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Age of Autism Spectrum Disorder Diagnosis and Comorbidity in Children and Adolescents with Autism Spectrum Disorder

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ABSTRACT

Aim: Research is required to study the relationship between age of autism spectrum disorder (ASD) diagnosis and the presence of comorbidities. Method: The Gastrointestinal Symptom Inventory, Autism Spectrum Disorder-Comorbid for Children, Behavior Problem Inventory-Short Form and Social Communication Questionnaire were completed by parents of 129 children and adolescents with a diagnosis of ASD. Results: Results revealed significant relationships between the age of ASD diagnosis, the presence of comorbidities and intellectual disability. Significant correlations were found between the age of ASD diagnosis and self-injurious and stereotyped behavior. Comorbid psychopathology significantly predicted the presence of GI symptoms. In addition, the relationship between comorbid psychopathology and challenging behavior in this study was reported as bi-directional as both comorbidities predicted one another in the sample. Conclusion: Future research needs to consider the role of comorbidities in relation to ASD diagnosis.

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Autism spectrum disorder; diagnosis; gastrointestinal symptoms; challenging behavior; comorbid psychopathology; comorbidity

Introduction

Autism Spectrum Disorder

Autism Spectrum Disorder (ASD) is a lifelong neurodevelopmental disorder characterized by deficits in social communication and social interaction, as well as restricted, repetitive patterns of behavior, interests or activities.[1] ASD is expressed on a continuum ranging from mild to severe. Some children may have strong language and intellectual abilities while others may not be verbal and may require lifelong care.

Age of Diagnosis

Research suggests that ASD can be reliably diagnosed as early as 24 months.[2] More recently, studies have found that the average age a child receives an ASD diagnosis is between four and five years.[3,4] Despite the growing prevalence of ASD and ASD awareness, previous research found that the age of ASD diagnosis has not decreased.[3]

An ASD diagnosis is important to access early intervention. Early intervention is associated with reduced intellectual, behavioral and functional impairments in ASD.[5] Research has also reported that early intervention increases adaptive functioning and intelligence quotient (IQ), as well as decreasing challenging behaviors in individuals with ASD.[6–8] A delayed diagnosis may result in ineffective treatment,[9] school placement, and limited access to programs and resources beneficial for ASD children.[3] Whereas an early diagnosis of ASD can expedite early intervention and effective outcomes[10] thus, highlighting the importance of early ASD diagnosis.

There are several factors that may influence the age a child receives a diagnosis. Firstly, those with a sibling already diagnosed are more likely to be receiving earlier diagnosis than those who are the first in the family seeking a diagnosis.[11] Secondly, socio-economic status (SES) also influences age of diagnosis, with those from lower SES receiving later diagnoses.[11] It has also been reported that those in rural areas are more likely to receive later diagnosis that those in urban settings.[12]

Comorbidity in Autism Spectrum Disorder

Comorbidity is defined as the existence of two or more disorders in the same individual.[13] The awareness of comorbid conditions related to ASD is extremely important in order to accurately diagnose one disorder as primary and another as secondary.[13] Common comorbid conditions in ASD include epilepsy, sleep problems, GI symptoms, toileting problems, behavioral problems, attention-deficit/hyperactivity disorder (AD/HD), anxiety and depression.[14–20] Research has found that 70% of children and adolescents with ASD have a minimum of one comorbid condition with social anxiety being the most reported symptom.[21]

Symptoms of a comorbidity may overlap and mask the symptoms of ASD, therefore leading to significant delays in an ASD diagnosis. For instance, one study found that ASD co-occurred with AD/HD in 59% of children with an ASD

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diagnosis.[22] Findings from this study revealed that age of ASD diagnosis was significantly later for children with a comorbidity. More specifically, age of diagnosis was on average 4 years older for children with a comorbid diagnosis of ASD and AD/HD, compared to ASD alone. Similarly, another study found that children with an initial diagnosis of AD/HD did not receive an ASD diagnosis for an average of 3 years later than those without comorbid AD/HD.[23]

Research focusing on how comorbidities can affect the age of ASD diagnosis is limited. Therefore, research exploring the specificity of this relationship requires further investigation. Accurately diagnosing comorbidities with ASD can significantly assist healthcare professionals in providing the best possible medication regiments for children while minimizing possible side effects.[24,25] In addition, the awareness of disorders comorbid with ASD is extremely important in order to eliminate the occurrence of diagnostic overshadowing biases.[21] This phenomenon occurs when the clinician fails to recognize, and consequently underdiagnoses the co-occurring disorder by falsely attributing the symptoms to the primary disorder.[26]

Gastrointestinal Symptoms

Numerous studies reveal greater incidence of GI symptoms in individuals with ASD compared to the general population.[27–29] Prevalence rates of GI symptoms in ASD range from 9% to 90%.[17,30] The presence of GI symptoms in ASD has been linked to various negative outcomes such as increased sleep problems, aggressive behavior, comorbid psychopathology, language regression, intellectual disabilities and social skills impairments.[31–34]

One study reported that the main GI symptoms include abdominal pain, chronic constipation, nausea, diarrhea and bloating.[30] Other symptoms include disaccharides deficiencies, abnormalities of the enteric nervous system, inflammation of the GI tract, and gastroesophageal reflux disease.[30] GI issues can cause immense discomfort and pain to an individual, which can result in increased levels of challenging behavior.[30]

Previous research has also found a relationship between GI symptoms and comorbid psychopathology.[32,33] Specifically, nausea can impact worry/depressed behavior, avoidant behavior and conduct behavior in children with ASD.[32,33] Abdominal pain and constipation is also related to higher levels of conduct behavior.[33] There is a need for further examination of the relationship between comorbid psychopathology and GI symptoms. Additionally, research investigating the impact of age of diagnosis of ASD on the presentation of GI symptoms is currently limited. This is an area that requires further investigation.

Challenging Behaviors

Challenging behaviors are defined as "behaviors that are culturally abnormal of such duration, intensity or frequency that places the person or others around them in physical jeopardy or behavior which is likely to seriously limit the use of or result in the person being denied the access to ordinary community facilities".[35 (p.3)] For children, the definition has been further refined to include aggression, self-injury and property destruction, and any behavior that inhibits with the learning or social interactions or is considered problematic by the child's family.[36] Research found that the prevalence for challenging behavior in children and adolescents with ASD is 93.7%.[37]

Challenging behaviors can occur as a reaction to experiencing physical pain or as a means of gaining attention from others.[17,38] Individuals with ASD sometimes lack the verbal ability to effectively communicate this information to others.[30,39,40] Parents or caregivers may not recognize the child's underlying reasons for displaying challenging behavior, which in turn can cause frustration for both the child and parent. Early identification of ASD symptoms is crucial so that the child can receive the most appropriate and effective interventions. Early intervention during the toddler and preschool years improves outcomes for most children with ASD.[41] Research has not yet focused on how challenging behavior can impact age of ASD diagnosis.

Comorbid Psychopathology

The most common comorbid psychopathological disorders that co-occur with ASD include depression, anxiety and AD/HD.[42] Prevalence rates in the literature for comorbid psychopathology range from 11% to 84%, depending on the comorbid psychopathologies being considered.[43] Little is known about the relationship between age of ASD diagnosis and comorbid psychopathology.

Current Study

Given the prevalence of comorbidity in ASD, research is needed to evaluate the age of ASD diagnosis and its relationship with comorbid conditions. Previous research has identified that a comorbid AD/HD diagnosis suggests a later ASD diagnosis,[22] yet little is known about how other comorbid conditions affect age of ASD diagnosis. Research investigating how comorbid conditions affect age of diagnosis of ASD is imperative, as an early diagnosis of ASD is important in order to access early intervention. The rationale for the current study aimed to expand on previous research by examining the age at which each participant was diagnosed with ASD, and how age of ASD diagnosis is related to other comorbid conditions such as GI symptoms, comorbid psychopathology and challenging behavior. The rationale behind choosing these comorbid conditions in the present study is that the relationships between these comorbidities and age of diagnosis have yet to be investigated in research. Previous research has also identified gender,[44] overshadowing of an ID,[45] medication[46] and early intervention[47] as influential factors on the age of ASD diagnosis. These variables were included as controls in this study.

Method

Participants

The participants in this study consist of 129 children and adolescents with a diagnosis of ASD in accordance with DSM-IV-TR criteria.[48] Diagnoses of each child were provided by

a licensed psychologist or pediatrician prior to participation in the study. Of the 129 children, 77.5% (n = 100) were males and 22.5% (n = 29) were female, ranging from 3 to 18 years (M = 111.56 months, SD = 46.13). An intellectual disability (ID) was reported in 45% (n = 71) of participants. Within those participants with an ID, 31 (23.1%) reported a mild ID, 19 (14.2%) reported a moderate ID, and 8 (6%) reported a severe ID.

Procedure and Informants

Informants were recruited through parent support groups, social media, and special schools. During the recruitment process it was stated that this study was looking for parents of children and adolescents with comorbid conditions and with no comorbid conditions to take part, as this would help us learn more about why some children present with these conditions and others do not. If parents/guardians wished to participate in the study, they were provided with a participant information sheet and a consent form to complete. After providing consent, parents received a battery of the below questionnaires to complete in their own time. Rating scales were completed independently by parents of children and adolescents diagnosed with ASD. Instructions were printed on the top of each questionnaire.

Measures

Demographic Information

A questionnaire constructed by the researchers provided information on the participant's age, gender, the age of ASD diagnosis, the presence/absence of an ID, and level of ID. Interventions participants were undergoing were asked to be stated, including Applied Behavior Analysis, eclectic intervention, other interventions, such as special needs assistance, or no intervention at all. Further, participants were asked to state if any medication was taken. Presence or absence of any current comorbid diagnosis such as epilepsy, AD/HD and an anxiety disorder were also reported.

Gastrointestinal Symptom Inventory

The Gastrointestinal Symptom Inventory[49] is a 35-item questionnaire that assesses GI symptoms. This measure includes questions about the presence, duration, and nature of various GI symptoms. The inventory is scored initially dichotomously (i.e. whether or not the child has any GI symptoms), whereby higher scores imply the presence of more GI symptoms. This tool has not been validated. It is based on previous questionnaires and on clinical symptom assessment for children with ASD and identified GI disorders. However, it has been successfully implemented in previous published research with children and adolescents with ASD.[50–54] The Cronbach alpha coefficient in this study was .72.

Autism Spectrum Disorder – Comorbid for Children (ASD-CC)

The ASD-CC[55] is a 39-item, informant-based rating scale designed to assess symptoms of psychopathology and emotional disturbances which commonly occur with ASD. Each symptom is rated on the extent to which it has been a recent problem (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). Mean scores and standard deviations for the subscales within the ASD-CC are calculated and compared to the established cutoffs of no/minimal impairment, moderate impairment, and severe impairment.[24] Factor analysis yielded seven subscales in the ASD-CC: tantrums, repetitive behavior, worry/depressed, avoidant behavior, under-eating, conduct and over-eating.[55] Interrater and test–retest reliability for the ASD-CC has been found to be moderately good,[56] with very good internal consistency reported (α = .91).[57]

Behavior Problems Inventory – Short Form (BPI-S)

The BPI-S[58] is a shortened version of the BPI-01.[59] Behaviors were categorized into three subscales: self-injurious behavior (8 items), aggressive/destructive behavior (10 items), and stereotyped behavior (12 items). Each item is rated by frequency (0 = never, to 4 = hourly) and severity (0 = no problem, to 3 = severe problem) using a Likert-Scale. The BPI-S is a widely used measure and yields strong psychometric properties with high internal consistency, presenting a Cronbach's alpha of (α = .91), with total frequency and severity subscales ranging from .89 to .83, respectively.[60] This instrument also depicts good test-retest and interrater reliability ranging from .65 to .91[60], as well as having strong evidence for confirmatory and discriminant validity.[61]

The Social Communication Questionnaire (SCQ)

The SCQ[62] is a 40-item parent report based on the Autism Diagnostic Interview-Revised (ADI-R).[63] The total score represents the severity of symptoms associated with ASD (range 0–39 for verbal and 0–33 for non-verbal children) with a higher score indicating greater severity of ASD symptoms. The suggested cut-off score for children under the age of five is 11[64,65] and 15 for children older than five years of age. The scale has high reliability ranging from .84 to .93, as well as diagnostic validity.[63] It has been established as a valuable screening tool in children.[64,66–68] Cronbach's Alpha in this study was .81.

Results

Descriptive Statistics

Demographic Information

Over a third of the participants (36%; n = 46) reported taking medication, with hormones, laxatives and anticonvulsant medications being the most prevalent (see Table 1). It was reported that 47.3% (n = 61) had a psychological or medical comorbid diagnosis, including AD/HD (14.7%, n = 19), anxiety disorder (18.6%, n = 24), dyspraxia (6.2%, n = 8), and epilepsy (1.5%, n = 2). Regarding interventions, 18.6% (n = 24) received Applied Behavior Analysis, while a further 17.1% (n = 22) reported receiving eclectic intervention. The remainder (64.3%) of the participants (n = 83) reported receiving other interventions, such as special needs assistance, or received no intervention at all.

Age of ASD Diagnosis

Age of ASD diagnosis was reported in months, ranging from 1 year and 6 months (18 months) to 17 years and 6 months

Table 1. Demographic information of study sample (N = 129).

		n	%
Age of Diagnosis			
	0–24 Months	7	5.4
	25–48 Months	53	41.1
	49–72 Months	31	24.0
	73–96 Months	16	12.4
	97–120 Months	8	6.2
	121–144 Months	8	6.2
	145–168 Months	2	1.6
	169–192 Months	3	2.3
	Above 193 Months	1	0.8
Medication			
	Anticonvulsants	8	6.2
	Antidepressants	7	5.5
	Stimulants	4	3.1
	Atypical Antipsychotics	4	3.1
	Laxatives	12	9.3
	Antihistamines	4	3.1
	Proton-pump Inhibitors	2	1.6
	Antispasmodic	3	2.3
	Corticosteroids	2	1.6
	Alpha2 Adrenergic Agonists	2	1.6
	Central Alpha Agonists	2	1.6
	Hormones	23	17.8
	Nutritional Supplements	5	3.9
	Other	8	6.2
Intervention			
	Applied Behavior Analysis	24	18.6
	Eclectic	22	17.1
	Other	83	64.3

(210 months), with the mean age of diagnosis being 5 years 5 months (64.66 months; *SD* = 38.22). Table 1 gives a summary of the ages of diagnoses across the study sample.

ASD Symptoms

ASD symptoms was measured using the SCQ. The mean SCQ score was 20.19 (*SD* = 6.5). Cutoff scores for ASD ranges from 11 for children under the age of five to 15 for those over 5 years.

Gastrointestinal Symptoms

Within the last 3 months, 82.2% (n = 106) of the participants presented with at least one GI symptom. Of these participants, 17.2% (n = 23) presented with one symptom, 17.2% (n = 23) with two symptoms, while 21.6% (n = 29) reported experiencing three symptoms. A further 11.2% (n = 15) presented with four symptoms and only 7.5% (n = 10) reported experiencing all five symptoms. The most common GI symptom reported was constipation (53.5%; n = 69) and abdominal pain (52.7%; n = 68). Diarrhea was reported in 42.64% (n = 55) of participants. Nausea affected 35.66% (n = 46) of the participants in the last 3 months. The least common symptom was bloating, with just 29.46% (n = 38) reporting symptoms.

Table 2. Means and standard deviations for subscales of the BPI-S (N = 129).

Subscale	*M*	*SD*
SIB Frequency	4.78	4.53
SIB Severity	3.93	3.62
Aggressive/Destructive Behavior Frequency	8.47	7.89
Aggressive/Destructive Behavior Severity	7.22	6.64
Stereotyped Behavior Frequency	15.64	8.91

Challenging Behavior

Challenging behavior was measured using the BPI-S, for which the mean and standard deviations were calculated for the three subscales (See Table 2). All participants (N = 129) reported at least one form of challenging behavior. All three forms were reported in 67.9% (n = 91), while 20.9% (n = 28) reported to present with two behaviors, and 7.5% (n = 10) presented with only one form of challenging behavior.

Comorbid Psychopathology

Comorbid Psychopathology was measured using the ASD-CC. The total score averaged at a mean of 37.74 (*SD* = 16.03), with subscales as follows: tantrum behavior (M = 10.28; *SD* = 4.84), repetitive behavior (M = 8.48; *SD* = 4.53), worry/depressed (M = 4.98; *SD* = 3.29), avoidant behavior (M = 7.35; *SD* = 3.07), under-eating (M = 1.75; *SD* = 2.14), conduct (M = 2.91; *SD* = 2.67), and over-eating (M = 1.89; *SD* = 1.77).

Analyses

A fixed effects Pearson's correlation was conducted to assess the relationship between the age of ASD diagnosis and the presence of an ID. To further investigate this relationship, an independent samples t-test was employed. Pearson's correlation was conducted to assess the association between the age of ASD diagnosis and parent reported medical or psychological comorbid conditions. To further investigate this relationship, an independent samples t-test was conducted. Pearson's correlations were carried out to examine the relationship between the age of ASD diagnosis and total GI symptoms, comorbid psychopathology, and challenging behavior with a Bonferroni adjusted alpha level of .008 per test (.05/6) as multiple comparisons were made. A series of hierarchical multiple regression analyses was conducted to determine predictors of GI symptoms, comorbid psychopathology, and challenging behavior.

Analyses of Age of ASD Diagnosis and Comorbid Conditions

Analyses of Age of ASD Diagnosis and Intellectual Disability

Pearson's correlation revealed a significant moderate correlation between the age of ASD diagnosis and the presence of an ID (r (129) = .30, p < .001). An independent t-test indicated a significant difference in age of diagnosis of ASD between individuals who had an ID and those who did not (t (125.19) = −3.71, p < .001). Children with an ID (M = 51.86, *SD* = 29.77) were diagnosed with ASD much earlier than children without an ID (M = 75.11, *SD* = 41.28).

Analyses of the Age of ASD Diagnosis with Medical or Psychological Comorbid Conditions

Pearson's correlation was carried out to examine the association between the age of ASD diagnosis and parent reported medical or psychological comorbid conditions. A negative correlation was found between the age of ASD diagnosis and the presence of a medical or psychological comorbid condition (r (129) = −.17, p < .05). An independent t-test indicated a significant difference in age of diagnosis of ASD between individuals who presented with a medical or psychological

comorbid condition and those who did not (t (122.74) = 2.01, p < .05). Children with a medical or psychological comorbid condition (M = 71.03, SD = 42.24) were diagnosed with ASD much later than children without a medical or psychological comorbid condition (M = 75.11, SD = 41.28).

Correlation Analyses of the Age of ASD Diagnosis with GI Symptoms and Comorbid Psychopathology

Pearson's correlations were carried out to examine the associations between age of ASD diagnosis and total GI symptoms; as well as the age of ASD diagnosis and comorbid psychopathology (as measured by the ASD-CC total scores). No significant correlations were found between these variables.

Correlation Analyses of the Age of ASD Diagnosis and Challenging Behavior

Pearson's correlations were conducted to investigate the relationship between age of ASD diagnosis and challenging behavior, as measured using the BPI-S. Analyses were conducted for each of the three subscales of the BPI-S (self-injurious behavior {SIB}; aggressive/destructive behavior; stereotyped behavior), including the frequency and severity of the SIB and the aggressive/destructive behavior subscales and the frequency of stereotyped behavior. Significant correlations were found between age of ASD diagnosis and the three subscales as presented in Table 3. A small negative correlation was reported between age of diagnosis and SIB frequency as well as SIB severity. A negative correlation was also found between age of diagnosis and stereotyped behavior frequency.

Hierarchical Multiple Regression Analyses

Predictors of GI Symptoms

At Block 1, age, gender, presence of an ID, medication and intervention were entered as control variables and were not significant in predicting GI symptoms. At Block 2, the addition of age of ASD diagnosis was not significant in predicting GI symptoms ($F_{(6,121)}$ = 1.50, p = .18, R^2 = .07). Comorbid psychopathology (as measured by the ASD-CC total scores) was entered in Block 3, and the model became statistically significant ($F_{(7,120)}$ = 2.19, p = .04, R^2 = .11), explaining 11% of the variance in GI symptoms. As can be seen in Table 4, total ASD-CC scores was the only significant predictor in Block 3 (p = .02). The addition of total BPI-S scores measuring challenging behavior in Block 4 was not significant in predicting GI symptoms ($F_{(8,119)}$ = 2.11, p = .04, R^2 = .13).

Table 3. Pearson's Correlations of age of ASD Diagnosis and Challenging Behavior subcategories (BPI-S).

		1	2	3	4	5	6
1	Age of ASD Diagnosis						
2	SIB Frequency	−.25**	−.08				
3	SIB Severity	−.19*	−.07	.89**			
4	Aggressive/Destructive Behavior Frequency	−.05	.12	.64**	.59**		
5	Aggressive/Destructive Behavior Severity	.02	.07	.58**	.57**	.92**	
6	Stereotyped Behavior Frequency	−.28**	−.29*	.54**	.58**	.42**	.39**

Note. * significant at the .05 level; **significant at the .01 level.

Table 4. Hierarchical regression for predictors of GI symptoms (GSI total).

Step	Variable	ß	ΔR²	Δ Adj R²	F change
1	Age	.08			
	Gender	.12			
	ID	.06			
	Medication	−.15			
	Intervention	−.09	.05	.02	1.38
2	Age of ASD Diagnosis	.17	.07	.02	2.06
3	Total ASD-CC	.22**	.11	.06	5.95**
4	Total BPI-S	.13	.12	.07	1.46

Note. Significance level: *p < .05, **p < .01.

Table 5. Hierarchical regression for predictors of challenging behavior (BPI-S total).

Block	Variable	ß	ΔR²	Δ Adj R²	F change
1	Age	−.17			
	Gender	−.03			
	ID	−.13			
	Medication	−.16			
	Intervention	−.01	.07	.03	1.83
2	Age of ASD Diagnosis	.11	.08	.03	.95
3	Total ASD-CC	.50**	.31	.27	40.53**
4	Total GSI	.10	.32	.27	1.46

Note. Significance level: *p < .05, **p < .01

Predictors of Challenging Behavior

At Block 1, the model including age, gender, presence of an ID, medication and intervention was not significant in predicting challenging behavior based on BPI-S total scores ($F_{(5,122)}$ = 1.82, p = .11, R^2 = .07). At Block 2, the addition of age of ASD diagnosis was not a significant predictor of challenging behavior. The addition of comorbid psychopathology (as measured by the ASD-CC total scores) in Block 3 measuring comorbid psychopathology significantly predicted challenging behavior, $F_{(7,120)}$ = 7.70, p = .001, R^2 = .31, explaining 31% of the variance. As can be seen in Table 5, comorbid psychopathology was the only significant predictor in Block 3 (p = .001). The addition of total GI symptoms scores in Block 4 was not significant in predicting challenging behavior.

Predictors of Comorbid Psychopathology

At Block 1, the model including age, gender, presence of an ID, medication and intervention was not significant in predicting comorbid psychopathology (as measured by the ASD-CC total scores). At Block 2, the addition of age of ASD diagnosis was not significant in predicting challenging behavior. At Block 3, the addition of BPI-S total scores measuring challenging behavior significantly predicted comorbid psychopathology, $F_{(7,120)}$ = 7.31, p = .001, R^2 = .299, explaining 29.9% of the variance. As can be seen in Table 6, total ASD-

Table 6. Hierarchical regression for predictors of comorbid psychopathology (ASD-CC total).

Block	Variable	ß	ΔR²	Δ Adj R²	F change
1	Age	.06			
	Gender	.04			
	ID	−.10			
	Medication	−.20*			
	Intervention	−.02	.06	.02	1.61
2	Age of ASD Diagnosis	.02	.06	.02	.040
3	Total BPI-S	.51**	.30	.26	40.53**
4	Total GSI	.12	.31	.27	2.27

Note. Significance level: *p < .05, **p < .01.

CC scores was the only significant predictor in Block 3 (p = .001). The addition of GI symptoms total scores in Block 4 was not significant in predicting comorbid psychopathology.

Discussion

This study investigated the age of ASD diagnosis and comorbid psychopathology, GI symptoms, and challenging behavior in children and adolescents with ASD. The current study found that the average age of ASD diagnosis was 5 years and 5 months. Despite the potential for early diagnosis of ASD with the advancement of ASD screening and diagnostic tools, diagnosis occurred at a later age. Previous research implies that a later diagnosis can result in a lack of early intervention affecting access to appropriate school placement and to beneficial resources for children with ASD.[3] In addition to this, early diagnosis is crucial for parents as a later diagnosis may mean they are lacking an understanding of their child's difficulties, not receiving the appropriate support, help and management strategies they need. Therefore, early diagnosis of ASD is imperative in order for children to access early intervention.

Results from this study found a relationship between the presence of a medical or psychological comorbid condition and the age at which the participant was diagnosed with ASD. On average, children with a medical or psychological comorbid condition were being diagnosed thirteen months later than children without a medical or psychological comorbid condition. Consistent with previous research,[22] this finding indicates that participants received a later diagnosis of ASD if they presented with a medical or psychological comorbid condition, which in turn can affect the provision of receiving early intervention. Diagnostic overshadowing bias can occur where clinicians focus on the presence and symptoms of one condition, and not another condition. A greater awareness of the co-occurrence of other conditions with ASD is vital in order for children to receive a correct diagnosis. It is also important that children receive the treatment needed for the comorbid conditions that they present with.

Children diagnosed with an ID were diagnosed with ASD on average 23 months earlier than children without a co-occurring diagnosis of ID. It may be the case that when children were diagnosed with an ID, they also showed symptoms of ASD and were therefore, screened for ASD earlier. This is an important finding as it highlights the need to screen for ASD and other co-occurring conditions earlier when diagnosing ID.

Age of diagnosis of ASD was found to be associated with challenging behavior. Specifically, there was a relationship between age of ASD diagnosis and self-injurious behavior, and stereotyped behavior. It was found that participants exhibited slightly lower SIB frequency and severity and stereotyped behavior when their age of diagnosis of ASD was later. This may be due to parents seeking professional help at an earlier stage if their child presented with symptoms such as SIB and stereotyped behavior. Where children with ASD do not present with SIB or stereotyped behavior, their diagnosis may be received later, as some professionals may associate ASD with more severe symptoms such as SIB or stereotyped behavior.

Comorbid psychopathology predicted GI symptoms. It may be hypothesized that individuals with ASD experience more GI symptoms when psychopathology is present. Previous research has identified a relationship between these comorbidities in ASD. Research has indicated that anxiety significantly contributed to the prediction of chronic constipation, chronic abdominal pain, chronic bloating, and chronic nausea in children and adolescents with ASD.[53] Research has reported that chronic GI symptoms were more common in children with ASD and clinical anxiety than children with ASD without anxiety.[54] Given the complexity of brain–gut connections, complex bidirectional relationships among these variables are also evident in the ASD population.[55,69,70] The relationship between comorbid psychopathology and GI symptoms is one that needs to be further examined.

Comorbid psychopathology and challenging behavior were found to be predictors of one another within this sample. This suggests that the relationship between these two comorbidities are bi-directional. Previous research has found that there is a relationship between comorbid psychopathology and challenging behaviors in ASD.[31–34,71] This finding is important as the clinical significance found between these comorbidities predicting one another suggests that individuals with ASD may require more support.

The findings of this study present significant practical implications for ASD assessment and early intervention. As later age of diagnosis predicts more self-injurious behavior particularly in those who present with a medical condition, this suggests a need to improve the early assessment of ASD which may improve treatment outcomes for those with a comorbid condition. The findings from this study also present implications for the additional support for those with comorbid psychopathology, as the relationship between comorbid psychopathology and challenging behavior has been shown to be bi-directional. Overall, the process of obtaining an ASD diagnosis is complex, there is a fundamental need to ensure that families have access to appropriate interventions as well as timely and accurate ASD diagnoses.

The current study had some limitations. The data obtained was by parental report, which can be argued to be a subjective measure of behavior. However, previous research has found that parental reports of GI symptoms are highly correlated with the findings of the evaluations of clinicians.[31] In addition, there is potential for sampling bias in this research. It may have been the case that mainly parents of children and adolescents presenting with comorbid conditions decided to participate rather than parents of children and adolescents without these issues. However, every effort was made when recruiting participants to also involve parents of children and adolescents who do not have such comorbidities. The current sample had a relatively late age of diagnosis, which could be considered a limitation of the current study as this may be due to geographical constraints. The majority of the sample were from Ireland and the United Kingdom. It should also be noted there may be external factors responsible for delayed age of diagnosis, as two-thirds of child health ASD assessment teams in the United Kingdom do not maintain a well-defined time scale for assessment, with the other third of teams reporting not meeting targets for early diagnosis, suggesting a systematic delay in ASD diagnosis.[3] Data were not collected on racial/

ethnic backgrounds. Children from minoritized racial/ethnic backgrounds often have later diagnosis of ASD. Future research needs to consider the impact of racial/ethnic backgrounds on age of diagnosis of ASD and also needs to consider how this could impact comorbid conditions.

The need for future research in ASD diagnosis is imperative as the age of diagnosis is an important factor for long-term outcomes for children with ASD. The findings highlight the importance of promoting awareness about the early signs of ASD, encouraging parents to raise their concerns with their child's pediatrician from a young age and promoting vigilant routine checkups with respect to developmental delays and core features of ASD, thereby allowing the provision of early intervention if necessary. There is often a high prevalence of comorbid disorders that get diagnosed alongside ASD.[42] Our findings show that children with some comorbid disorders are more likely to receive an earlier diagnosis of ASD than those without a comorbid disorder. This may be due to ASD symptoms being discovered while screening for a comorbid disorder and shows that awareness of early ASD signs in children without a comorbid disorder is important in identifying and diagnosing ASD earlier. In addition, the findings show that lower frequencies of challenging behavior are associated with later diagnosis. This shows the importance of awareness of the early signs of ASD in any form. It may be possible that this result is due to individuals not taking ASD symptoms as seriously if they do not come in more obvious or severe symptoms such as SIB.

In conclusion, this study investigated the relationship between age of ASD diagnosis with a number of comorbid conditions including challenging behaviors, GI symptoms, and comorbid psychopathology. A number of novel findings were reported such as the relationship between the age of ASD diagnosis and challenging behavior. Relationships between comorbid psychopathology and the presence of GI symptoms and challenging behavior were also found. Future research needs to consider comorbid conditions when researching age of ASD diagnosis.

Disclosure Statement

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

Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the National University of Ireland Galway and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent

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

References

1. American Psychiatric Association. 2013. Diagnostic and statistical manual of mental disorders (DSM-5). Washington, DC: American Psychiatric Pub.
2. Steiner AM, Goldsmith TR, Snow AV, Chawarska K. Practitioner's guide to assessment of autism spectrum disorders in infants and toddlers. J Autism Dev Disord. 2012;42(6):1183–96. doi:10.1007/s10803-011-1376-9.
3. Brett D, Warnell F, McConachie H, Parr JR. Factors affecting age at ASD diagnosis in UK: no evidence that diagnosis age has decreased between 2004 and 2014. J Autism Dev Disord. 2016;46(6):1974–84. doi:10.1007/s10803-016-2716-6.
4. Zwaigenbaum L, Bauman ML, Stone WL, Yirmiya N, Estes A, Hansen RL, McPartland JC, Natowicz MR, Choueiri R, Fein D, et al. Early identification of autism spectrum disorder: recommendations for practice and research. Pediatrics. 2015;136 (Supplement):S10–S40. doi:10.1542/peds.2014-3667C.
5. Fountain C, King MD, Bearman PS. Age of diagnosis for autism: individual and community factors across 10 birth cohorts. J Epidemiol Community Health. 2011;65(6):503–10. doi:10.1136/jech.2009.104588.
6. Magiati I, Tay XW, Howlin P. Cognitive, language, social and behavioural outcomes in adults with autism spectrum disorders: a systematic review of longitudinal follow-up studies in adulthood. Clin Psychol Rev. 2014;34(1):73–86. doi:10.1016/j.cpr.2013.11.002.
7. McGarrell M, Healy O, Leader G, O'Connor J, Kenny N. Six reports of children with autism spectrum disorder following intensive behavioral intervention using the Preschool Inventory of Repertoires for Kindergarten (PIRK®). Research in Autism Spectrum Disorders. 2011;65(3):503–10. doi:10.1016/j.rasd.2009.02.006.
8. Oono IP, Honey EJ, McConachie H. Parent-mediated early intervention for young children with autism spectrum disorders (ASD). Evidence-Based Child Health: A Cochrane Review Journal. 2013;8 (6):2380–479. doi:10.1002/ebch.1952.
9. Harris SL, Handleman JS. Age of IQ at intake as predictors of placement for young children with autism: a four-to six-year follow-up. J Autism Dev Disord. 2000;30(2):137–42. doi:10.1023/A:1005459606120.
10. Dawson G. Early behavioral intervention, brain plasticity, and the prevention of autism spectrum disorder. Dev Psychopathol. 2008;20(3):775–803. doi:10.1017/S0954579408000370.
11. Emerson ND, Morrell HE, Neece C. Predictors of age of diagnosis for children with autism spectrum disorder: the role of a consistent source of medical care, race, and condition severity. J Autism Dev Disord. 2016;46(1):127–38. doi:10.1007/s10803-015-2555-x.
12. Mandell DS. Factors associated with age of diagnosis among children with autism spectrum disorders. Pediatrics. 2005;116 (6):1480–86. doi:10.1542/peds.2005-0185.
13. Matson JL, Nebel-Schwalm MS. Comorbid psychopathology with autism spectrum disorder in children: an overview. Research in Developmental Disabilities. 2007;28(4):341–52. doi:10.1016/j.ridd.2005.12.004.
14. Francis K, Mannion A, Leader G. The assessment and treatment of toileting difficulties in individuals with autism spectrum disorder and other developmental disabilities. Review Journal of Autism and Developmental Disorders. 2017;4(3):190–204. doi:10.1007/s40489-017-0107-3.
15. Mannion A, Leader G. Attention-deficit/hyperactivity disorder (AD/HD) in autism spectrum disorder. Res Autism Spectr Disord. 2014a;8(4):432–39. doi:10.1016/j.rasd.2013.12.021.
16. Mannion A, Leader G. Epilepsy in autism spectrum disorder. Res Autism Spectr Disord. 2014b;8(4):354–61. doi:10.1016/j.rasd.2013.12.012.
17. Leader G, Mannion A. Gastrointestinal Disorders. In: Matson JL, editor. Comorbid conditions among children with autism spectrum disorders (pp.257-281). Cham, Switzerland: Springer. 2016b.
18. Mannion A, Leader G. Sleep problems in autism spectrum disorder: a literature review. Review Journal of Autism and Developmental Disorders. 2014c;1(2):101–09. doi:10.1007/s40489-013-0009-y.

19. Mayes SD, Calhoun SL, Murray MJ, Zahid J. Variables associated with anxiety and depression in children with autism. J Dev Phys Disabil. 2011;23(4):325–37. doi:10.1007/s10882-011-9231-7.
20. Williams S, Leader G, Mannion A, Chen J. An investigation of anxiety in children and adolescents with autism spectrum disorder. Res Autism Spectr Disord. 2015;10:30–40. doi:10.1016/j.rasd.2014.10.017.
21. Simonoff E, Pickles A, Charman T, Chandler S, Loucas T, Baird G. Psychiatric disorders in children with autism spectrum disorders: prevalence, comorbidity, and associated factors in a population-derived sample. J Am Acad Child Adolesc Psychiatry. 2008;47(8):921–29. doi:10.1097/CHI.0b013e318179964f.
22. Stevens T, Peng L, Barnard-Brak L. The comorbidity of ADHD in children diagnosed with autism spectrum disorder. Research in Autism Spectrum Disorders. 2016;31:11–18. doi:10.1016/j.rasd.2016.07.003.
23. Yee MM, Millichap JG. Relationship between Age at Diagnosis of ADHD and ASD.. Pediatric Neurology Briefs. 2015;29(10):78. doi:10.15844/pedneurbriefs-29-10-5.
24. Thorson RT, Matson JL. Cutoff scores for the Autism Spectrum Disorder – comorbid for Children (ASD-CC). Res Autism Spectr Disord. 2012;6(1):556–59. doi:10.1016/j.rasd.2011.07.016.
25. Van Steensel FJ, Bögels SM, De Bruin EI. Psychiatric comorbidity in children with autism spectrum disorders: a comparison with children with ADHD. J Child Fam Stud. 2013;22(3):368–76. doi:10.1007/s10826-012-9587-z.
26. Neil N, Moum L, Sturmey PC Comorbidity among children and youth with autism spectrum disorder. Children and youth with autism spectrum disorder: recent advances and innovations in assessment, education, and intervention. 2014:26–41.
27. Chaidez V, Hansen RL, Hertz-Picciotto I. Gastrointestinal problems in children with autism, developmental delays or typical development. J Autism Dev Disord. 2014;44(5):1117–27. doi:10.1007/s10803-013-1973-x.
28. Fulceri F, Morelli M, Santocchi E, Cena H, Del Bianco T, Narzisi A, Calderoni S, Muratori F. Gastrointestinal symptoms and behavioral problems in preschoolers with Autism Spectrum Disorder. Digestive and Liver Disease. 2016;48(3):248–54. doi:10.1016/j.dld.2015.11.026.
29. McElhanon BO, McCracken C, Karpen S, Sharp WG. Gastrointestinal symptoms in autism spectrum disorder: a meta-analysis. Pediatrics. 2016;46(5):127–38. doi:10.1542/peds.2013-3995.
30. Buie T, Campbell DB, Fuchs GJ, Furuta GT, Levy J, Van De Water J, Whitaker AH, Atkins D, Bauman ML, Beaudet AL, et al. Evaluation, diagnosis, and treatment of gastrointestinal disorders in individuals with ASDs: a consensus report. Pediatrics. 2010;125 (Supplement 1):1–18. doi:10.1542/peds.2009-1878C.
31. Gorrindo P, Williams KC, Lee EB, Walker LS, McGrew SG, Levitt P. Gastrointestinal dysfunction in autism: parental report, clinical evaluation, and associated factors. Autism Res. 2012;5 (2):101–08. doi:10.1002/aur.237.
32. Mannion A, Leader G. An analysis of the predictors of comorbid psychopathology, gastrointestinal symptoms and epilepsy in children and adolescents with autism spectrum disorder. Research in Autism Spectrum Disorders. 2013;7(12):1663–71. doi:10.1016/j.rasd.2013.10.002.
33. Mannion A, Leader G. An investigation of comorbid psychological disorders, sleep problems, gastrointestinal symptoms and epilepsy in children and adolescents with autism spectrum disorder: a - two year follow-up. Research in Autism Spectrum Disorders. 2016;22:20–33. doi:10.1016/j.rasd.2015.11.002.
34. Valicenti-mcdermott MD, McVicar K, Cohen HJ, Wershil BK, Shinnar S. Gastrointestinal symptoms in children with an autism spectrum disorder and language regression. Pediatr Neurol. 2008;39(6):392–98. doi:10.1016/j.pediatrneurol.2008.07.019.
35. Emerson E. Challenging behavior: analysis and intervention in people with severe intellectual disabilities. 2nd. Cambridge: Cambridge University Press; 2001.
36. Doubet SL, Ostrosky MM. The impact of challenging behavior on families: i don't know what to do. Topics Early Child Spec Educ. 2015;34(4):223–33. doi:10.1177/0271121414539019.
37. McTiernan A, Leader G, Healy O, Mannion A. Analysis of risk factors and early predictors of challenging behavior for children with autism spectrum disorder. Res Autism Spectr Disord. 2011;5 (3):1215–22. doi:10.1016/j.rasd.2011.01.009.
38. Leader G, Mannion A. Challenging behaviors. In: Matson JL editor. Handbook of assessment and diagnosis of autism spectrum disorder. Cham Switzerland: Springer 2016a. p. 209–32.
39. Devlin S, Healy O, Leader G, Reed P. The analysis and treatment of problem behavior evoked by auditory stimulation. Res Autism Spectr Disord. 2008;2(4):671–80. doi:10.1016/j.rasd.2008.02.001.
40. Mulloy A, Lang R, O' Reilly M, Sigafoos J, Lancioni G, Rispoli M. Gluten-free and casein-free diets in the treatment of autism spectrum disorders: a systematic review. Res Autism Spectr Disord. 2010;4(3):328–39. doi:10.1016/j.rasd.2009.10.008.
41. Filipek PA, Accardo PJ, Ashwal S, Baranek GT, Cook EH, Dawson PG, Gordon JB, Gravel JS, Johnson CP, Kallen RJ, et al. Practice parameter: screening and diagnosis of autism: report of the Quality Standards Subcommittee of the American Academy of Neurology and the Child Neurology Society. Neurology. 2000;55 (4):468–79. doi:10.1212/WNL.55.4.468.
42. Matson JL, Cervantes PE. Commonly studied comorbid psychopathologies among persons with autism spectrum disorder. Res Dev Disabil. 2014;35(5):952–62. doi:10.1016/j.ridd.2014.02.012.
43. Grondhuis SN, Aman MG. Assessment of anxiety in children and adolescents with autism spectrum disorders. Research in Autism Spectrum Disorders. 2012;6(4):1345–65. doi:10.1016/j.rasd.2012.04.006.
44. Giarelli E, Wiggins LD, Rice CE, Levy SE, Kirby RS, Pinto-Martin J, Mandell D. Sex differences in the evaluation and diagnosis of autism spectrum disorders among children. Disabil Health J. 2010;3(2):107–16. doi:10.1016/j.dhjo.2009.07.001.
45. Pedersen AL, Pettygrove S, Lu Z, Andrews J, Meaney FJ, Kurzius-Spencer M, Lee L-C, Durkin MS, Cunniff C. DSM criteria that best differentiate intellectual disability from autism spectrum disorder. Child Psychiatry Hum Dev. 2017;48(4):537–45. doi:10.1007/s10578-016-0681-0.
46. Zuckerman K, Lindly OJ, Chavez AE. Timeliness of Autism spectrum disorder diagnosis and use of services among U.S. Elementary school–aged children. Psychiatric Services. 2017;68(1):33–40. doi:10.1176/appi.ps.201500549.
47. Clark ML, Vinen Z, Barbaro J, Dissanayake C. School age outcomes of children diagnosed early and later with autism spectrum disorder. J Autism Dev Disord. 2018;48(1):92–102. doi:10.1007/s10803-017-3279-x.
48. American Psychiatric Association. 2000. Diagnostic criteria from DSM-IV-TR. Washington, DC: American Psychiatric Pub.
49. Autism Treatment Network. GI Symptom Inventory Questionnaire, vers. 3.0. New York (NY): Autism Speaks; 2005.
50. Leader G, Francis K, Mannion A, Chen J. Toileting problems in children and adolescents with parent-reported diagnoses of autism spectrum disorder. J Dev Phys Disabil. 2018;30(3):307–27. doi:10.1007/s10882-018-9587-z.
51. Mazefsky CA, Schreiber DR, Olino TM, Minshew NJ. The association between emotional and behavioral problems and gastrointestinal symptoms among children with high-functioning autism. Autism. 2014;18(5):493–501. doi:10.1177/1362361313485164.
52. Mazurek MO, Kanne SM, Wodka EL. Physical aggression in children and adolescents with autism spectrum disorders. Res Autism Spectr Disord. 2013;7(3):455–65. doi:10.1016/j.rasd.2012.11.004.
53. Mazurek MO, Vasa RA, Kalb LG, Kanne SM, Rosenberg D, Keefer A, Murray DS, Freedman B, Lowery LA. Anxiety, sensory over-responsivity, and gastrointestinal problems in children with autism spectrum disorders. J Abnorm Child Psychol. 2013;41 (1):165–76. doi:10.1007/s10802-012-9668-x.
54. Williams KC, Christofi FL, Clemmons T, Rosenberg D, Fuchs GJ. Association of chronic gastrointestinal symptoms with sleep problems may help identify distinct subgroups of autism spectrum

disorders. Gastroenterology. 2012;142(5):S–714. doi:10.1016/S0016-5085(12)62767-X.
55. Williams KC, Fuchs GJ, Furuta GT, Marcon MA, Coury DL. 511 Clinical Features Associated With GI Symptoms in Autism Spectrum Disorders (ASD). Gastroenterology. 2010;138(5):S–74. doi:10.1016/S0016-5085(10)60337-X.
56. Matson JL, González ML. Autism spectrum disorders–comorbidity–child version. Baton Rouge (LA): Disability Consultants, LLC; 2007.
57. Matson JL, LoVullo SV, Rivet TT, Boisjoli JA. Validity of the Autism Spectrum Disorder-Comorbid for Children (ASD-CC). Research in Autism Spectrum Disorders. 2009;3(2):345–57. doi:10.1016/j.rasd.2008.08.002.
58. Matson JL, LoVullo SV. Encopresis, soiling and constipation in children and adults with developmental disability. Res Dev Disabil. 2009;30(4):799–807. doi:10.1016/j.ridd.2008.12.001.
59. Rojahn J, Rowe EW, Sharber AC, Hastings R, Matson JL, Didden R, Kroes DBH, Dumont ELM. The Behavior Problems Inventory-Short Form for individuals with intellectual disabilities: part I: development and provisional clinical reference data. J Disability Res. 2012a;56(5):527–45. doi:10.1111/j.1365-2788.2011.01507.x.
60. Rojahn J, Matson JL, Lott D, Esbensen AJ, Smalls Y. The Behavior Problems Inventory: an instrument for the assessment of self-injury, stereotyped behavior, and aggression/destruction in individuals with developmental disabilities. J Autism Dev Disord. 2001;31(6):577–88. doi:10.1023/A:1013299028321.
61. Mascitelli AN, Rojahn J, Nicolaides VC, Moore L, Hastings RP, Christian-Jones C. The Behaviour Problems Inventory-Short Form: reliability and factorial validity in adults with intellectual disabilities. Journal of Applied Research in Intellectual Disabilities. 2015;28(6):561–71. doi:10.1111/jar.12152.
62. Rojahn J, Rowe EW, Sharber AC, Hastings R, Matson JL, Didden R, Kroes DBH, Dumont ELM. The behavior problems inventory-short form for individuals with intellectual disabilities: part II: reliability and validity. J Disability Res. 2012b;56(5):546–65. doi:10.1111/j.1365-2788.2011.01506.x.
63. Rutter M, Bailey A, Lord C. The social communication questionnaire: manual. Los Angles (LA): Western Psychological Services; 2003.
64. Rutter M, Le Couteur A, Lord C. Autism diagnostic interview-revised. Los Angeles ((CA)): Western Psychological Services. 2003; Vol. 29 (2003) 30.
65. Allen CW, Silove N, Williams K, Hutchins P. Validity of the social communication questionnaire in assessing risk of autism in preschool children with developmental problems. Journal of Autism and Developmental Disorders. 2007;37(7):1272–78. doi:10.1007/s10803-006-0279-7.
66. Wiggins L, Bakeman R, Adamson L, Robins D. The utility of the Social Communication Questionnaire in screening for autism in children referred for early intervention. Focus Autism Other Dev Disabl. 2007;22(1):33–38. doi:10.1177/10883576070220010401.
67. Chandler S, Charman T, Baird G, Simonoff E, Loucas T, Meldrum D, Scott M, Pickles A. Validation of the social communication questionnaire in a population cohort of children with autism spectrum disorders. Journal of the American Academy of Child & Adolescent Psychiatry. 2007;46(10):1324–32. doi:10.1097/chi.0b013e31812f7d8d.
68. Hanley S, Mulligan A, Houlihan B, Sodipo T. P01-209-Validation study of the modified social communication questionnaire. European Psychiatry. 2010;25:419. doi:10.1016/S0924-9338(10)70415-6.
69. Mayer EA. Gut feelings: the emerging biology of gut–brain communication. Nat Rev Neurosci. 2011;12(8):453–66. doi:10.1038/nrn3071.
70. Nikolov RN, Bearss KE, Lettinga J, Erickson C, Rodowski M, Aman MG, McCracken JT, McDougle CJ, Tierney E, Vitiello B, et al. Gastrointestinal symptoms in a sample of children with pervasive developmental disorders. J Autism Dev Disord. 2009;39(3):405–13. doi:10.1007/s10803-008-0637-8.
71. Holden B, Gitlesen JP. A total population study of challenging behaviour in the county of Hedmark, Norway: prevalence, and risk markers. Res Dev Disabil. 2006;27(4):456–65. doi:10.1016/j.ridd.2005.06.001.