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Running Head: ADHD symptoms in ASD

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Attention Deficit Hyperactivity Disorder (ADHD) Symptoms, Comorbid
Psychopathology, Behaviour Problems and Gastrointestinal Symptoms in Children and
Adolescents with Autism Spectrum Disorder

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Abstract

Objectives. The study aims to investigate Attention Deficit Hyperactivity Disorder (ADHD) symptoms, gastrointestinal (GI) symptoms, comorbid psychopathology, and behaviour problems in children and adolescents with autism spectrum disorder (ASD).

Methods. Parents of 147 children and adolescents with ASD aged 6-18 years completed the Conners-3 Parent-Short Form, Gastrointestinal Symptom Inventory, Behavior Problems Inventory-Short Form, and Autism Spectrum Disorder-Comorbid for Children.

Results. Fifty six percent of children and adolescents had a comorbid diagnosis of ADHD, yet over 70% presented with clinically significant ADHD symptoms. Forty percent of participants received a diagnosis of ADHD before ASD and 25.6% received a diagnosis of ASD first. Relationships were found between ADHD symptoms and comorbid psychopathology, gastrointestinal symptoms, and behaviour problems.

Conclusions. The outcomes suggest that ADHD is being under-estimated as a comorbid disorder of ASD. This may have implications on treatment and interventions for children and adolescents who have a diagnosis of both ASD and ADHD.

Keywords: Autism spectrum disorder; Attention Deficit Hyperactivity Disorder (ADHD); comorbidity; gastrointestinal symptoms; behaviour problems.

Attention Deficit Hyperactivity Disorder (ADHD) Symptoms, Comorbid Psychopathology,

Behaviour Problems and Gastrointestinal Symptoms in Children and Adolescents with

Autism Spectrum Disorder

Introduction

Autism Spectrum Disorder

Autism spectrum disorder (ASD) is a complex behavioural disorder characterised by social deficits, communication difficulties, stereotyped or repetitive behaviours and interests and cognitive delays according to the DSM-5 (American Psychiatric Association, 2013). The Center for Disease Control and Prevention has found that 1 in 54 children is diagnosed with ASD (Maenner et al., 2020). The most recent data on the prevalence of ASD in Ireland was reported in a study (Boilson et al., 2016) which determined that 1.5% of children in Ireland have a diagnosis of ASD. Research conducted by the United Kingdom Department of Health reported that 4.2% of children in Northern Ireland have a diagnosis of ASD (Rodgers & McCluney, 2020). It was previously thought that the male-to-female ratio with ASD was 4:1, but a recent study by Loomes et al. (2017) determined that this statistic is closer to 3:1. ASD is usually identified in children by the age of two when delays in language and social interactions begin to become noticeable (Lord et al. 2006).

Attention Deficit Hyperactivity Disorder (ADHD)

Attention Deficit Hyperactivity Disorder (ADHD) is a disorder that co-occurs with ASD (Mannion et al. 2014). ADHD is associated with behaviour problems including inattention, hyperactivity and impulsivity. According to the DSM-5 (American Psychiatric Association, 2013), 5% of children in the general population have ADHD. In order to be diagnosed according to the DSM-5, a person must exhibit at least six symptoms from the categories of

either or both Inattention/Hyperactivity and Impulsivity (American Psychiatric Association, 2013). In Ireland, it has been found that less than 1% of children have received a formal diagnosis of ADHD (Adamis et al., 2019; Williams et al., 2009). ADHD has been found to have a negative effect on occupational status and social interactions in people diagnosed with the disorder (Barkely, 2002; Mannuzza et al. 1993; Mannuzza & Klein, 2000).

Comorbid Psychopathology in ASD

Comorbid psychopathology describes the presence of at least two forms of psychopathology within one individual (Matson & Nebel-Schwalm, 2007). It is important that the primary diagnosis is asserted so that future treatment and correct prioritization of intervention goals occurs (Matson & Nebel-Schwalm, 2007). Comorbid conditions in ASD and other developmental disorders include sleep problems, epilepsy, toileting problems, stimulus overselectivity, behaviour problems (Devlin et al. 2008; Francis et al. 2017; Kelly et al. 2015; Leader & Mannion, 2016a; Mannion & Leader, 2014a; 2014b; Newman et al., 2015).

Several studies have been conducted to examine the effect of comorbidity in individuals with ASD. Mannion et al. (2013) found that 46.1% of children and adolescents diagnosed with ASD had a comorbid disorder. This rose to 78% when an intellectual disability (ID) was included. Furthermore, the researchers found that 18% of these children and adolescents had a comorbid diagnosis of ADHD. Thomas, Lycett, Papadopoulos, Sciberras, and Rinehart (2018) found that out of a sample of 392 children with ADHD, 93 participants had a comorbid diagnosis of ASD, whereas 299 participants had ADHD alone. Ashwood et al (2015) determined that in a sample of 86 children, 38 participants had a comorbid diagnosis of ADHD and ASD, whereas 17 had ASD alone, and 31 had ADHD alone.

ASD and **ADHD**

In the DSM-IV-TR (American Psychiatric Association, 2000) an ASD diagnosis did not allow for a comorbid diagnosis with certain disorders. Examples of these disorders were ADHD, stereotyped movement disorder and psychiatric conditions such as schizophrenia and anxiety states (Wing et al. 2010). In the area of ASD, the DSM-5 (American Psychiatric Association, 2013) has allowed for dual diagnosis between ASD and ADHD. Recent research has found that symptoms of ADHD occur in children and adolescents with ASD without a comorbid diagnosis. May et al. (2012), found that children with ASD had higher scores of ADHD symptoms compared to typically developing children (TD). Additionally, within the ASD group, young boys had higher levels of impulsivity and hyperactivity compared to girls and older children.

Other disorders such as dyspraxia frequently co-occur with ASD and ADHD as their impairments in motor skills commonly overlap. For example, research investigating ADHD have found that 50% of ADHD cases also have motor problems severe enough to be diagnosed with dyspraxia (Piek et al., 1999, Pitcher et al., 2003). Further, children initially diagnosed with dyspraxia have been found to also meet moderate to severe diagnosis for ADHD (Kadesjö & Gillberg, 1999). Significant motor impairments such as grip selection, fine and gross motor abilities and the production of gestures are evident as overlapping across individuals diagnosed with ASD and dyspraxia (Dewey et al., 2007; van Swieten et al., 2010). Investigating comorbid disorders associated with ASD such as ADHD has crucial implications for treatment and diagnosis. Treatments available for individuals with ADHD have been shown to have positive effects (De Crescenzo et al., 2017).

Gastrointestinal Symptoms

Gastrointestinal (GI) symptoms describe problems affecting the gastrointestinal tract of an individual, leading to abnormalities such as constipation, diarrhoea, or abdominal pain (Leader & Mannion, 2016b). Children with ASD are more likely to present with GI symptoms than typically developing children and special needs children (Chandler et al. 2013). The most common GI symptoms affecting individuals with ASD are constipation and abdominal pain with or without diarrhoea (Buie et al., 2010). Nausea and bloating are also common symptoms in children with ASD (Mannion & Leader, 2013; 2016). Chandler et al (2013) showed that 46.5% of children with ASD had at least one GI symptom in the past compared to 21.8% of TD children, and 29.2% of special needs children. Mannion et al. (2013) determined that 79.3% of children and adolescents with ASD had presented with at least one GI problem in the past three months. Additionally, the researchers found a relationship between GI symptoms and comorbid psychopathology, such as conduct, tantrum, avoidant and worry/depressed behaviours in children and adolescents with ASD. Further studies have also found links between language regression (Valicenti et al., 2008) and behavioural aetiologies for GI symptoms (Ibrahim et al., 2009) in children with ASD. Williams et al. (2015) also examined the relationship between anxiety and GI symptoms and found that higher levels of anxiety are associated with higher levels of GI symptoms. Consistently, Mazurek et al. (2013) found in a study that participants who reported nausea and constipation symptoms had higher levels of anxiety than those without GI symptoms.

GI symptoms have also been linked to ADHD. In a cohort study by McKeown et al. (2013), it was found that children with ADHD had a higher rate of both constipation (4.1% in children with ADHD compared to 1.5% without) and faecal incontinence (0.9% in children with ADHD compared to 0.15% without) than children without ADHD.

Behaviour Problems

Challenging behaviour is a well-documented, recurrent issue in the literature. Challenging behaviours are mainly defined as behaviours which are not socially acceptable, physically dangerous, and those that negatively influence education (Jang et al. 2011; Matson et al. 2010). Hutchins and Prelock (2014) reported that recent prevalence estimates of challenging behaviours in individuals with ASD/ID range from 35.8% to 64.3% with most studies reporting that more than half of these individuals engage in more than one challenging behaviour. A comorbid diagnosis with ASD can amplify the effects of challenging behaviour (Matson et al. 2011). This can increase the severity of the primary disorder (Sprenger et al. 2013; Rao & Landa, 2013; Yerys et al. 2009).

Maskey et al. (2013) found that half of the children with ASD in the study presented with at least four of ten common behaviour problems. Behaviours presented consisted of sleep problems, toileting, hyperactivity, temper, aggression, self-injury, reluctance to separate from parent, anxiety, eating problems, and sensory issues. The study is consistent with past studies such as Leyfer et al (2006) and Simonoff et al (2008). Behaviour problems can cause increased issues in areas unrelated to the behaviours themselves. It has been found that greater levels of behaviour problems can be associated with lower IQ and expressive/receptive language in children with ASD (Dominick et al. 2007).

A comorbid diagnosis of ADHD and ASD increases impairment in challenging behaviour (Jang et al. 2011). Goldin et al. (2013) investigated the impact a comorbid diagnosis of ADHD and ASD can have on tantrum behaviours. In this study, the comorbid group was found to be significantly higher in tantrum behaviours than the other two groups (ASD only and ADHD only). Comorbid symptoms targeted by the ASD-CC (Matson & González, 2007) was highest in the ADHD and ASD comorbid group. Konst et al. (2013) found that children with ASD had a higher rate of tantrum behaviours than the ADHD group.

The ASD and ADHD group presented with even higher rates of tantrum behaviour compared to the other two groups.

Current Study

The present study aims to assess the impact of ADHD on children and adolescents with ASD. Additionally, the relationship between ADHD symptoms and challenging behaviour, comorbid psychopathology, and gastrointestinal symptoms will be examined. The aim is to better understand whether children and adolescents with both ASD and ADHD symptoms are at an increased risk of challenging behaviour, comorbid psychopathology, and gastrointestinal symptoms. A hypothesis of this study is that children and adolescents with ASD without a diagnosis of ADHD will still exhibit ADHD symptoms.

Method

Participants

The sample for this study was 147 children and adolescents aged 6 to 17 years with a diagnosis of ASD in accordance with DSM-IV-TR criteria (American Psychiatric Association, 2000). Diagnoses were provided by a licensed psychologist or paediatrician independent of the study. The participants received their diagnosis as a result of the formal diagnostic protocol which employs multiple diagnostic measures. Caregiver information on professional diagnosis, diagnostic setting/organization and professional(s) who made the diagnosis was obtained. Eighty-one percent of children and adolescents included in the study were male (n=119), and 19% were female (n=28). The mean age for this study was 10.09 years (SD=3.21). Nearly half of all participants (44.9%; n=66) had an intellectual disability (ID). Of those diagnosed with an ID, 16.7% (n=30) had a mild ID, 17.8% (n=32) had a moderate ID, while 4.4% of participants (n=8) had a severe ID.

Informants and Procedure

Informants were parents of children and adolescents with ASD. Rating scales were completed by parents independently according to the instructions which were printed on the top of each questionnaire. Parents were recruited through schools, ASD service providers and parent support groups. If parents wished to participate in the study, they were provided with a participant information form and a consent form to complete. Once consent was obtained, the informants were provided with the battery of questionnaires to complete in their own time.

Measures

Demographic Information Questionnaire

Parents were asked to complete a self-constructed demographic information questionnaire which inquired about age and gender of the child. Parents were also asked about diagnosis of ASD, ADHD, ID (and severity), anxiety disorders, other comorbid disorders, and at what age the child received their diagnoses.

Conners 3-Parent (Short Form)

The Conners 3-Parent (Short Form) (Conners, 2008a) was used to assess the comorbid symptoms of ADHD. The scale is a 43-item parent-rated scale which asks parents to report on the previous month of the child's behaviour to screen for ADHD symptoms. Inattention, Hyperactivity/Impulsivity, Learning Problems, Executive Functioning, Aggression, and Peer Relations were the norms assessed on the scale. The Conners 3 has been extensively researched and developed over a four-year period and has been found to be reliable and valid (Izzo, Donati, Novello, Maschietto, & Primi, 2019). Internal consistency coefficients range between .77 to .97, Cronbach's alpha ranges between .71 and .98, and inter-rater reliability

lies between .7 and .94 (Conners, 2008b). Conners 3 has been tested for factorial, construct validity, and predictive reliability. These reliability and validity accounts origin from a normative sample of 3,400 children from Canada and the United States (Conners, 2008b). Cut-off scores for clinically elevated scores were set at a *t*-score of 65. However, an upper limit of 70 on the *t*-score can also be applied according to the Conners 3 Manual as very elevated (Conners, 2008b).

Gastrointestinal Symptom Inventory

The Gastrointestinal Symptom Inventory (Autism Treatment Network, 2005) was used to assess gastrointestinal symptoms. The scale consisted of a 35-item questionnaire which was based on experience of symptoms in the past three months, allowing assessment of presence and absence of different symptoms. The questionnaire allows branching of specific symptomatology i.e. bowel movements, constipations etc. The Gastrointestinal Symptom Inventory was formed from previous questionnaires and clinical symptom assessment (Autism Treatment Network, 2005). This tool has not yet been validated. However, previous literature has used this scale (Leader et al., 2018; Mazurek et al., 2013).

Behavior Problems Inventory (BPI-S)

The Behavior Problems Inventory-Short Form (Rojahn et al. 2012b) scale consisted of 30 items to assess challenging behaviors in terms of self-injurious behavior (item 1-9), aggressive/destructive behaviors (item 10-18) and stereotyped behavior (item 19-30). The scale assesses both frequency (monthly, weekly, daily, hourly) and severity of problem (mild, moderate, and severity). The short form correlates with the BPI-01 (r=0.96 to 0.99) and held sensitivity at 0.92 to 0.99 (Rojahn et al. 2012a). Internal consistency for both the frequency and severity scales on the BPI-S was reported to be 0.70 to 0.89 (Rojahn et al. 2012b).

Convergent validity, discriminate validity and factorial validity are all robust in the BPI-S (Rojahn et al. 2012b).

Autism Spectrum Disorder-Comorbidity for Children (ASD-CC)

The Autism Spectrum Disorder-Comorbidity for Children (Matson & González, 2007) assesses comorbid psychopathology in children and adolescents with ASD. The scale consisted of 39 items which were marked on a 3-point Likert scale. It consists of seven subscales: Tantrum Behavior, Repetitive Behavior, Worry/Depressed, Avoidant Behavior, Under Eating, Over Eating, and Conduct. Matson et al. (2009) showed that the ASD-CC has validity with construct validity being established for Tantrum Behavior, Repetitive Behavior, Worry/Depressed, Conduct, Over Eating and to a lesser extent, Under-eating. Matson and Wilkins (2008) determined interrater, test-retest and internal reliabilities for the ASD-CC showing reliability for all items in the scale.

Results

Analyses

Descriptive statistics including means, standard deviations and frequencies were calculated for the variables. Clinically elevated t-scores from the Conners T-scores in each of its subscales were generated. A one-way ANOVA was conducted to assess the effect of ADHD diagnosis on the Conners subscales. Two ANOVAs were conducted to examine the relationship between ADHD symptoms and ID severity and anxiety. Correlations were conducted to assess the effects of the Conners subscales on the BPI-S, GI Symptom Inventory, and the ASD-CC. Two independent *t*-tests were conducted to compare learning problems in those with GI symptoms compared to those with no GI symptoms.

Descriptive Statistics

Respondents were asked if their child had a diagnosis of ADHD, ID and/or an anxiety disorder. A diagnosis of ADHD was present in 56.5% (n=83) of participants. Table 1 provides a summary of demographic information. Additionally, ADHD diagnosis was evaluated through diagnosis dates and it was found that 40.2% of participants had a diagnosis of ADHD before being diagnosed with ASD. It was also found that 25.6% were diagnosed with ASD first and 34.1% were diagnosed with ASD and ADHD at the same time.

---Insert Table 1 about here---

Mean differences between the group with ADHD and the group without ADHD were examined in terms of GI symptoms (as measured by the GI Symptom Inventory), behaviour problems (as measured by the BPI-S), and comorbid psychopathology (as measured by the ASD-CC). It was found that 75.5% of participants presented with between one and six GI symptoms. In relation to the groups with ADHD and without ADHD, there were differences between types of GI symptoms experienced. The group with ADHD had higher mean scores for experiencing bloating and constipation.

Mean scores for behaviour problems based on the BPIS (self-injurious behavior frequency and severity, aggressive/destructive behavior frequency and severity, and stereotyped behavior frequency) were higher in the group without ADHD across all domains.

Mean scores for comorbid psychopathology assessed by the ASD-CC showed higher means scores across tantrum, undereating, and conduct behaviours in participants with a diagnosis of ADHD compared to those without ADHD. Very little difference in mean scores were observed between the two groups based on overeating, repetitive and worry behaviour domains.

Clinically elevated T-scores from the Conners T-scores were assessed in each of the subscales; Hyperactivity, Inattention, Learning Problems, Executive Functioning,

Aggression, and Peer Relations. Over seventy percent of the total population scored above 65, indicating clinically elevated scores on the Conners Scale. Ninety-one percent reported clinically elevated scores on hyperactivity, 91% for inattention, 71% for learning problems, 80% for executive functioning, 65% for aggression, and 65% for peer relations.

Inferential Statistics

A one-way ANOVA was conducted to assess the effect of ADHD diagnosis on Conners subscales. A difference between groups was found in the subscale inattention (F(1,145)=8.18, p < .005). Descriptively, inattention had a mean score of 82.39 in the ADHD diagnosis group, compared to 77.14 without an ADHD diagnosis group. All other areas were similar in mean scores and did not show significant differences between the groups.

Two one-way between subjects ANOVA was conducted to examine the relationships between the presence of an anxiety disorder and the severity of an ID on the Conners subscales. Results found that the presence of an anxiety disorder (F(1,145)=8.12, p<.005) and ID severity was significant in one subscale, learning problems (F(3,143)=17.90, p<.000). Post hoc comparisons using the Tukey HSD test indicated that the mean score for no ID (M=66.21, SD=12.26) was significantly different than the mild ID (M=75.30, SD=10.51), moderate ID (M=81.59, SD=8.43), and severe ID (M=81.00, SD=8.19) conditions.

A correlation was conducted to assess Conners subscales effect on the BPI-S.

Aggression significantly correlated with all sub-scores of the BPI-S. Inattention,

Hyperactivity/impulsivity, Learning Problems, Executive functioning, Aggression and Peer relations also significantly correlated with some areas of the BPI-S as can be seen in Table 2.

---Insert Table 2 about here---

A correlation between scores of ASD-CC and Conners subscales was performed.

Tantrum behavior significantly correlated with all subscales of the Conners scale. A summary of the results can be seen in Table 3.

---Insert Table 3 about here---

Significant correlations were also found between total GI symptoms and the Conners subscales. Table 4 presents a summary of the results.

---Insert Table 4 about here---

A series of independent t-tests were conducted to compare learning problems in children with GI symptoms to those without GI symptoms. Results revealed a significant difference in learning problems between individuals who experienced bloating compared to those who did not experience bloating ($t_{(145)}$ =-2.95, p = .004). Children and adolescents experiencing bloating had more learning problems (M = 77.34, SD = 12.22) than children and adolescents who did not experience bloating (M = 70.43, SD = 12.52). There was a significant difference in learning problems between the presence of other GI symptoms (other than constipation, diarrhoea, abdominal pain, bloating, and nausea) compared to those who had no other GI symptoms ($t_{(145)}$ =-2.42, $t_{(145)}$

Discussion

One of the central aims of this study was to determine the frequency of both ADHD diagnosis and symptoms of ADHD in children and adolescents with ASD. The study found that children and adolescents with ASD without a diagnosis of ADHD still exhibited symptoms of ADHD. Over half of the participants (56.5%) included in this study had a comorbid diagnosis of ADHD with ASD. However, over 70% of participants presented with

clinically significant ADHD symptoms. The study examined the relationship between ADHD symptoms and GI symptoms, behaviour problems and comorbid psychopathology.

Relationships were found between inattention and comorbid psychopathology. Specifically, relationships were found between inattention and tantrum, repetitive, conduct, and overeating behaviours. Inattention is defined by poor attention and difficulty concentrating (Conners, 2008b). The results indicate that tantrum, repetitive, conduct and overeating behaviours are contingent on the child's inability to focus. Relationships were also found between inattention and behaviour problems. Specifically, relationships were found between inattention and the severity and frequency of aggressive/destructive behaviours and the frequency of stereotyped behaviour. These findings are supported by the Individuals with Disabilities Act (2004) which found that children with ADHD inattention type are at a higher risk for both learning disabilities and emotional disturbances (Conners, 2008b).

A relationship was found between hyperactivity and behaviour problems. The results indicate that children and adolescents with ASD who exhibit hyperactivity display more aggressive/destructive behavior, stereotyped behavior, and self-injurious behavior. Significant relationships were found between hyperactivity and all the ASD-CC subscales measuring comorbid psychopathology. Hyperactivity is associated with restlessness and impulsivity (Conners, 2008b) and according to the Individuals with Disabilities Act (2004), this puts children with high scores on this scale at risk of emotional disturbances.

A relationship was found between executive functioning scores and comorbid psychopathology, specifically tantrum, repetitive, worry/depressed, avoidant, undereating and conduct behaviours. Executive functioning was associated with behaviour problems such as the frequency and severity of aggressive/destructive behaviour and the frequency of stereotyped behaviours. Executive functioning is associated with poor organisation and

difficulty beginning projects (Conners, 2008b). This is line with previous research which found that ADHD can have a negative effect on occupational status and social interactions, which may result from poor executive functioning (Barkley, 2002; Mannuzza et al., 1993; Mannuzza & Klein, 2000).

Relationships were found between the Conners subscale of aggression and comorbid psychopathology. Specifically, relationships were found between aggression and tantrum behaviour, repetitive behaviour, worry/depressed behaviour, and conduct behaviour. Additionally, aggression was found to correlate significantly with of the BPI-S subscales based on the frequency and severity of self-injurious, aggressive/destructive and stereotyped behaviours. The correlation between aggression on both scales indicate that the scales showed reliability and were consistent in measurement of behaviours. The results of the study show that challenging behaviour is influenced by comorbid disorders, as demonstrated in past studies (Matson et al. 2011; Goldin et al. 2013; Konst et al. 2013). Aggression, like hyperactivity, has an effect on behaviours that can be challenging to treat (Matson & Nebel-Schwalm, 2007).

Based on the Conners Scale, peer relations relate to having difficulty with friendships, poor social skills, or seems to be unaccepted by groups (Conners, 2008b). This scale showed the highest level of difficulty in the group with 97.3% of children and adolescents with ASD showing clinically elevated scores. This may demonstrate the relationship between ASD and difficulties in peer relations. This could be related more to the diagnosis of ASD rather than the diagnosis of ADHD, as ASD is characterised by issues with social communication according to the DSM-5 (American Psychiatric Association, 2013). Relationships were found between peer relations and comorbid psychopathology, specifically tantrum, worry/depressed and avoidant behaviours. Peer relations was also associated with the severity of aggressive/destructive behaviours based on the BPI-S.

A significant relationship was found between GI symptoms and learning problems. Further analysis revealed that learning problems were more prevalent in children and adolescents who experienced bloating and other GI symptoms compared to those who did not. Learning problems are understood as difficulties with learning or understanding material that may indicate a specific learning disability in children with ADHD (Conners, 2008b). Chandler et al (2013) found no link between intellectual ability and GI symptoms. Ibrahim et al. (2009) found that GI symptoms could be linked to behavioural aetiologies, particularly constipation and feeding issues/selectivity, and it may be these behaviours influencing significance in the learning problems subscale.

Learning problems also had a significant relationship with comorbid psychopathology, correlating with all subscales on the ASD-CC. Results also indicated that children and adolescents diagnosed with an anxiety disorder in the study showed more learning problems than those without an anxiety disorder. This finding indicates that comorbid psychopathology in children and adolescents with ASD and ADHD is linked to increased learning problems. Results also suggested that a mild, moderate or severe ID were linked to more learning problems in children with ASD and ADHD.

There are multiple strengths to this study. Unlike other studies which focused on ADHD and ASD comorbidity (May et al. 2012; Goldin et al. 2013; Konst et al. 2013) this study did not use an ADHD only group and TD children and adolescents as controls. However, by looking at an ASD only group to study ADHD comorbidity, it was possible to determine the effect the subscales had on these children and adolescents. A limitation was that data collection through parental report. Parents were the only caregivers that were asked to respond to the questionnaire, however, a child's behaviours may be different in various settings. For example, some studies have found that parent and teacher ratings have low agreement in ADHD symptoms (Antrop et al. 2002; Murray et al. 2007). Future research

investigating the relationship between parent and teacher ratings with children and adolescents with a comorbid diagnosis of ASD and ADHD is recommended. This would further develop understanding of these disorders. A strength of this study was the construct validity between the scales used. Behaviours like aggression in the Conners correlated to their counter parts in the BPI-S.

Future research examining the relationship between ASD and ADHD diagnosis is needed. In this study, the age at which diagnosis was made were examined. Forty percent of participants received a diagnosis of ADHD before ASD and 25.6% received a diagnosis of ASD first. Previous diagnosis may indicate primary diagnosis; however, future studies may find that symptomology may be affected by primary and secondary diagnosis of ADHD. Finally, research examining comorbidity in ASD and ADHD in adulthood would add to the understanding of the research area. As the DSM-5 has only begun to allow for a comorbid diagnosis between these two disorders, individuals who were previously diagnosed under the DSM-IV-TR could have symptoms of ADHD without a diagnosis.

This study has implications for the diagnosis of ADHD in an ASD population. Nearly all children and adolescents in the study were found to have clinically elevated scores in the Conners subscales and further studies may investigate if parents were aware of an ADHD diagnosis or whether parents had referred to medical professionals to investigated comorbidity. Additionally, due to the relative new allowance of ADHD and ASD in the same individual from the DSM-5 (American Psychiatric Association, 2000), there is potential for children and adolescents with a comorbid diagnosis to avail of better treatment and assessment to deal with the increased problems that arise from a comorbid diagnosis.

In conclusion, this was the first study to examine the differences in gastrointestinal symptoms, comorbid psychopathology and behaviour problems between children and adolescents with an ADHD diagnosis and ADHD symptoms and without a diagnosis and

symptoms in children and adolescents with ASD. Furthermore, by investigating these differences, it was possible to distinguish the different effects ADHD symptoms had on GI symptoms, comorbid psychopathology, and behaviour problems. The results found that ADHD symptoms increase behaviour problems and comorbidities that were related to ASD. Future research should examine these relationships in more detail to form better treatment and interventions for children and adolescents with a comorbid diagnosis of ADHD and ASD.

Compliance with Ethical Standards

Conflicts of interest: None.

Ethical Standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committee on human experimentation with the Helsinki Declaration of 1975, as revised in 2008. Informed consent was obtained from all individual participants included in the study. The study protocol was approved by the ethics committee of the participating institution.

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References

- Adamis, D., Tatlow-Golden, M., Gavin, B., & McNicholas, F. (2019). General practitioners' (GP) attitudes and knowledge about attention deficit hyperactivity disorder (ADHD) in Ireland. *Irish Journal of Medical Science*, **188**, 231-239.
- American Psychiatric Association. (2000). Diagnostic and statistical manual of mental disorders: DSM-IV-TR. Washington, DC: American Psychiatric Association.
- American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders: DSM 5. Arlington: American Psychiatric Association.
- Antrop, I., Roeyers, H., Oosterlaan, J., & Van Oost, P. (2002). Agreement between parent and teacher ratings of disruptive behavior disorders in children with clinically diagnosed ADHD. *Journal of Psychopathology and Behavioral Assessment*, 24, 67-73.
- Ashwood, K. L., Tye, C., Azadi, B., Cartwright, S., Asherson, P., & Bolton, P. (2015).

 Brief Report: Adaptive Functioning in Children with ASD, ADHD and ASD +

 ADHD. *Journal of Autism and Developmental Disorders*, **45**, 2235-42.
- **Autism Treatment Network.** (2005) GI symptom inventory questionnaire, version. 3.0 Autism Speaks, New York, NY.
- **Barkley, R. A.** (2002). Major life activity and health outcomes associated with attention-deficit/hyperactivity disorder. *Journal of clinical psychiatry*, **63**, 10-15.
- Boilson, A. M., Staines, A., Ramirez, A., Posada, M., & Sweeney, M. R. (2016).
 Operationalisation of the European Protocol for Autism Prevalence (EPAP) for autism spectrum disorder prevalence measurement in Ireland. *Journal of Autism and Developmental Disorders*, 46, 3054-3067.

- Buie, T., Campbell, D. B., Fuchs, G. J., Furuta, G. T., Levy, J., Vande Water, J., ... &
 Winter, H. (2010). Evaluation, diagnosis, and treatment of gastrointestinal disorders in individuals with ASDs: a consensus report. *Pediatrics*, 125, S1-S18.
- Chandler, S., Carcani-Rathwell, I., Charman, T., Pickles, A., Loucas, T., Meldrum, D., Simonoff, E., Sullivan, P., & Baird, G. (2013). Parent-reported gastro-intestinal symptoms in children with autism spectrum disorders. *Journal of Autism and Developmental Disorders*, **43**, 2737-2747.
- Conners, C. K. (2008a). Conners 3rd Edition. Multi-Health Systems: Toronto.
- Conners, C. K. (2008b). *Manual for the Conners 3*. Multi-Health Systems: Toronto.
- **De Crescenzo, F, Cortese, S., Adamo, N., & Janiri, L.** (2017). Pharmacological and non-pharmacological treatment of adults with ADHD: a meta-review. *Evidence-Based Mental Health*, **20**, 4-11.
- **Devlin, S., Healy, O., Leader, G., & Reed, P.** (2008). The analysis and treatment of problem behavior evoked by auditory stimulation. *Research in Autism Spectrum Disorders*, **2**, 671-680.
- **Dewey, D., Cantell, M., & Crawford, S. G.** (2007). Motor and gestural performance in children with autism spectrum disorders, developmental coordination disorder, and/or attention deficit hyperactivity disorder. *Journal of the International Neuropsychological Society*, **13**, 246-256.
- Dominick, K. C., Davis, N. O., Lainhart, J., Tager-Flusberg, H., & Folstein, S. (2007).

 Atypical behaviors in children with autism and children with a history of language impairment. *Research in Developmental Disabilities*, **28**, 145-162.
- **Francis, K., Mannion, A., & Leader, G**. (2017). The assessment and treatment of toileting difficulties in individuals with autism spectrum disorder and other developmental disabilities. *Review Journal of Autism and Developmental Disorders*, **4**, 190-204.

- Goldin, R. L., Matson, J. L., Tureck, K., Cervantes, P. E., & Jang, J. (2013). A comparison of tantrum behavior profiles in children with ASD, ADHD and comorbid ASD and ADHD. *Research in Developmental Disabilities*, **34**, 2669-2675.
- Hutchins, T. L., & Prelock, P. A. (2014). Using Communication to Reduce Challenging

 Behaviors in Individuals with Autism Spectrum Disorders and Intellectual Disability.

 Child and Adolescent Psychiatric Clinics of North America, 23, 41-55.
- Ibrahim, S. H., Voigt, R. G., Katusic, S. K., Weaver, A. L., & Barbaresi, W. J. (2009).

 Incidence of gastrointestinal symptoms in children with autism: a population-based study. *Pediatrics*, **124**, 680-686.
- Individuals with Disabilities Education Act (2014). Available at: https://sites.ed.gov/idea/
- Izzo, V. A., Donati, M. A., Novello, F., Maschietto, D., & Primi, C. (2019). The Conners 3–short forms: Evaluating the adequacy of brief versions to assess ADHD symptoms and related problems. *Clinical Child Psychology and Psychiatry*, **24**, 791-808.
- Jang, J., Dixon, D. R., Tarbox, J., & Granpeesheh, D. (2011). Symptom severity and challenging behavior in children with ASD. *Research in Autism Spectrum Disorders*, 5, 1028-1032.
- **Kadesjö, B., & Gillberg, C.** (1999). Developmental coordination disorder in Swedish 7-year-old children. *Journal of the American Academy of Child & Adolescent Psychiatry*, **38**, 820-828.
- **Kelly, M. P., Leader, G., & Reed, P.** (2015). Stimulus over-selectivity and extinction-induced recovery of performance as a product of intellectual impairment and autism severity. *Journal of Autism and Developmental Disorders*, **45**, 3098-3106.
- **Konst, M. J., Matson, J. L., & Turygin, N**. (2013). Comparing the rates of tantrum behavior in children with ASD and ADHD as well as children with comorbid ASD and ADHD diagnoses. *Research in Autism Spectrum Disorders*, **7**, 1339-1345.

- **Leader, G., Francis, K., Mannion, A., & Chen, J.** (2018). Toileting Problems in children and adolescents with parent reported diagnoses of autism spectrum disorder. *Journal of Developmental and Physical Disabilities*, **30**, 307-327.
- Leader, G., & Mannion, A. (2016a). Challenging Behaviors. In J.L. Matson (Ed.),Handbook of Assessment and Diagnosis of Autism Spectrum Disorder (pp. 209–232).Cham: Springer International Publishing.
- Leader, G., & Mannion, A. (2016b). Gastrointestinal Disorders. In J.L. Matson (Ed.), Comorbid Conditions Among Children with Autism Spectrum Disorders (pp.257-281). Cham: Springer.
- Leyfer, O. T., Folstein, S. E., Bacalman, S., Davis, N. O., Dinh, E., Morgan, J., Tager-Flusberg, H., & Lainhart, J. E. (2006). Comorbid psychiatric disorders in children with autism: Interview development and rates of disorders. *Journal of autism and developmental disorders*, 36, 849-861.
- Loomes, R., Hull, L., & Mandy, W. P. L. (2017). What Is the Male-to-Female Ratio in

 Autism Spectrum Disorder? A Systematic Review and Meta-Analysis. *Journal of the*American Academy of Child & Adolescent Psychiatry, 56, 466-474.
- Lord, C., Risi, S., DiLavore, P. S., Shulman, C., Thurm, A., & Pickles, A. (2006). Autism from 2 to 9 years of age. *Archives of general psychiatry*, **63**, 694-701.
- Maenner MJ, Shaw KA, Baio J, Washington A, Patrick M, DiRienzo M, Christensen DL, Wiggins LD, Pettygrove S, Andrews JG, et al. (2020). Prevalence of autism spectrum disorder among children aged 8 years—autism and developmental disabilities monitoring network11 sites, United States, 2016. MMWR. *Surveillance Summaries*. **69**, 1–12.
- **Mannion, A., & Leader, G.** (2013). 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*, **7**, 1663-1671.
- **Mannion, A., & Leader, G.** (2016). 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*, **22**, 20-33.
- Mannion, A., & Leader, G. (2014a). Attention-Deficit/Hyperactivity Disorder in Autism Spectrum Disorder. *Research in Autism Spectrum Disorders*, **8**, 432-439.
- **Mannion, A., & Leader, G.** (2014b). Epilepsy in autism spectrum disorder. *Research in Autism Spectrum Disorders*, **8**, 354-361.
- Mannion, A., Leader, G., & Healy, O. (2013). An investigation of comorbid psychological disorders, sleep problems, gastrointestinal symptoms and epilepsy in children and adolescents with Autism Spectrum Disorder. Research in Autism Spectrum Disorders, 7, 35-42.
- **Mannion, A., Brahm, M., & Leader, G**. (2014). Comorbid psychopathology in autism spectrum disorder. *Review Journal of Autism and Developmental Disorders*, **1**, 124-134.
- Mannuzza, S., & Klein, R. G. (2000). Long-term prognosis in attention-deficit/hyperactivity disorder. *Child and adolescent psychiatric clinics of North America*, **9**,711-726.
- Mannuzza, S., Klein, R. G., Bessler, A., & Malloy, P. (1993). Adult outcome of hyperactive boys: educational achievement, occupational rank, and psychiatric status. Archives of General Psychiatry, 50, 565-576.
- Maskey, M., Warnell, F., Parr, J. R., Le Couteur, A., & McConachie, H. (2013).

 Emotional and behavioural problems in children with autism spectrum disorder.

 Journal of autism and developmental disorders, 43, 851-859.

- Matson, J. L., & González, M. L. (2007). Autism Spectrum Disorders Comorbidity Child Version. Baton Rouge, La: Disability Consultants, LLC.
- Matson, J. L., LoVullo, S. V., Rivet, T. T., Boisjoli, J. A. (2009). Validity of the Autism Spectrum Disorder-Comorbid for Children (ASD-CC). *Research in Autism Spectrum Disorders*, **3**, 345–357.
- Matson, J. L., Mahan, S., Fodstad, J. C., Worley, J. A., Neal, D., & Sipes, M. (2011).

 Effects of symptoms of co-morbid psychopathology on challenging behaviours among infants and toddlers with Autistic Disorder and PDD-NOS as assessed with the Baby and Infant Screen for Children with aUtIsm Traits (BISCUIT). *Developmental Neurorehabilitation*, 14, 129-139.
- Matson, J. L., Mahan, S., Hess, J., Fodstad, J. C., & Neal, D. (2010). Progression of Challenging behaviors in children and adoslescents with autism spectrum disorders as measured by the autism spectrum disorder–problem behaviors for children (ASD–BPC). Research in Autism Spectrum Disorders, 4, 400–404.
- Matson, J. L., & Nebel-Schwalm, M. S. (2007). Comorbid psychopathology with autism spectrum disorder in children: An overview. *Research in developmental disabilities*, **28**, 341-352.
- Matson, J. L., & Wilkins, J. (2008). Reliability of the autism spectrum disorders-comorbid for children (ASD-CC). *Journal of Developmental and Physical Disabilities*, **20**, 327-336.
- May, T., Cornish, K., & Rinehart, N. J. (2012). Gender profiles of behavioral attention in children with autism spectrum disorder. *Journal of attention disorders*, **18**, 2-10.
- Mazurek, M. O., Vasa, R. A., Kalb, L. G., Kanne, S. M., Rosenberg, D., Keefer, A., Murray, D.S., Freedman, B., & Lowery, L. A. (2013). Anxiety, sensory over-

- responsivity, and gastrointestinal problems in children with autism spectrum disorders. *Journal of abnormal child psychology*, **41**, 165-176.
- McKeown, C., Hisle-Gorman, E., Eide, M., Gorman, G. H., & Nylund, C. M. (2013).

 Association of Constipation and Fecal Incontinence With AttentionDeficit/Hyperactivity Disorder. *Pediatrics*, **132**, 1210-1215.
- Murray, D. W., Kollins, S. H., Hardy, K. K., Abikoff, H. B., Swanson, J. M.,
 Cunningham, C., Vitiello, B., Riddle, M.A., Davis, M., Greenhill, L.L.,
 McCracken, J.T., McGough, J.J., Posner, K., Skrobala, A.M., Wigal, T., Wigal,
 S.B., Ghuman, J.K., & Chuang, S. Z. (2007). Parent versus teacher ratings of attention-deficit/hyperactivity disorder symptoms in the Preschoolers with Attention-Deficit/Hyperactivity Disorder Treatment Study (PATS). *Journal of Child and Adolescent Psychopharmacology*, 17, 605-619.
- Newman, I., Leader, G., Chen, J., & Mannion, A. (2015). An analysis of challenging behavior, comorbid psychopathology, and attention-deficit/hyperactivity disorder in Fragile X syndrome. *Research in Developmental Disabilities*, **38**, 7-17.
- **Piek, J.P., Pitcher, T.M., & Hay, D.A.** (1999). Motor coordination and kinaesthesis in boys with attention deficit-hyperactivity disorder. *Developmental Medicine & Child Neurology*, **41**, 159–165.
- **Pitcher, T.M, Piek, J. P., Hay, D, A.** (2003). Fine and gross motor ability in males with ADHD. *Developmental Medicine & Child Neurology*, **45**, 525–535.
- **Rao, P. A., & Landa, R. J.** (2013). Association between severity of behavioral phenotype and comorbid attention deficit hyperactivity disorder symptoms in children with autism spectrum disorders. *Autism*, **18**, 272-280.
- Rojahn, J., Rowe, E. W., Sharber, A. C., Hastings, R., Matson, J. L., Didden, R., Kroes, D.B.H.,& Dumont, E. L. M. (2012a). The Behavior Problems Inventory-Short Form

- for individuals with intellectual disabilities: Part I: development and provisional clinical reference data. *Journal of Intellectual Disability Research*, **56**, 527-545.
- Rojahn, J., Rowe, E. W., Sharber, A. C., Hastings, R., Matson, J. L., Didden, R., Kroes,
 D.B.H., & Dumont, E. L. M. (2012b). The Behavior Problems Inventory-Short Form
 for individuals with intellectual disabilities: Part II: reliability and validity. *Journal of Intellectual Disability Research*, 56, 546-565.
- Simonoff, E., Pickles, A., Charman, T., Chandler, S., Loucas, T., & Baird, G. (2008).

 Psychiatric disorders in children with autism spectrum disorders: prevalence, comorbidity, and associated factors in a population-derived sample. *Journal of the American Academy of Child & Adolescent Psychiatry*, **47**, 921-929.
- Sprenger, L., Bühler, E., Poustka, L., Bach, C., Heinzel-Gutenbrunner, M., Kamp-Becker, I., & Bachmann, C. (2013). Impact of ADHD symptoms on autism spectrum disorder symptom severity. *Research in developmental disabilities*, **34**, 3545-3552.
- Rodgers, H. & McCluney, J. (2020). The prevalence of autism (including Asperger's Syndrome) in school age children in Northern Ireland 2020. Department of Health. https://www.health-ni.gov.uk/publications/prevalence-autism-including-aspergers-syndrome-school-age-children-northern-ireland-2020
- **Thomas, S., Lycett, K., Papadopoulos, N., Sciberras, E., Rinehart, N.** (2018). Exploring Behavioral Sleep Problems in Children with ADHD and Comorbid Autism Spectrum Disorder. *Journal of Attention Disorders*, **22**, 947-958.
- Valicenti-McDermott, M. D., McVicar, K., Cohen, H. J., Wershil, B. K., & Shinnar, S. (2008). Gastrointestinal symptoms in children with an autism spectrum disorder and language regression. *Pediatric Neurology*, **39**, 392-398.

- van Swieten, L. M., van Bergen, E., Williams, J. H., Wilson, A. D., Plumb, M. S., Kent,
 S. W., & Mon-Williams, M. A. (2010). A test of motor (not executive) planning in developmental coordination disorder and autism. *Journal of Experimental Psychology: Human Perception and Performance*, 36, 493-499.
- Williams, J., Greene, S., Doyle, E., Harris, E., Layte, R., McCoy, S., McCrory, C.,
 Murray, A., Nixon, E., O'Dowd, T., O'Moore, M., Quail, A., Smyth, E., Swords, L.,
 & Thornton, M. (2009). Growing up in Ireland: The lives of 9 year olds. Dublin: The Stationery Office.
- Williams, S., Leader, G., Mannion, A., & Chen, J. (2015). An investigation of anxiety in children and adolescents with autism spectrum disorder. *Research in Autism Spectrum Disorders*, **10**, 30-40.
- Wing, L., Gould, J., & Gillberg, C. (2010). Autism spectrum disorders in the DSM-V: better or worse than the DSM-IV?. *Research in developmental disabilities*, **32**, 768-773.
- Yerys, B. E., Wallace, G. L., Sokoloff, J. L., Shook, D. A., James, J. D., & Kenworthy, L. (2009). Attention deficit/hyperactivity disorder symptoms moderate cognition and behavior in children with autism spectrum disorders. *Autism Research*, **2**, 322-333.

Table 1.

Demographic Information

		No ADHD diagnosis	ADHD diagnosis	All Participants
		(n=64, 43.5%)	(<i>n</i> =83, 56.5%)	(<i>N</i> =147)
		M (SD)	M (SD)	M(SD)
Age		10.34 (3.54)	9.85 (2.94)	10.07 (3.21)
		n (%)	n (%)	n (%)
Gender	Male	48 (75%)	71 (85.5%)	119 (81%)
	Female	16 (25%)	12 (14.5%)	28 (19%)
		n (%)	n (%)	n (%)
Presence of an Intellectual Disability (ID)	Yes	28 (43.8%)	38 (45.8%)	66 (44.9%)
` ,	No	36 (56.3%)	45 (54.2%)	81 (55.1%)
		N (%)	N (%)	N (%)
Presence of an Anxiety	Yes	11 (17.2%)	23 (27.7%)	34 (23.1%)
Disorder	No	53 (82.8%)	60 (72.3%)	113 (76.9%)

Note: *M*= *Mean SD*=*Standard Deviation*

Table 2.

Correlation between Conner's subscales and BPI-S.

	IN	HYP	LP	EF	A	PR
Self-injurious behavior frequency	.14	.16*	.18*	.10	.24**	.06
Self-injurious behavior severity	.14	.16	.20*	.15	.24**	.10
Aggressive/destructive behavior frequency	.26**	.31**	.16	.26**	.64**	.16
Aggressive/destructive behavior severity	.22**	.26**	.14	.23**	.68**	.19*
Stereotyped behavior frequency	.19*	.36**	.19*	.21**	.19*	.15

p<0.05*, p<0.01**

IN=Inattention; HYP=Hyperactivity/Impulsivity; LP=Learning Problems; EF=Executive Functioning; A=Aggression; PR=Peer Relations.

Table 3.

Correlations between ASD-CC and Conners subscales.

	IN	HY	LP	EF	A	PR
Tantrum Behavior	.27**	.31**	.22**	.37**	.66**	.23**
Repetitive Behavior	.26**	.39**	.27**	.34**	.19*	.12
Worry/Depressed	.14	.16	.18*	.32**	.29**	.20*
Avoidant Behavior	.11	.18*	.21**	.31**	.16	.30**
Under-eating	.05	.14	.18*	.19*	.07	.11
Conduct	.20*	.30**	.18*	.29**	.51**	.16
Over-eating	.16*	.18*	.33**	.12	.04	.08
Total	.27**	.37**	.32**	.42**	.44**	.25**

p<0.05*, p<0.01**

Table 4.

Correlations between total GSI and Conners subscales.

	IN	HY	LP	EF	A	PR	
Total	.06	.05	.18*	.23**	.03	.14	
Gastrointestinal							
Symptoms							
0 0 7 1 0 0 1 1 1							

p<0.05*, *p*<0.01**