children with ASD exhibited more food refusal and had a more limited food repertoire than typically developing children.
Emond, Emmett, Steer & Golding (2010).	To investigate the feeding, diet and growth of young children with ASD.	6-54 months.	86	Questionnaires designed by the Avon Longitudinal Study of Parents and	ASD children showed feeding symptoms from infancy and had a

Comorbidity in autism spectrum disorder
Children (ALSPAC). less varied at 15

See <http://www.bristol.ac.uk/alspac/> months, but energy intake and growth were not impaired.

Fodstad & Matson (2008).	To compare feeding and mealtime problems in adults with intellectual disabilities with and without autism.	18-69 years.	60	Screening Tool of Feeding Problems (STEP) (Matson & Kuhn, 2001).	Those with ASD+ ID displayed more behaviorally-based feeding problems, such as food selectivity and refusal related difficulties compared to those with ID alone.
Nadon, Ehrmann Feldman, Dunn	To examine the relationship between sensory processing	3-10 years.	95	Eating Profiles (Nadon, 2007).	Sensory processing problems were

& Gisel (2011). problems and the number of eating problems in children with ASD.

significantly related to an increase in the number of eating problems.

Schreck, Williams & Smith (2004). To compare eating behaviors in children with and without autism. 7-9.5 years. 436

Children's Eating Behavior Inventory (CEBI) (Archer, Rosenbaum & Streiner, 1991). Food Preference Inventory. Children with autism have significantly more feeding problems and eat a narrower range of foods than children without autism.

Seiverling, Hendy & Williams (2011). To examine psychometric qualities of the STEP-CHILD. 2-18 years. 142

STEP-CHILD (Matson & Kuhn, 2001; Seiverling, Hendy & Stealing food was more common in children with autism.

Comorbidity in autism spectrum disorder

Williams (2011).

Sharp, Jaquess & Lukens (2013).
 To assess feeding problems using multi-method assessment.
 3-8 years.
 30

Food Preference Inventory. Brief Autism Mealtime Behavior Inventory (BAMBI) (Lukens & Linscheid, 2008). Standardized Mealtime Observation. Increased food selectivity was positively correlated with problem behaviors during the observation, while ASD symptom severity and growth parameters were unrelated to feeding data.

Table 9.

Summary of toileting problems articles.

Study	Research Question	Age of participants	Number of participants	Measures used	Outcome
Dalrymple & Ruble (1992).	To examine age of toilet training, toilet training methods, and toileting skills and behaviors in individuals with autism.	9-38 years.	100	Survey of Toilet Habits (STH) (Dalrymple & Ruble, 1992).	Lower cognitive level, being non-verbal and needing continued help with toileting was associated with age of accomplishing toilet training.