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An investigation of sleep problems, gastrointestinal symptoms, comorbid psychopathology and challenging behavior in children and adolescents with Down Syndrome

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ABSTRACT

Background: Down syndrome (DS) is one of the most common chromosomal abnormalities, and children with DS have increased risks of receiving diagnoses of specific comorbidities.
Aims: This study aimed to assess the frequencies and relationships between sleep problems, gastrointestinal (GI) symptoms, comorbid psychopathology, and challenging behavior.
Methods and procedures: The Children's Sleep Habits Questionnaire, Gastrointestinal Symptom Inventory, Autism Spectrum Disorder-Comorbid for Children, and Behavior Problems Inventory-Short Form were completed by 123 parents of children and adolescents with DS.
Outcomes and results: The frequency of GI symptoms was 74.8 %, with high frequencies also found for: sleep problems (100 %), challenging behavior (100 %), and moderate to severe levels of comorbid psychopathology (tantrum=80 %; repetitive behavior=63 %; avoidant behavior=82 %; worry/depressed=61 %; conduct behavior=100 %; over-eating=100 %; under-eating=100 %). A significant moderate correlation was found between total GI symptoms and self-injurious behavior frequency. Children who presented with abdominal pain engaged in self-injurious behavior more frequently than those with no abdominal pain.
Conclusions and implications: Findings indicated a high frequency of sleep problems, comorbid psychopathology, GI symptoms, and challenging behavior and demonstrated a relationship between GI symptoms and self-injurious behavior in children and adolescents with DS. This research illustrated the importance of investigating comorbid conditions in individuals with DS.
What this paper adds?: Down Syndrome (DS) is a genetic condition characterized by trisomy 21 and is a leading cause of intellectual disability worldwide. The prevalence of DS is commonly associated with advanced maternal age and is associated with multiple comorbid conditions. The current study aimed to investigate the frequency of and relationship between sleep problems, gastrointestinal symptoms, comorbid psychopathology, and challenging behavior in children and adolescents with DS. High-frequency levels were found for sleep problems (100 %), challenging behavior (100 %), gastrointestinal symptoms (74.8 %), and moderate to severe levels of the different comorbid psychopathologies (tantrum=80 %; repetitive behavior=63 %; avoidant

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behavior=82 %; worry/depressed=61 %; conduct behavior=100 %; over-eating=100 %; under-eating=100 %). Results indicated a significant difference in self-injurious behavior frequency between individuals who presented with abdominal pain and those who did not. This study is the first to investigate the relationship of multiple comorbid conditions in a sample of children with DS. This paper adds to the literature by demonstrating the frequency of a number of comorbid conditions in children and adolescents with DS. The paper also adds novel findings to the literature by investigating the relationships between comorbid conditions in this population. The findings of this paper highlighted the frequency and comorbidities that exist between gastrointestinal symptoms, sleep problems, comorbid psychopathology, and challenging behavior. Analyses indicated that those who presented with abdominal pain, engaged in self-injurious behavior more frequently.

Sleep problems, gastrointestinal symptoms, comorbid psychopathology, and challenging behavior in children and adolescents with Down Syndrome.

1. Introduction

1.1. Down syndrome

Down syndrome (DS) is one of the most common chromosomal abnormalities (Weijerman & de Winter, 2010) and is a leading cause of intellectual disability worldwide (Asim et al., 2015). The prevalence of DS is commonly associated with advanced maternal age (Morris et al., 2002). According to the National Birth Defects Prevention Network annual data report from 2010–2014, it is estimated that the prevalence of DS in the United States is 14.14 per 10,000 live births and 15.74 per 10,000 live births when adjusted for maternal age (Mai et al., 2019).

There are a number of phenotypes associated with DS, including memory and learning issues, congenital heart disease, leukemia, cancers, and Hirschsprung disease (Asim et al., 2015). Children with DS have increased risks of DS-specific comorbidities, including vision disorders, wheezing airway disorders, congenital defects of the gastrointestinal tract, obesity, transient myeloproliferative disorder, and atlantoaxial instability (Asim et al., 2015; Weijerman & de Winter, 2010).

Furthermore, compared to children without DS, children with DS are at a higher risk of hearing loss, ear infections, obstructive sleep apnea (OSA), hip dislocation, thyroid disease and iron deficiency anemia (Chen et al., 2007; Gibson et al., 2005; Murphy et al., 2008; Prasher, 2005). Poor muscle tone is associated with infants with DS, affecting the strength, mobility, and range of motion of the muscles in the mouth, face, and neck (Kumin et al., 1991). Heart defects can also be prevalent in up to 40 % of children with DS (Lewis & Kritzinger, 2004). Medical problems associated with behavior changes include vision or hearing deficits, thyroid function, celiac disease, anemia, gastroesophageal reflux, constipation, depression, anxiety, and sleep apnea (Patterson, 2020). Physiological characteristics associated with DS also pose an increased risk of developing numerous sleep problems.

1.2. Down syndrome and sleep problems

Sleep problems are common, with up to 74.1 % of children and adolescents with DS presenting with sleep problems (Maris et al., 2016). Sleep problems include bedtime resistance, sleep duration, sleep anxiety, night waking, parasomnias, daytime sleepiness, and sleep-disordered breathing (Hoffmire et al., 2014). Behavioral sleep problems were found to affect 65 % of children with DS, compared to 23 % of typically developing children. Previous research has identified obstructive sleep apnea as a pervasive sleep disorder for up to 84 % of children with DS, compared to 35 % of typically developing children (Bassell et al., 2015). This is linked to the pre-existing physical characteristics typical of DS, including craniofacial and upper airway abnormalities, obesity, generalized hypotonia, tonsil and adenoid hypertrophy, macroglossia, glossoptosis, hypoplastic trachea, midfacial, and mandibular hypoplasia (Angriman et al., 2015). Untreated OSA has multiple health-related consequences, including increased risks for cardiovascular disease and impaired cognitive function (Robinson-Shelton & Malow, 2016). Children with DS and OSA scored 9 points lower on Verbal IQ tests than children with DS without OSA (Breslin et al., 2014).

The etiology of sleep problems in children and adolescents with DS is unknown, although a number of attributes increase susceptibility including medical and neurological disorders such as gastroesophageal reflux and epileptic seizures, poor sleep hygiene and environmental factors, medication use, anxiety and restless legs syndrome (Robinson-Shelton & Malow, 2016). Frequent arousals due to respiratory disruption resulting from OSA is likely to impede normal development of the frontal-subcortical circuits implicated in disruptive behavioral disorders such as Attention-deficit/hyperactivity disorder (AD/HD) (Hodges et al., 2012).

1.3. Down syndrome and gastrointestinal symptoms

Digestion, absorption, excretion, and protection are the primary functions of the gastrointestinal tract. There are a series of organs from the mouth to the anus that play distinct roles to achieve these functions (Cheng et al., 2014). Gastrointestinal (GI) symptoms that may be exhibited by children with DS include vomiting, diarrhea, abdominal pain and discomfort, and constipation (Holmes, 2014). Children displaying these symptoms can develop structural and functional disorders of the GI tract and related structures (Holmes, 2014).

According to Spaphis and Wilson (1999), over three-quarters of neonates attending special clinics for DS may present with GI problems, including feeding difficulties and developmental anomalies. Approximately 5 % of infants with DS are born with an anomaly of the GI tract (Davidson, 2008), including duodenal atresia, annular pancreas, imperforate anus, and esophageal atresia with tracheoesophageal fistula (Pameijer et al., 2000).

It is possible for obstructions of the GI tract to be detected pre-birth. However, on the occasion that a diagnosis is not made, symptoms indicating abdominal pain that suggest the presence of bowel obstruction and the need for surgical intervention include no bowel action, vomiting, and a distressed baby (Holmes, 2014). The prevalence of celiac disease is between 5 % and 15 % among individuals with DS, making it more common than among the general population (Mackey et al., 2001). This is also the case for Hirschsprung disease (Davidson, 2008).

1.4. Down syndrome and comorbid psychopathology

Comorbid psychopathology is a term used to describe the occurrence of two or more psychopathology in the same individual (Matson & Nebel-Schwalm, 2007). Comorbid psychopathology consists of a number of psychological disorders, including mood disorders, anxiety disorders, conduct and oppositional defiant disorders (ODD), AD/HD, and schizophrenia (Lanyi et al., 2022). Specific to children with DS, the most common psychopathological disorders are AD/HD, anxiety and mood disorders, ODD, and autism spectrum disorder (ASD) (Marino et al., 2019).

The developmental disorder AD/HD affects 5 % of the general population (Banaschewski et al., 2017), 14–43.9 % of the population with DS (American Psychological Association, 2013), and approximately 30 % of children (aged 2–4 years) with DS (Green et al., 1989). According to Ersoy et al. (2018), the three main symptoms of AD/HD are inattention, impulsivity, and hyperactivity. Conduct disorders have a lower prevalence than other psychopathologies in children with DS, affecting approximately 10 % (Coe et al., 1999). In a study carried out on 211 children with DS, stubbornness was reported in 79 %, and disobedience was reported in 74 % (Dykens & Kasari, 1997). Additionally. the presence of DS is a risk factor for developing depression (McGuire & Chicoine, 1996). Common symptoms of depression in DS are changes in sleep and appetite patterns (81.8 %), agitation (72 %), and anxiety (40.9 %; Myers & Pueschel, 1995). Depressive symptoms were recorded in a retrospective study of 832 children with DS, showing a prevalence of symptoms of 9.6 % in children aged 5–11 years and 7.6 % in children aged 12–21 years (Downes et al., 2015).

1.5. Down syndrome and challenging behavior

Challenging behavior, defined by Emerson (2001), includes aggression, self-injurious behaviors, stereotypies, and behaviors considered damaging to the individual or others. Research found that challenging behavior among individuals with intellectual disabilities has a prevalence rate of 10–15 % (Emerson et al., 2001). Children with DS show higher rates of attention problems, social withdrawal, noncompliance, and compulsions than typically developing children (Evans & Gray, 2000). Challenging behavior scores were also found to be higher in adolescents with DS than in the normative sample of adolescents without DS and increased with the severity of intellectual disability (van Gameren-Oosterom et al., 2013).

The increased risk for children with DS to engage in challenging behavior due to a characteristic behavioral phenotype, including the early development of avoidant and attention-motivated behavior, can lead to reduced learning opportunities (Feeley & Jones, 2006). Early intervention for challenging behaviors is important for children with DS as persistent challenging behaviors pose a risk for social exclusion from community settings such as schools. This is notable as education settings have been found to lead to more positive outcomes for children with DS (Buckley et al., 2002). The rationale for investigating the relationship between these comorbidities is to assess the frequency and severity with which a cohort of children with DS display each condition. These findings will then highlight the importance of developing broad and multi-dimensional treatment options to meet such common yet complex needs.

1.6. Pilot study

Caregivers of children with DS utilize a wide variety of treatments for their child, with and without empirical support. Neil et al. (2018) assessed the number and type of treatments used, the child characteristics which influence the number of treatments used, and the caregiver's rating of treatment efficacy in a study of 162 participants. The study found that caregivers access an average of five treatments for their child. Child characteristics such as age and race can influence the number of treatments used, and therefore need better access to educational materials to make informed decisions regarding treatment options (Neil et al., 2018). While data were collected on treatments, the current study focused on data that were collected on comorbid conditions.

1.7. Current study

The first aim of the current study is to investigate the frequency of sleep problems, GI symptoms, comorbid psychopathology, and challenging behavior in children and adolescents with DS. The second aim is to determine if there is a relationship between GI symptoms, sleep problems, comorbid psychopathology, and challenging behavior. The third aim is to investigate if any of these comorbid conditions are predictors of GI symptoms.

2. Method

2.1. Sample

The study sample comprised 123 children and adolescents with a diagnosis of DS. The age range of the children was from 1 to 17 years ($M = 7.35$; $SD = 4.95$). Within the current sample, 54 % of children ($n = 66$) were male, while 46 % ($n = 57$) were female.

2.2. Procedure and Informants

The study protocol was reviewed and approved by the Institutional Review Board at Michigan State University. The web-based survey was distributed via chapters of the Global DS Foundations [http://www.globaldownsyndrome.org] and via colleagues, who then distributed it to caregivers of children with DS. The survey was live from June 2016 to January 2017. Participants accessed the questionnaire after providing informed consent, and all submitted responses were stored on a secure, university-controlled server. Participation was confidential, as no identifying information was collected, and participants did not receive compensation. Participants were parents of children and adolescents diagnosed with DS who then completed rating scales independently according to the instructions printed on the online questionnaire.

2.3. Measures

2.3.1. Demographic information

The first and second authors developed the questionnaire based on existing literature investigating caregiver treatment use among individuals with other developmental disabilities (Green et al., 2006; Goin-Kochel et al., 2009; Hume et al., 2005; Martin et al., 2013). As reported in the pilot study (Neil et al., 2018), twenty-five questions assessed the demographic characteristics of primary and secondary caregivers and the child with DS (e.g., country of residence, age, gender, race/ethnicity, education, marital status).

2.3.2. Children's sleep habits questionnaire (CSHQ)

The CSHQ (Owens et al., 2000) is a 52-item parental-report, sleep-screening instrument designed for typically developing children ages 4 to 10 years. However, it has been used with younger (Goodlin-Jones et al., 2008) and older children with ASD (Goldman et al., 2011). Forty-two of the items are rated on a three-point Likert scale, with the responses being 'Rarely' (never or one time a week), 'Sometimes' (2 to 4 times a week), and 'Usually' (5 or more times a week). Each question was asked in relation to the previous week. The second column of questions is to determine if the item is considered a problem for caregivers. Besides each item, parents can choose 'Yes,' 'No,' or 'N/A' under the 'Problem?' column. Thirty-three of the items are used in deriving the total sleep disturbance score and the subscales of the questionnaire. There are 8 subscales of the CSHQ, including bedtime resistance, sleep onset delay, sleep duration, sleep anxiety, night wakings, parasomnias, daytime sleepiness, and sleep-disordered breathing. The CSHQ is not intended to be used to diagnose specific sleep disorders but rather to identify sleep problems and the possible need for further evaluation. While there are no established "norms" for the total subscale scores, a total CSHQ score of 41 has been reported to be a sensitive clinical cut-off for identification of probable sleep problems (Owens et al., 2000). The CSHQ has been used in a number of studies with children with DS (Arias-Trejo et al., 2021; Breslin et al., 2011; Carter et al., 2008; Choi et al., 2019; Churchill et al., 2015; Esbensen & Hoffman, 2017, 2018; Esbensen, Hoffman, Beebe et al., 2018; Esbensen, Hoffman, Stansberry et al., 2018; Fernandez et al., 2017; Hoffmire, 2012; Hoffmire et al., 2014; Kelmanson, 2017; Lukowski & Milojevich, 2017; Lukowski et al., 2020; Maris et al., 2016).

2.3.3. Gastrointestinal symptom inventory

The Gastrointestinal Symptom Inventory (Autism Treatment Network, 2005) is a 35-item questionnaire that was developed by the Autism Treatment Network (ATN) with additional items should a child exhibit certain symptomatology, and therefore includes 77 items in total. The ATN is the first network of hospitals and physicians dedicated to developing a model of comprehensive medical care for children and adolescents with autism through seventeen participating institutions in the U.S. and Canada. The questionnaire was based on previous questionnaires and on clinical symptom assessments for children with autism and identified GI disorders. The inventory is scored initially dichotomously (i.e., whether the child has any GI symptoms) and then allows branching into specific areas of symptomatology: abdominal pain, abnormal bowel movements, reflux, and food insensitivity. These branches allow the determination of rates of these symptoms in the child. The GI Inventory has been employed in published research (Leader, O'Reilly et al., 2021; Mazefsky et al., 2014; Mazurek et al., 2013; Williams et al., 2012a; Williams et al., 2012b; Williams et al., 2010). While the Gastrointestinal Symptom Inventory has not been used with individuals with DS, it has been used in a number of published studies with children with developmental and genetic conditions, such as cerebral palsy, 22q11.2 deletion syndrome, and Duplication 15q syndrome (Leader et al., 2020; Leader, Forde et al., 2021; Leader, Molina Bonilla et al., 2021).

2.3.4. Autism spectrum disorder – comorbid for children (ASD-CC)

The ASD-CC (Matson & González, 2007) is a 39-item informant-based rating scale designed to assess symptoms of psychopathology and emotional difficulties commonly occurring with ASD. Items are included to address conditions such as AD/HD, depression, conduct disorder, eating disorders/difficulties, OCD, specific phobias, and tic disorders. Caregivers rate each item to the extent it has been a recent problem as either 0 = "not a problem or impairment; not at all," 1 = "mild problem or impairment," 2 = "severe problem or impairment," or X = "does not apply or don't know." Inter-rater and test–retest reliability for the ASD-CC has been found to be

moderately good ($k = .46$ and $k = .51$, respectively) with very good internal consistency ($\alpha = .91$) reported (Matson & Dempsey, 2008). Factor analysis yielded seven subscales for the ASD-CC: 1) Tantrum Behavior, 2) Repetitive Behavior, 3) Worry/Depressed, 4) Avoidant Behavior, 5) Under-Eating, 6) Conduct, and 7) Over-Eating. Construct validity was established for Tantrum Behavior, Worry/Depressed, Repetitive Behavior, Conduct, and Over-Eating factors. While the ASD-CC has not been used with individuals with DS, it has been used in a number of published studies with children with other developmental and genetic conditions (Leader et al., 2020; Leader, Forde et al., 2021; Leader, Molina Bonilla et al., 2021).

2.3.5. Behavior problems inventory - short form (BPI-S)

The BPI-S (Rojahn et al., 2012a) is an informant-based behavior rating tool designed to evaluate maladaptive behaviors in individuals with intellectual disabilities. The rating scale uses the same system as the BPI-01 (Rojahn et al., 2001) but has fewer items. It consists of 30 items and has three subscales: Self-injurious behavior (eight items), Aggressive/destructive behavior (10 items), and Stereotyped behavior (12 items). Each item on the Self-injurious behavior and Aggressive/destructive behavior subscales is rated on frequency and severity scales. The Stereotyped behavior subscale is rated on a frequency scale only. Each frequency scale was rated from 'Never/No problem,' 'Monthly,' 'Weekly,' 'Daily,' to 'Hourly.' Each severity scale was rated from 'Mild,' 'Moderate,' to 'Severe.' Rojahn et al. (2012b) investigated the reliability and validity of the BPI-S, which was deemed psychometrically sound. The internal consistency values on the BPI-S frequency sub-scales ranged from fair (Self-injurious Behavior) to good (Aggressive/Destructive Behavior and Stereotyped Behavior). The BPI-01 has been used with young children and adults with DS (Lundqvist, 2013; Medeiros et al., 2013). The BPI-S has been used in studies with adults with intellectual disabilities, including a study that included 36 individuals who had DS (Bowring et al., 2017).

3. Results

3.1. Data analyses

Some data from children were excluded from analyses as not all sections of the questionnaires were completed. Therefore, each scale was completed by a different number of children; CSHQ ($n = 88$), the GI Symptom Inventory ($n = 123$), the BPI-S ($n = 44$), and the ASD-CC scale ($n = 105$). The correlation analysis conducted was assessed using Pearson's correlation matrix between GI symptoms (measured by GI symptom inventory), sleep problems (measured by CSHQ), comorbid psychopathology (measured by ASD-CC), and challenging behaviors (measured by BPI-S). Based on the findings of the correlation analyses, a *t*-test was conducted to assess if there was a difference in the severity and/or frequency of self-injurious behavior if they presented with one or more GI symptoms or not. A multiple regression was conducted to further explore whether sleep problems, challenging behavior, and comorbid psychopathology predicted GI symptoms in children and adolescents diagnosed with DS.

3.2. Sleep problems

Of the 88 participants who completed the CSHQ, the frequency of sleep problems in this sample was 100 % ($n = 88$), whereby a sleep problem was classified if a child presented with a score of 41 or more on the CSHQ. This study's mean score on the CSHQ was 83.73 ($SD = 6.61$). A summary of the subscale means and standard deviations of the subscales is included in Table 1.

3.3. Gastrointestinal symptoms

Of the 123 caregivers who completed the Gastrointestinal Symptom Inventory, the frequency of GI symptoms was 74.8 % ($n = 92$), with children and adolescents with DS experiencing at least one GI symptom within the previous three months. The mean number of total GI symptoms was 1.61 ($SD = 1.44$). The types of GI symptoms and the number of GI symptoms are presented in Table 2.

3.4. Comorbid psychopathology

The means and standard deviations were calculated for behaviors associated with psychopathology in the Autism Spectrum Disorder-Comorbid for Children (ASD-CC; $n = 105$). The mean score for the ASD-CC was 61.37 ($SD = 25.77$). The means and standard

Table 1
Means and standard deviations for subsales of CSHQ.

Variable	*M*	*SD*
Bedtime Resistance	15.32	2.54
Sleep Onset Delay	2.52	0.76
Sleep Duration	8.02	1.61
Sleep Anxiety	10.24	1.64
Night Wakings	7.64	1.66
Parasmonia	18.45	1.73
Sleep Disordered Breathing	7.88	1.60
Daytime Sleepiness	18.57	2.66

Table 2;
Frequency and Percentage of Specific Gastrointestinal Symptoms and Frequency and Percentage of Number of Gastrointestinal Symptoms.

Symptom	*n*	%	Number of Symptoms	*n*	%
Constipation	58	47.2 %	One symptom	34	27.6 %
Diarrhea	40	32.5 %	Two symptoms	31	25.2 %
Abdominal Pain	40	32.5 %	Three symptoms	16	13.0 %
Bloating	26	21.1 %	Four symptoms	3	2.4 %
Nausea	18	14.6 %	Five symptoms	6	4.9 %
Other GI Symptom	16	13.0 %	Six Symptoms	2	1.6 %

deviations for the subscales of the ASD-CC are shown in Table 3.

Although there is no cut-off for the total score, there are cut-offs for the seven subscales, and the value for each cut-off changes per subscale, as establisbed by Thorson and Matson (2012). Cut-offs are divided into no/minimal, moderate, and severe, depending on how far the score falls from the mean. Frequency and percentages represent how many children fell within that level of impairment for each subscale. A summary of the scores, frequency, percentages, and level of impairment are provided for each subscale in Table 3.

3.5. Challenging behavior

Table 4 shows the means and standard deviations, frequency and percentage of individuals with challenging behavior for all children ($n = 44$). In this study, all children were reported to have challenging behavior.

3.6. Correlation analyses

3.6.1. Correlations between GI symptoms, comorbid psychopathology, sleep problems, and challenging behavior

Pearson's correlation matrix was run between total GI symptoms and total comorbid psychopathology, total CSHQ, and BPI-S subscales. No significant relationship was found between the GI Symptom inventory and the total ASD-CC or between the GI Symptom inventory and the total CSHQ. A positive significant correlation with a medium effect size ($r = .27$, $p = .04$) was found between GI symptoms and the frequency of self-injurious behavior, as seen in Table 5. Therefore, further analysis was conducted to assess whether a significant relationship between GI symptoms and self-injurious behavior was present.

3.6.2. Correlations between comorbid psychopathology and challenging behavior

Pearson's correlation matrix was run between total comorbid psychopathology and BPI-S subscales. No significant relationship was found between the total ASD-CC with the BPI-S subscales, as shown in Table 5.

3.7. t-Tests

A series of independent *t*-tests were conducted to assess whether children with or without GI symptoms engaged in more frequent or more severe self-injurious behavior (SIB). Twelve independent *t*-tests were conducted with each GI symptom type (abdominal pain,

Table 3
ASD-CC subscale means, standard deviations and level of impairment.

Factor	*M*	*SD*	Level of Impairment	Frequency	Percentage
Tantrum	15.51	6.05	Mild	21	20.0 %
			Moderate	38	36.2 %
			Severe	46	43.8 %
Repetitive Behaviors	12.15	5.82	Mild	39	37.1 %
			Moderate	33	31.4 %
			Severe	33	31.4 %
Avoidant Behaviors	9.81	4.13	Mild	19	18.1 %
			Moderate	48	45.7 %
			Severe	38	36.2 %
Worry/Depressed	8.59	4.77	Mild	41	39.0 %
			Moderate	31	29.5 %
			Severe	33	31.4 %
Conduct Behaviors	6.50	3.96	Mild	0	0.00 %
			Moderate	55	52.4 %
			Severe	50	47.6 %
Over-Eating	4.68	2.18	Mild	0	0.00 %
			Moderate	63	60.0 %
			Severe	42	40.0 %
Under-Eating	4.13	2.49	Mild	0	0.00 %
			Moderate	77	73.3 %
			Severe	28	26.7 %

Table 4
Behavior Problems Inventory-Short Form (BPI-S) subscale means and standard deviations, frequency and percentage of individuals with challenging behavior.

Subscale	*M*	*SD*	*n*	%
At least 1 type of Challenging Behavior			44	100 %
Self-Injurious Behavior			32	73 %
Frequency	3.45	3.19		
Severity	9.14	2.63		
Aggressive/ Destructive Behavior			32	73 %
Frequency	3.77	5.87		
Severity	11.52	4.31		
Stereotyped Behavior			32	73 %
Frequency	7.91	10.21		

Table 5
Pearson's Correlation statistics for total scores for CSHQ, ASD-CC and GI Symptom Inventory and BPI-S subscales.

Variable	1.	2.	3.	4.	5.	6.	7.
1. Total GI Symptoms	-						
2. Total ASD-CC	-.04	-					
3. SIB frequency	.27 *	.02	-				
4. SIB severity	.17	-.10	.23	-			
5. Aggressive/Destructive Behavior frequency	.08	-.07	.51 * *	.10	-		
6. Aggressive/Destructive Behavior severity	.03	-.13	.14	.65 * *	.63 * *	-	
7. Stereotyped Behavior frequency	.10	.04	.59 * *	.21	.61 * *	.36 * *	-
8. Total CSHQ	-.14	.20	.06	-.06	.00	-.11	.19

Note:
* $p < .05$,
* * $p < .01$.

nausea, bloating, diarrhea, constipation, other GI symptoms) as the independent variable and with SIB frequency and SIB severity subscales of the BPI-S as the dependent variable. A Bonferroni correction was applied to control for multiple comparisons, and the alpha level was adjusted to.01. Results showed that only one of the *t*-test analyses was significant: abdominal pain and SIB frequency.

3.7.1. Abdominal pain and SIB frequency

Levene's test for equality of variance was not significant ($F = 2.94$, $p = 0.09$), ensuring homogeneity of variance. Results showed that there was a significant difference in self-injurious behavior frequency between those who presented with abdominal pain and those who did not ($t_{(42)} = -3.46$, $p = .001$). Children who had abdominal pain ($M = 6.20$, $SD = 3.58$), on average, engaged in self-injurious behavior more frequently than those without abdominal pain ($M = 2.65$, $SD = 2.62$), as represented by Figure 1.

3.8. Multiple regression analysis

3.8.1. Predictors of GI symptoms

A hierarchical multiple regression was conducted to examine if sleep problems, challenging behavior, and comorbid psychopathology predicted total GI symptoms in children and adolescents with DS. GI symptoms were chosen as the criterion variable in the regression based on the initial correlational analyses conducted where GI symptoms were found to be significantly correlated with SIB. Predictor variables were sleep problems, challenging behavior, and comorbid psychopathology. Multicollinearity was not present in the data. Pearson's correlation statistics for predictor variables were less than.7 (see Table 5). The variance inflation factor (VIF) scores were less than 10 (range 1.04–7.98) and tolerance scores were greater than.1 (range.13–.96). The results of the multiple regression as displayed in Table 6 show that the overall model was not significant, and did not contribute to the variance in frequency to GI

Table 6
Summary of Hierarchical Multiple Regression Model.

Variable	β	ΔR^2	Adjusted ΔR^2	*F* Change
ASD-CC Total	-.05			
CSHQ Total	-.18			
SIB frequency	.15			
SIB severity	.38			
Aggressive/Destructive Behavior frequency	.25			
Aggressive/Destructive Behavior severity	-.36			
Stereotyped Behavior frequency	-.12	.13	-.04	.77

symptoms ($F_{(7,\ 36)} = .77$, $p = .62$, $R^2 = .13$, adjusted $R^2 = -.04$).

4. Discussion

The current study investigated the frequency of GI symptoms, sleep problems, comorbid psychopathology, and challenging behavior in children and adolescents with DS. It was the first study to investigate the relationship between a number of comorbid conditions in children and adolescents with DS. Findings revealed high rates of sleep problems, GI symptoms, comorbid psychopathology, and challenging behavior among the sample.

One hundred percent of children and adolescents who completed the CSHQ presented with at least one sleep problem, with daytime sleepiness and parasomnias being the most common variables. This is a higher result than Breslin (2011), who found that 85 % of children with DS presented with sleep problems, and Choi et al. (2019), who found 83 %. The current study found no significant link between sleep problems and GI symptoms. However, older children may not be waking caregivers at night, so they may not know exact sleep patterns of their children. Kelmanson (2017) found that more sleep problems were associated with increased AD/HD in children and adolescents with DS. Contrary to previous research, sleep problems were not associated with increased instances of comorbid psychopathology in this study.

Over three-quarters (75.6 %) of the children presented with at least one GI symptom. This is similar to Spaphis and Wilson's (1999) findings with neonates with DS. Various GI symptoms were present in children and adolescents with DS, with constipation being the most prevalent (47.2 %) symptom as well as diarrhea and abdominal pain in 32.5 % each. GI symptoms, particularly abdominal pain, were correlated with self-injurious behavior frequency. This demonstrates a possible and interesting relationship between self-injurious behavior and abdominal pain in children and adolescents with DS. Self-injurious behaviors may have been used to communicate abdominal pain in children with less verbal ability. However, the relationship between this outcome and the communication abilities of the children and adolescents with DS was not addressed in this study, and is an avenue for future research.

Moderate and severe impairment levels of comorbid psychopathology were prevalent in this study, with tantrums, and repetitive and avoidant behaviors being the most severely reported psychopathologies. This supports findings from ASD studies (Tureck et al., 2014). Findings from the current study reported no correlation between comorbid psychopathology and challenging behavior in children and adolescents with DS. This finding contrasts with literature regarding infants and toddlers with ASD, where findings revealed greater levels of comorbid psychopathology were associated with more challenging behaviors (Matson et al., 2010). In addition, results revealed that comorbid psychopathology did not predict the presence of GI symptoms. Although previous ASD studies (Leader, Browne et al., 2022) showed that there was a relationship between GI symptoms and comorbid psychopathology, the current study did not indicate that comorbid psychopathology had a significant relationship with either sleep problems, challenging behavior, or GI symptoms for individuals with DS. This result suggests the relationship between these comorbid conditions is present in ASD but not in DS. Future research in this area is warranted.

Similar to sleep problems, challenging behavior was reported for all 44 children. All three subscales of challenging behavior – self-injurious behavior, aggressive/destructive behavior, and stereotyped behavior – were equally highly prevalent at 73 % among this sample. There was no significant relationship between comorbid psychopathology and challenging behavior which contrasts findings from a study conducted by Bowring et al. (2017) that used the BPI-S and found a link between DS and increased aggressive/destructive behavior but not with self-injurious behavior, stereotyped behavior, or challenging behavior. In the current study, correlational analyses showed that a positive significant correlation was found between GI symptoms and the frequency of self-injurious behavior. Children with abdominal pain engaged in self-injurious behavior more frequently than those without abdominal pain. This finding could be due to abdominal pain being the starting point of several other GI symptoms. An explanation for this finding may be that the function of children engaging in self-injurious behavior is to communicate their abdominal pain to caregivers. Children who are non-verbal may instead display their pain through challenging behavior (Leader, Abberton et al., 2022; Leader & Mannion, 2016).

Medeiros et al. (2013) measured the frequency and severity of challenging behaviors over one year using the BPI and found that rates of self-injurious behavior and stereotyped behavior had a stable frequency, while severity was unstable over time. Furthermore, aggressive/destructive behavior was stable in severity, while the frequency was unstable over time. Due to these findings, future research may be necessary into the frequency and severity of challenging behavior and GI symptoms over time. This result corresponds with findings from Peebles and Price (2012), in which individuals with intellectual disabilities initiate self-injurious behaviors in order to address the presence of irritating and painful sensations. Although there is no literature on this relationship in children and adolescents with DS, there are findings in ASD studies that show an increase in GI symptoms that appear to be associated with self-injurious behaviors (Soke et al., 2018). Based on these findings, future research should explore the relationship between communication levels and self-injurious behavior and abdominal pain.

There were a number of limitations which should be highlighted for the current study. Firstly, the scales used were completed by the children's caregivers, so there could be limitations to how reliable their verdict of abdominal pain versus another GI symptom may be. However, studies have found that parental reports are a valid measure for children diagnosed with cerebral palsy and ASD (Gorrindo et al., 2012; Salavati et al., 2018). Gorrindo et al. (2012) discussed how they would encourage the use of parental reports as their findings implied that parents were receptive to the existence of a gastrointestinal problem and were 92 % accurate when compared with the physicians' eventual diagnosis.

Another limitation of the current study was that not all parents completed every questionnaire. As stated above, 88 participants completed the CSHQ (sleep problems), 123 for the GI Symptom Inventory (GI symptoms), 44 completed the BPI-S (challenging behavior), and 105 completed the ASD-CC scale (comorbid psychopathology). A further critique of the findings of this paper could be in relation to sampling bias. Parents of children who are more likely to present with comorbid issues may have been more interested in

the topic and get involved in research in the area. In addition, another limitation of this study concerns the diversity of the sample. Future research could be conducted widening the diversity of the sample, in terms of race, ethnicity, and gender.

In conclusion, this study highlighted the frequency and comorbidities that exist between GI symptoms, sleep problems, comorbid psychopathology, and challenging behavior with an investigation into the relationships between comorbid conditions in this population. Several of our findings have clinical implications for practitioners in the area. First, the high frequency and percentages reported among this population for children and adolescents diagnosed with DS were also noted as having other comorbidities, including approximately 75 % reporting at least one GI symptom, high mean scores in sleeping problems, large frequencies in the moderate and severe ranges with comorbid psychopathologies and all children having challenging behavior with 73 % meeting the criteria for self-injurious behavior, aggressive/ destructive behavior, and stereotyped behavior respectively. Future research is needed to determine how comorbid conditions potentially interact with each other and how these conditions may further exacerbate those with DS's health and quality of life. Also, research needs to include additional objective measures of the comorbid conditions to complement the parental report. This could remove any potential sampling bias which may arise from parents reporting. Therefore, these findings can alert healthcare professionals working with individuals diagnosed with DS to these characteristics when screening/developing intervention plans. This may give practitioners currently working in the field a more thorough understanding of the comorbidities or challenges a person diagnosed with DS may be experiencing.

Compliance with ethical standards

None.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study protocol was reviewed and approved by the Institutional Review Board at Michigan State University.

Informed consent

Informed consent was obtained from all individual participants included in the study.

Declaration of Competing Interest

All the authors of this article declare that they have no conflict of interest.

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