ORIGINAL ARTICLE

Autistic Characteristics, Cognitive Impairment, and Sex as Predictors of Anxiety and Depression among Autistic Youth

Erin E. Long[1] · Mary F. Johnson[2] · Laura A. Carpenter[3]

Abstract

Although it is well established that autistic youth are at high risk for anxiety and depression, factors associated with heightened risk within this population are poorly understood. The purpose of this study was to evaluate whether autistic characteristics and cognitive impairment interact to predict anxiety and depression symptoms, and whether the impacts of autistic characteristics and cognitive impairment on anxiety and depression differ for male and female children. Participants comprised 7989 youth (M = 11.23 years) enrolled in SPARK, a national cohort of autistic individuals. Autistic characteristics were assessed via the Social Communication Questionnaire. Anxiety and depression were assessed via the Child Behavior Checklist. Linear regressions were conducted to examine associations between autistic characteristics, cognitive impairment, and symptoms and to test for interactions. The effect of parent-reported autistic characteristics on anxiety was stronger for males than for females, while the effect of cognitive impairment on anxiety was stronger for females than for males. A different pattern was observed for depression. The effect of autistic characteristics on depression was the same for males and females, while cognitive impairment was not associated with depression per parent report. Findings indicate that both male and female children with high levels of autistic characteristics are susceptible to experiencing anxiety and depression, and that autistic female children with intact cognitive abilities are uniquely vulnerable to experiencing anxiety based on parent report. Results have implications for the prevention of internalizing problems in autistic youth, and highlight future directions for longitudinal work examining mechanisms of comorbidity.

Keywords Autism · Cognitive impairment · Anxiety · Depression · Sex

Autism spectrum disorder is a neurodevelopmental condition characterized by impairments in social communication and the presence of restricted and repetitive behaviors (Ozonoff et al., 2007). Autism is highly prevalent; current estimates indicate that 1 in 36 children is autistic (Maenner et al., 2023). Autism is also associated with a number of co-occurring conditions, including other neurodevelopmental disorders as well as psychiatric disorders (Leyfer et al., 2006). Evidence indicates that autistic youth are at elevated risk for experiencing depression and anxiety disorders, relative to non-autistic youth (Gillott et al., 2001; Kerns et al., 2021; Kim et al., 2000; Vasa et al., 2013). However, our understanding of specific factors that confer risk for these internalizing outcomes among autistic youth is limited. The present study aimed to examine whether autistic characteristics interact with cognitive impairment to predict anxiety and depression among autistic youth, and whether the impacts of autistic characteristics and cognitive impairment on internalizing symptoms differs for male and female children.

✉ Erin E. Long
  erinlong@mcw.edu

1 Department of Pediatrics, Division of Pediatric Psychology and Developmental Medicine, Medical College of Wisconsin, 8915 W. Connell Ct, Milwaukee, WI 53226, USA

2 Department of Neuroscience, Neuroscience Administration Research Team, Children's Hospital of Colorado, Aurora, CO, USA

3 Department of Pediatrics, Division of Developmental-Behavioral Pediatrics, Medical University of South Carolina, Charleston, SC, USA

Internalizing Symptoms in Autistic Youth

A large body of literature demonstrates that autistic children are at elevated risk for internalizing disorders, including anxiety (Lai et al., 2019; Vasa et al., 2013, 2020). Meta-analytic work suggests that 40% of autistic children and adolescents have at least one co-occurring anxiety disorder (van Steensel et al., 2011). Although it is clear that autistic children experience anxiety at higher rates than non-autistic children, specific prevalence estimates range widely across studies, from 11 to 84% (Kerns & Kendall, 2012; Muris et al., 1998). Further, diagnostic prevalence rates may not capture the full scope of the impact of anxiety on autistic youth, as many autistic youth with symptoms of anxiety that do not meet diagnostic thresholds still experience significant distress and impairment (Strang et al., 2012; Vasa et al., 2013). The impacts of anxiety at both clinical and sub-clinical levels on autistic youth include increased interpersonal impairment, poorer quality relationships with teachers, peers, and family members, and more aggressive behaviors (Kim et al., 2000).

Autistic youth are additionally at increased risk for experiencing depression, relative to their non-autistic peers (Kanne et al., 2009; Kim et al., 2000; Mayes et al., 2011a, b; Strang et al., 2012). Meta-analytic work and reviews indicate that the current prevalence of depression in autistic youth is four times higher than the current prevalence of depression in non-autistic youth (Hudson et al., 2019; Smith & White, 2020). Even more autistic youth experience sub-threshold symptoms of depression that are also associated with significant distress and impairment (Simonoff et al., 2008; Strang et al., 2012), including higher rates of sleep problems, increased use of maladaptive coping strategies, more frequent peer victimization, and suicidality (Pouw et al., 2013; Richdale & Baglin, 2015; Storch et al., 2013). However, as with the anxiety literature, prevalence rates of depression are highly variable across studies, ranging from 1 to 76% (Hudson et al., 2019; Menezes et al., 2018).

Risk for Anxiety and Depression in Autistic Youth

Taken together, a wealth of literature indicates that anxiety and depression are pervasive concerns negatively impacting the lives of autistic children and adolescents. However, the wide prevalence estimates reported in the literature indicate that significant questions remain about which autistic youth are at greatest risk for experiencing these problems, and under what circumstances. Identifying factors associated with risk for depression and anxiety among autistic children and adolescents is critically important to identify which groups of youth are must vulnerable to these outcomes, and to target prevention and intervention efforts towards these groups.

One factor that may be associated with risk for anxiety and depression is level of autistic characteristics. Some researchers have hypothesized that autistic traits may play a causal role in the development of anxiety (Wood & Gadow, 2010) and depression (Smith & White, 2020) via mechanisms such as social impairment associated with autism. In support of this hypothesis, studies have found evidence that symptoms of anxiety and depression increase with increasing levels of both social communication difficulties (Kanne et al., 2009) and restricted repetitive behaviors (Baribeau et al., 2020; Sukhodolsky et al., 2008). One study of autistic children found that maternal report of anxiety and depression symptoms increased with increasing autistic characteristics, and that level of autistic characteristics was a stronger predictor of both anxiety and depression than age, IQ, or sex (Mayes et al., 2011a, b). Another study similarly found that autistic traits were a stronger predictor of emotional problems than age, IQ, sex, or socioeconomic status (Colvert et al., 2022). A number of studies have focused solely on anxiety symptoms among autistic youth, and have found that higher levels of autistic characteristics predict increased symptoms of anxiety (Ben-Itzchak et al., 2020; Spackman et al., 2022). Overall, anxiety has been more extensively studied in relation to autistic characteristics than depression, highlighting the need for additional work focused on understanding associations between autistic traits and depression symptoms.

While some studies examining associations of autistic characteristics with internalizing symptoms have found positive associations, other studies have found evidence that symptoms of anxiety and depression decrease as levels of autistic characteristics increase. For example, one study found that increased levels of autistic characteristics were associated with lower levels of both anxiety and depression (Mazurek & Kanne, 2010). Another study found that higher levels of autistic traits were associated with lower parent-reported emotional problems broadly (Stringer et al., 2020). Still other studies find no evidence for an association between autistic characteristics and symptoms of anxiety or depression (Simonoff et al., 2008; Wright et al., 2023). Finally, while some work has used broad measures of emotional problems or internalizing symptoms (e.g., Colvert et al., 2022; Stringer et al., 2020), other evidence indicates that autistic characteristics may differentially associate with anxiety and depression, highlighting the importance of assessing and modeling them separately. For example, one study found that higher levels of traits associated with autism were related to increased risk for depression but not anxiety (Kreiser & White, 2015).

Several factors may contribute to the inconsistent findings regarding the association of autistic characteristics with symptoms of anxiety and depression, as well as the heterogeneity in estimated prevalence rates of anxiety and depression in the extant literature. One possibility is that moderators of the relation between autistic characteristics and internalizing symptoms may exist, such that autistic characteristics may associate with anxiety and/or depression for certain youth, but not for others. Both cognitive ability and sex have been hypothesized to impact internalizing symptoms in autistic youth specifically, and evidence also indicates that they are both associated with internalizing outcomes in non-autistic youth (Buckley et al., 2020; Hankin et al., 1998; Lewinsohn et al., 1998). Further, intellectual functioning and sex are associated with heterogeneity in prevalence rates of mental health diagnoses in autistic people across the lifespan (Lai et al., 2019). However, limited empirical work has explored these factors as possible moderators of the association between autistic characteristics and symptoms of anxiety and depression.

Moderators of the Association Between Autistic Characteristics and Internalizing Symptoms

In addition to higher observed rates of co-occurring internalizing disorders, autistic youth are also at elevated risk for cognitive impairment. Epidemiological work indicates that approximately one third of autistic children have co-occurring intellectual disability (ID) (Maenner et al., 2023). Among youth with ID who are not autistic, high levels of co-occurring psychiatric symptoms are reported, with anxiety symptoms being the second most common following ADHD symptoms (Buckley et al., 2020). Given the frequent co-occurrence of cognitive impairment with autism, and observed associations of both cognitive impairment and autism with mental health problems, a growing body of empirical (Dunn et al., 2020; Gotham et al., 2015; Kerns et al., 2021; Spackman et al., 2022) and meta-analytic (Edirisooriya et al., 2021; Mingins et al., 2021) work has examined the mental health outcomes of autistic youth with varied cognitive abilities. Interestingly, despite evidence that cognitive impairment is associated with more internalizing symptoms among non-autistic youth (Buckley et al., 2020), the findings regarding associations between cognitive impairment and internalizing problems among youth on the autism spectrum are more equivocal (for a meta-analysis see Edirisooriya et al., 2021).

It has been hypothesized that, as cognitive mechanisms (e.g., rumination; negative cognitive biases) are central to dominant theories of depression and anxiety (Beck &

Haigh, 2014; Nolen-Hoeksema et al., 2008), autistic children with stronger cognitive abilities may therefore be at increased risk for experiencing these disorders (Mazurek & Kanne, 2010). It has also been suggested that children with stronger cognitive abilities may have greater insight into their social difficulties, which may lead to increased distress (Rao et al., 2008). Consistent with these hypotheses, some evidence indicates that autistic youth with stronger cognitive skills experience higher levels of anxiety and depression than autistic youth with impaired cognitive skills (Mazurek & Kanne, 2010; Sukhodolsky et al., 2008). Autistic youth with stronger cognitive skills also had more severe caregiver-reported anxiety (Gotham et al., 2015; Spackman et al., 2022) and were more likely to have a history of a depression (Greenlee et al., 2016). Meta-analytic work further supports that autistic youth with higher IQs are more vulnerable to depression (Edirisooriya et al., 2021).

On the other hand, some researchers have hypothesized that youth with both autism and ID may experience compounded risk for poor mental health outcomes (Dunn et al., 2020). In line with this theory, some studies have found that cognitive impairment is associated with increased risk for mental health problems broadly in autistic people across the lifespan (Dunn et al., 2020), as well as with increased risk for anxiety symptoms specifically (van Steensel et al., 2011). Still other studies have not found an association between IQ and anxiety or depression in autistic youth (Hollocks et al., 2023; Mayes et al., 2011a, b, 2020; Simonoff et al., 2008; Strang et al., 2012; Wright et al., 2023).

However, this body of work is characterized by several limitations. First, some work examining associations of cognitive ability with internalizing outcomes has limited the range of IQ in the sample to ≥70 (Strang et al., 2012; van Steensel et al., 2011; van Steensel & Heeman, 2017), which may obscure associations between cognitive ability and internalizing symptoms that may exist at lower levels of cognitive ability. Meta-analytic work has highlighted the need for additional studies including children with a full range of cognitive abilities (Edirisooriya et al., 2021). Second, measurement issues may impact reported rates of anxiety and depression in autistic children with cognitive impairment. In particular, meta-analytic work indicates that relying on formal diagnostic categories may underestimate the degree of anxiety and depression problems experienced by children and adolescents with cognitive impairment, and that using rating scales like the CBCL may better capture the true scope of internalizing symptoms in this population (Buckley et al., 2020). Third, girls are often underrepresented in studies of the association between cognitive functioning and internalizing outcomes among autistic youth, resulting in studies that are underpowered to detect potential sex and/or gender differences.

The underrepresentation of autistic girls in studies examining risk for internalizing outcomes is especially important, as sex and gender[1] represent additional potential moderators of the association between autistic characteristics and anxiety and depression symptoms. It is well-established that sex and gender are associated with risk for anxiety and depression among non-autistic youth, such that girls are at increased risk for experiencing anxiety and depression relative to boys and report greater symptom levels (Axelson & Birmaher, 2001; Costello, 1996; Hankin et al., 1998; Hankin & Abramson, 2001). The literature examining sex and gender differences in internalizing problems in autistic children and adolescents is more equivocal, however (for a review on sex and gender differences, see Hull et al., 2017). Some evidence indicates that similar sex differences in internalizing problems exists among autistic youth, such that females experience greater levels of anxiety and depression relative to males. This sex difference been hypothesized to reflect a female autism phenotype which is characterized by internalizing problems, along with other aspects (e.g., camouflaging) that differentiate it from a male phenotype (Hull et al., 2020). In support of this hypothesis, Horwitz and colleagues found trajectories of anxiety and depression symptoms during adolescence that were similar across sex, regardless of autism diagnostic status. That is, both autistic and non-autistic females evidenced increases in symptoms of anxiety and depression over time, while both autistic and non-autistic males demonstrated decreasing symptoms (Horwitz et al., 2023). Notably, this sample did not include youth with co-occurring cognitive impairment. Another study found that, while autistic females displayed increasing levels of anxiety and depression from childhood to adolescence, autistic males reported high initial levels of both anxiety and depression that remained stable through adolescence. This pattern resulted in levels of anxiety and depression that were equal across sexes by early adulthood (Gotham et al., 2015). Other studies find evidence for sex differences in symptoms of anxiety and depression in autistic children beginning in early childhood, with females reporting more symptoms than males (Wright et al., 2023)

Other studies find no sex difference in levels of internalizing problems in autistic children and adolescents. For example, in a study of autistic children ages 6 to 12 with IQs > 70, Nasca and colleagues found no sex differences in symptoms of anxiety or depression across males and females (Nasca et al., 2020). Similar findings have been observed in samples that are more heterogeneous in terms of IQ and age, indicating that autistic boys and girls experience similar levels of anxiety and depression across childhood and adolescence (Baribeau et al., 2020; Colvert et al., 2022; Greenlee et al., 2016; Hollocks et al., 2023; Mayes et al., 2011b, 2020; Spackman et al., 2022).

Importantly, even among studies that examine sex and gender differences, many are limited by small sample sizes of autistic girls, resulting in analyses that are underpowered. It is possible that samples with larger numbers of girls would be better able to detect whether sex and/or gender moderate associations between autistic traits and internalizing symptoms. In support of this hypothesis, one study examining gender as a moderator of the association between psychiatric diagnoses and autistic traits found that levels of subthreshold autistic traits were more strongly associated with mood disorders for women than men in a sample of undergraduates without autism diagnoses (Kreiser & White, 2015). Whether sex similarly moderates associations between autistic characteristics and symptoms of anxiety and depression in samples of children and adolescents with autism diagnoses remains to be tested.

The Present Study

An abundance of literature demonstrates that autistic youth are at increased risk for experiencing anxiety and depression, and autistic characteristics are one factor implicated in increased risk. It has also been hypothesized that autistic youth with cognitive impairment and autistic girls may be uniquely vulnerable to experiencing internalizing outcomes, but evidence thus far has been equivocal and is limited by small samples of girls, limited ranges of IQs, and reliance on diagnostic categories rather than rating scales which may better capture symptoms in this population. Meta-analytic and review work has emphasized the need to focus on girls and children and adolescents with low IQ, who currently represent understudied populations in the autism literature (Edirisooriya et al., 2021; Hull et al., 2017). The present study therefore aimed to address these gaps by examining interactive effects of level of autistic characteristics, cognitive impairment, and sex on anxiety and depressive symptoms in a large national sample of autistic children and adolescents, including a large sample of female children (n = 1837) with diverse cognitive abilities. We specifically aimed to test (1) whether autistic characteristics and cognitive impairment interact to predict anxiety and depression symptoms and (2) whether the impacts of autistic characteristics and cognitive impairment on anxiety and depression differ for male and female children. We hypothesized that autistic characteristics would interact with cognitive

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[1] We use the terms "males" and "females" throughout this manuscript when discussing the present study as well as other studies that examine sex differences, and we use "girls" and boys" when discussing studies that examine gender differences. When discussing a broad body of literature regarding both sex and gender differences, we use "girls" and "boys."

impairment to predict levels of anxiety and depression, such that risk for anxiety and depression conferred by level of autistic characteristics would be amplified among youth without cognitive impairment. We additionally hypothesized that the association between autistic characteristics and internalizing outcomes would be stronger for females relative to males, based on empirical work demonstrating increased risk for anxiety and depression among both autistic and neurotypical girls.

Method

Participants

Participants comprised 7989 children ages 6 to 17 (M = 11.23, SD = 3.31; 77% male children) from the Simons Foundation Powering Autism Research for Knowledge (SPARK) registry (Feliciano et al., 2018). In order to enroll in the SPARK registry, individuals must have a professional diagnosis of autism according to parent report. Children ages 6 to 17 enrolled in SPARK whose parent or guardian completed the Child Behavior Checklist for Ages 6–18 were included in the present study. Sample sociodemographic characteristics are reported in Table 1.

Measures

Social Communication Questionnaire

Level of autistic characteristics was assessed via caregiver report on the Social Communication Questionnaire (SCQ) (Rutter et al., 2003). The SCQ is a parent-report questionnaire of 40 yes-or-no items that represent characteristics associated with autism, including problems with communication and reciprocal social interaction, and restricted, repetitive, and stereotyped behaviors. Scores range from 0

to 39, with higher scores indicating greater levels of autistic characteristics.

Cognitive Impairment

Presence or absence of cognitive impairment was a manually derived composite variable that was calculated by SPARK. The variable reflects an aggregate across many indicators of cognitive impairment, including actual IQ scores and intellectual impairment or disability indicated from medical records when available (i.e., FSIQ or NVIQ < 80), parent-reported intellectual disability or cognitive impairment, Vineland Communication SS < 80, an absence of fluent complex speech if the participant's age > 48 months, parent-reported significant delays in cognitive level or a mental age < 80% chronological age, parent-reported IQ test score of < 80, presence of both language and total physical disability, or unresolved language regression. There were no weightings. This variable was evaluated by comparing it against IQ from medical record data and intellectual disability diagnosis data on a sample of 3845 youth (Brooks et al., 2023). Sensitivity of the derived variable was 80%, specificity was 69%, the positive predictive value was 72%, and the negative predictive value was 78% (Brooks et al., 2023). The Area Under the Curve (AUC) fell in the acceptable range (AUC = 0.812) (Çorbacıoğlu & Aksel, 2023; Nahm, 2022). Cognitive impairment was coded as a binary variable where 0 = absence of cognitive impairment and 1 = presence of cognitive impairment.

Child Behavior Checklist for Ages 6–18

Symptoms of anxiety and depression were assessed via the Anxiety Problems and Depressive Problems DSM-Oriented Scales on the Child Behavior Checklist for ages 6–18 (CBCL) (Achenbach & Rescorla, 2001, 2014). The CBCL is a broadband parent-report questionnaire of child symptoms occurring within the past 6 months for children from 6 to 18 years of age. The CBCL consists of 100 items, which are rated on a scale from 0 (*not true*) to 2 (*very true or often true*). The Anxiety Problems scale comprises 9 items that assess generalized anxiety disorder, separation anxiety disorder, and specific phobia. The Depressive Problems scale comprises 13 items that assess dysthymic and major depressive disorders. For the present analyses, t-scores on the Anxiety Problems and Depressive Problems scales were used. T-scores have a mean of 50 and standard deviation of 10. According to the CBCL interpretation guidelines, t-scores between 65 and 69 fall in the borderline clinical range, and t-scores above 70 fall in the clinical range. The DSM-Oriented Scales have good reliability, as well as strong convergent and discriminant validity in samples of

Table 1 Sample demographic characteristics

	Mean (SD)/N (%)
Age (years)	11.23 (3.31)
Sex	
Male	6152 (77%)
Female	1837 (23%)
Race/Ethnicity	
Asian	148 (1.9%)
Black or African American	412 (5.2%)
American Indian or Alaska Native	31 (0.4%)
Native Hawaiian	7 (0.1%)
White	6241 (78.1%)
Another Race	256 (3.2%)
More than one race	850 (10.6%)
Hispanic or Latinx	1266 (15.8%)

non-autistic youth (Nakamura et al., 2009). Although the literature examining the psychometric properties of the CBCL in samples of autistic youth is limited, some investigators have found evidence supporting the reliability of the CBCL, including the DSM-5 scales, in samples of autistic youth (Magyar & Pandolfi, 2017; Pandolfi et al., 2012).

Sex and Gender

Sex assigned at birth was coded as a binary variable (0 = male; 1 = female). It was determined based on parent report at the time of enrollment of participants' sex assigned at birth. Given a wealth of research demonstrating gender diversity among autistic individuals (Brunissen et al., 2021; Corbett et al., 2023; Strang et al., 2012, 2014, 2020), we also examined gender identity in the present sample. Gender identity was also based on parent report at the time of enrollment in SPARK. In the present sample, 5426 (76.8%) of participants were assigned male at birth, and 1635 (23.2%) of participants were assigned female at birth. Based on parent-reported gender identity, 5326 (75.4%) of participants identified as boys, 1615 (22.9%) of participants identified as girls, and 27 (0.4%) of participants identified as another gender. Although according to parent report, 99.2% of participants had a gender identity that matches their sex assigned at birth, based on the existing empirical work on gender diversity in autistic people (Brunissen et al., 2021; Corbett et al., 2023; Strang et al., 2012, 2014, 2020) we believe this is an underestimate of the number of gender diverse youth in the present sample. We attribute this to the young average age of registration in SPARK (M = 7.89 years, SD = 4.78) and to the fact that gender is a parent-report variable in this sample, and youth may not have disclosed their gender identity to their parent. Given the very small number of gender diverse youth in the present sample based on parent report, and the limitations of this variable, present analyses are limited to participants' sex assigned at birth.

Data Analysis

Analyses were conducted using the 'lavaan' library in R (Rosseel, 2012). Descriptive statistics were first calculated in order to characterize symptom levels in the present sample and assist with interpretation of tests of study hypotheses. Pearson correlations were conducted to examine the strength and direction of associations between study variables. Independent samples t-tests were conducted to compare mean scores on the Anxiety Problems and Depressive Problems scales across females and males, and across youth with and without cognitive impairment.

To test the hypotheses that level of autistic characteristics interacts with cognitive impairment and with sex to predict anxiety and depression, a series of linear regressions were conducted. Cognitive impairment was dummy-coded (0 = absence of cognitive impairment; 1 = presence of cognitive impairment), as was sex (0 = male; 1 = female). Scores on the SCQ were mean-centered. The first model examined the impact of autistic characteristics, cognitive impairment, sex, and their interactions on anxiety, and the second model examined their impact on depression. In each model, the main effects of autistic characteristics, cognitive impairment, and sex were entered in the first step, all two-way interactions were entered in the second step, and the three-way interaction was entered in the third step. Effects for all predictors were entered in the same models to examine their unique contributions to explaining anxiety and depression. Significant interactions were probed using tests of simple slopes and comparisons of estimated marginal means (Holmbeck, 2002).

Results

Descriptive Statistics

Consistent with the diagnostic status of the present sample, the average score on the SCQ was 21.51, above the recommended cutoff of 15 (Chandler et al., 2007; Rutter et al., 2003). 67.8% of the sample was identified as likely to have cognitive impairment. This did not differ by sex; females (67.8%) and males (65.4%) were equally likely to be classified as having cognitive impairment, χ^2 (1, N = 7682) = 3.36, p = .067. Females evidenced higher levels of parent-reported anxiety compared to males, t(7049) = -4.46, p < .001), as well as higher levels of parent-reported depression compared to males, t(7049) = -5.24, p < 001. Additional sample descriptive statistics and preliminary analyses are reported in Table 2.

Correlations between study variables are reported in Table 3. Higher levels of autistic characteristics were associated with both depression and anxiety, per parent report. Presence of cognitive impairment was associated with depression symptoms but not anxiety symptoms. As expected, anxiety and depression were significantly and positively correlated. Likewise, autistic characteristics and cognitive impairment were positively correlated, such that participants with higher levels of autistic characteristics were more likely to have cognitive impairment. Sex was correlated with autistic characteristics, such that males had higher levels of autistic characteristics than did females.

Table 2 Descriptive statistics

	Group	N (%)	Mean (SD)	t	p
SCQ	Females	1800 (23%)	20.53 (7.46)	6.58	<0.001
	Males	6017 (77%)	21.80 (7.15)		
	No Cog Impair	2253 (34%)	18.30 (7.00)	-26.71	<0.001
	Cog Impair	4424 (66%)	23.08 (6.88)		
Anxiety	Females	1833 (23%)	66.01 (12.73)	-5.16	<0.001
	Males	6146 (77%)	64.41 (11.34)		
	No Cog Impair	2307 (34%)	65.23 (11.36)	1.27	0.203
	Cog Impair	4506 (66%)	64.85 (11.83)		
Depression	Females	1833 (23%)	65.63 (9.26)	-6.22	<0.001
	Males	6146 (77%)	64.12 (9.08)		
	No Cog Impair	2307 (34%)	63.88 (9.14)	-4.90	<0.001
	Cog Impair	4506 (66%)	65.03(9.14)		

Note Sex was coded a binary variable where 0 = male and 1 = female. Cognitive impairment was coded as a binary variable where 0 = absence of cognitive impairment and 1 = presence of cognitive impairment

Table 3 *Correlations between study variables*

	SCQ	Anxiety	Depression	Cognitive Impairment	Sex
Anxiety	0.107**	1			
Depression	0.171**	0.606**	1		
Cognitive Impairment	0.308**	−0.017	0.056**	1	
Sex	−0.074**	0.058**	0.069**	0.021	1

Note ** Correlation is significant at the 0.001 level

Sex is coded as a binary variable such that 0 = boy and 1 = girl. Cognitive impairment is coded as a binary variable such that 0 = absence of cognitive impairment and 1 = presence of cognitive impairment

Autistic Characteristics, Cognitive Impairment, and Sex Predicting Anxiety

Complete model results are reported in Table 4. A significant interaction was observed between level of autistic characteristics and sex ($\beta = -0.031$, $p = .024$). Simple slope analysis revealed that the effect of autistic characteristics on symptoms of parent-reported anxiety was stronger for males ($b = 0.24$, $p < .001$) than for females ($b = 0.14$, $p < .001$) (Fig. 1). While females were more anxious than males at low levels of autistic characteristics, females and males do not differ in their level of anxiety at high levels of autistic characteristics.

Table 4 Main effects and interactions among autistic characteristics, cognitive impairment, and sex in predicting anxiety and depression

	R^2	B	SE	β	p
Model 1: Anxiety					
Step 1	0.02				
SCQ		0.207	0.019	0.128	<0.001
Cog		-1.370	0.297	−0.055	<0.001
Sex		1.861	0.320	0.067	<0.001
Step 2	$\Delta R^2 = 0.001$				
SCQ x Cog		−0.039	0.041	−0.019	0.338
SCQ x Sex		−0.102	0.045	−0.031	0.024
Cog x Sex		-1.479	0.715	−0.046	0.039
Step 3	$\Delta R^2 = 0.000$				
SCQ x Cog x Sex		−0.046	0.096	−0.011	0.628
Model 2: Depression					
Step 1	0.04				
SCQ		0.218	0.015	0.172	<0.001
Cog		0.084	0.231	0.004	0.716
Sex		1.834	0.248	0.084	<0.001
Step 2	$\Delta R^2 = 0.000$				
SCQ x Cog		0.013	0.032	0.008	0.682
SCQ x Sex		−0.033	0.035	−0.013	0.344
Cog x Sex		−0.299	0.556	−0.012	0.590
Step 3	$\Delta R^2 = 0.000$				
SCQ x Cog x Sex		0.065	0.075	0.020	0.380

Note SCQ = Social Communication Questionnaire; Cog = cognitive impairment

A significant interaction was also observed between cognitive impairment and sex ($\beta = -0.046$, $p = .039$). The absence of cognitive impairment was associated with greater symptoms of anxiety across sexes. However, contrasts between estimated marginal means indicated that the difference in the impact of presence versus absence of cognitive impairment on anxiety symptoms was more pronounced for females ($b = -2.68$, $p < .001$) than for males ($b = -1.10$, $p = .001$) (Fig. 2).
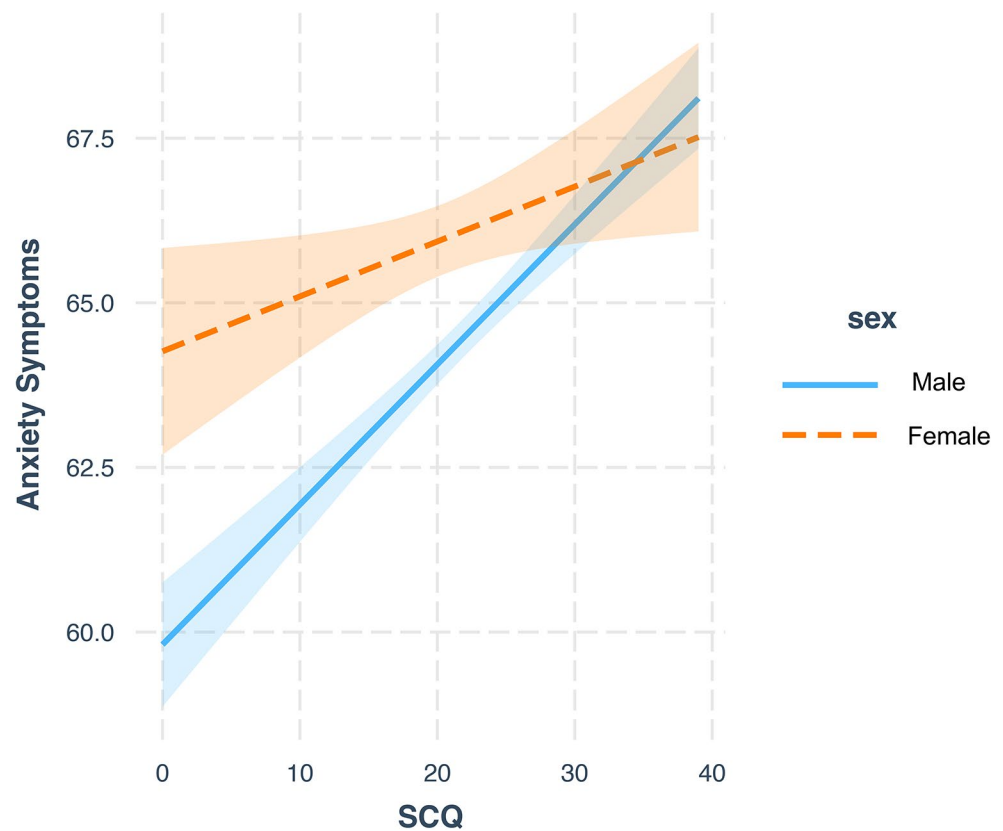
Finally, the three-way interaction between autistic characteristics, cognitive impairment, and sex predicting symptoms of anxiety was not significant ($\beta = -0.011$, $p = .628$).

Autistic Characteristics, Cognitive Impairment, and Sex Predicting Depression

Autistic characteristics predicted depression, such that greater levels of autistic characteristics were associated with higher levels of depression based on parent report ($\beta = 0.172$, $p < .001$). Sex also predicted depression ($\beta = 0.084$, $p < .001$); female sex was associated with higher levels of depression. However, presence of cognitive impairment was not associated with symptoms of depression ($\beta = 0.004$, $p = .716$).

Autistic characteristics did not interact with cognitive impairment ($\beta = 0.008$, $p = .682$) or with sex ($\beta = -0.013$,

Fig. 1 The association between autistic characteristics and anxiety symptoms for males and females. *Note.* SCQ = Social Communication Questionnaire scores. Anxiety Symptoms = t-scores. Shaded areas reflect 95% confidence intervals

$p = .344$) to predict depression. Likewise, cognitive impairment and sex did not interact to predict depression ($\beta = -0.012, p = .344$). The three-way interaction between autistic characteristics, cognitive impairment, and sex predicting symptoms of depression was not significant ($\beta = 0.030, p = .380$).

Discussion

It is well-established that autistic children and adolescents are at increased risk for experiencing elevated levels of anxiety and depression relative to their non-autistic peers (Gillott et al., 2001; Kanne et al., 2009; Kim et al., 2000; Mayes et al., 2011a, b; Strang et al., 2012; Vasa et al., 2013). However, specific factors which may be associated with autistic youths' risk for anxiety and depression remain poorly understood. The present study investigated whether autistic characteristics and cognitive impairment interact to predict anxiety and depression among autistic youth based on parent report, and whether they do so similarly or differently for males and females. Findings show that the impact of autistic characteristics and cognitive impairment on symptoms of anxiety depends on sex. The effect of autistic characteristics on anxiety was stronger for males than for females, while the effect of cognitive impairment on anxiety

was stronger for females than for males. A different pattern was observed for depression. The effect of autistic characteristics on depression was the same for males and females, while cognitive impairment was not associated with depression. Overall, findings indicate that both females and males with high levels of autistic characteristics are susceptible to experiencing anxiety and depression, and that autistic females with intact cognitive abilities are uniquely vulnerable to experiencing anxiety.

The results of the present study indicating that high levels of autistic characteristics are associated with increased levels of both anxiety and depression for females and males is consistent with a growing body work suggesting that autistic characteristics are associated with risk for anxiety, and contribute to a smaller literature demonstrating positive associations between autistic characteristics and depression (Baribeau et al., 2020; Ben-Itzchak et al., 2020; Kanne et al., 2009; Mayes et al., 2011b; Pine et al., 1998; Schiltz et al., 2021; Spackman et al., 2022; Sukhodolsky et al., 2008). Autistic characteristics were the most robust indicators of risk in our models, consistent with work comparing the relative strength of predictors of internalizing problems in autistic youth that has found autistic traits to be more strongly correlated with both anxiety and depression than with demographic (e.g., age, gender, race) or cognitive (e.g.,
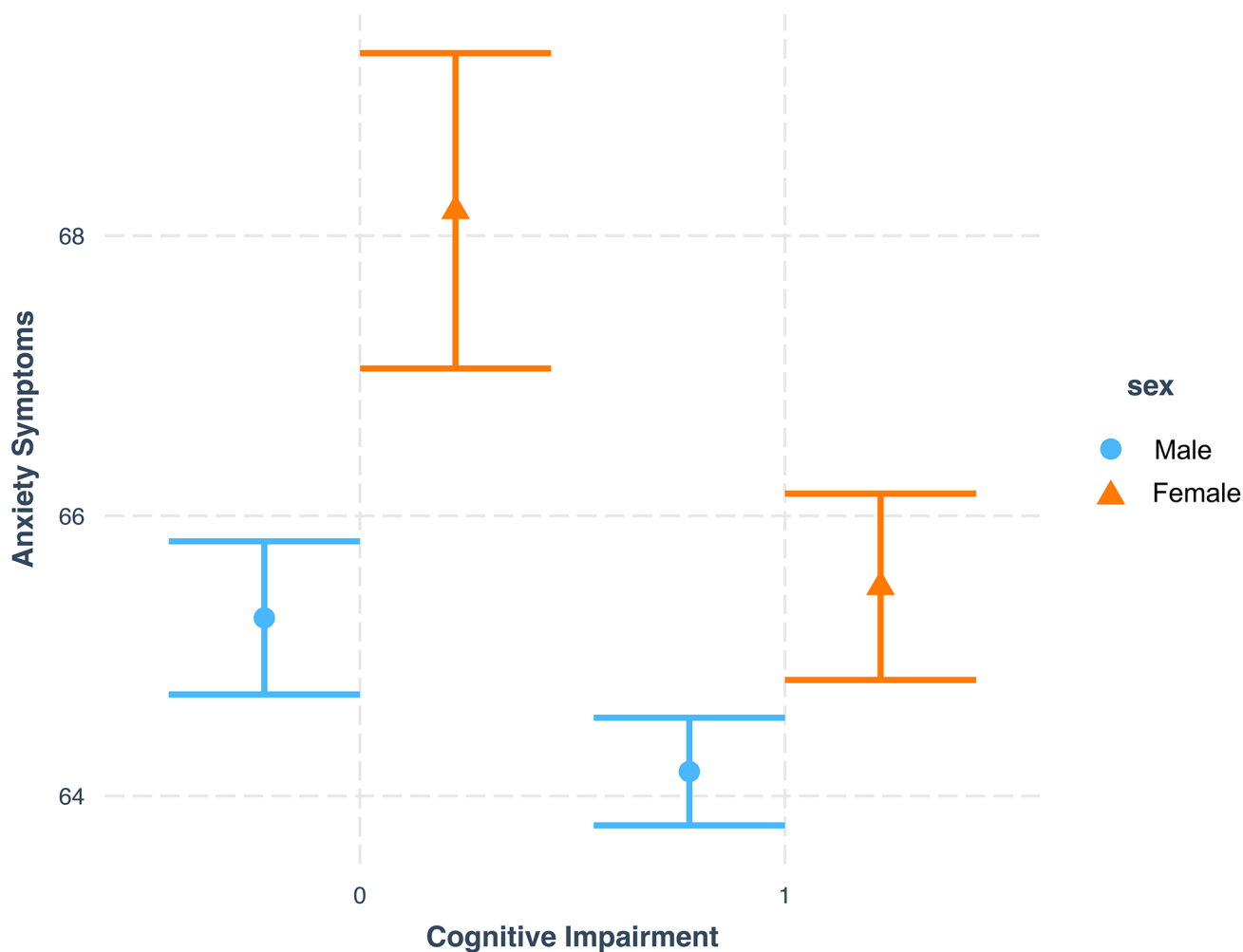
Fig. 2 The association between cognitive impairment and anxiety symptoms for males and females. *Note*. Cognitive impairment coded as 0 = absence of cognitive impairment and 1 = presence of cognitive impairment. Anxiety Symptoms = t-scores. Bars reflect 95% confidence intervals

verbal and nonverbal IQ) variables (Colvert et al., 2022; Mayes et al., 2011b).

It has been hypothesized that these strong observed associations between autistic characteristics, anxiety, and depression may be due to symptom overlap (Kerns & Kendall, 2012; Wood & Gadow, 2010). That is, symptoms that are commonly present in those with anxiety and depression are also commonly present in those with autism (e.g., somatic complaints, social withdrawal) (Mayes et al., 2011a, b), often to such an extent that some have debated whether features of anxiety should be considered part of autism rather than a co-occurring disorder (Kerns & Kendall, 2012). While evidence indicates that anxiety is indeed a separable condition from autism, forms of anxiety that are similar in their content to features of autism (e.g., insistence on sameness) are more strongly associated with autistic characteristics (Kerns et al., 2021). These findings support the idea that high observed rates of co-occurrence may in part be an artifact of symptom overlap, or may be reflective of a shared underlying risk factor (Kerns & Kendall, 2012).

However, others have posited that characteristics associated with autism may play a causal role in contributing to internalizing symptoms, suggesting that autistic traits impact symptoms via risk mechanisms such as social difficulties, loneliness, or sensory over- or under-responsivity (Ben-Sasson et al., 2008; Smith & White, 2020; Wood & Gadow, 2010). In support of hypotheses implicating social mechanisms for anxiety and depression, autistic children report experiencing more loneliness than their non-autistic peers (Bauminger & Kasari, 2000). Children with higher levels of autistic characteristics are less likely to have friends (Mazurek & Kanne, 2010; Rowley et al., 2012), and young adults with higher levels of autistic characteristics initiate fewer social contacts with friends (Schiltz et al., 2021) and report receiving less support from friendships (McKenney et al., 2024). Autistic young adults found that with greater levels of autistic characteristics also reported more symptoms of

social anxiety and depression, and that this association was mediated by loneliness (Schiltz et al., 2021). Loneliness is associated with higher levels of autistic traits in adults (Ee et al., 2019) and poorer social skills in children and adolescents (Deckers et al., 2017). Therefore, it may be that difficulties with social skills associated with autistic characteristics contribute to loneliness, which in turn causes internalizing problems. It has also been hypothesized that the loneliness and dissatisfaction with social connectedness reported by autistic individuals may arise from experiences of social marginalization and the double empathy problem, or the lack of mutual understanding and shared reciprocity that can occur when autistic individuals and non-autistic individuals interact (Milton, 2012; Mitchell et al., 2021). In support of this hypothesis, evidence indicates that non-autistic children and adults form rapid and unfavorable first impressions of autistic children and adults, and report lower intention to pursue social interactions based on these impressions (Sasson et al., 2017). Experiences of social marginalization are associated with mental health problems (for a review, see Han et al., 2022), and dissatisfaction with social connectedness is longitudinally associated with symptoms of depression (McKenney et al., 2024) in autistic adults. It will be important for future work to consider how the dynamics of social interactions with non-autistic individuals, including issues related to the double empathy problem, marginalization, and stigma, may impact feelings of loneliness and therefore internalizing problems among autistic youth. Finally, it has also been hypothesized that associations between autistic characteristics and internalizing symptoms may be bidirectional. For example, symptoms of anxiety may lead to social withdrawal, reducing a child's opportunities to practice social skills and increasing social impairment, further increasing anxiety. Although the body of literature testing this hypothesis thus far is limited, current evidence examining bidirectional associations between anxiety and autistic characteristics, including social communication impairment (Duvekot et al., 2018) and insistence on sameness (Baribeau et al., 2023) has supported a unidirectional model.

Notably, sex moderated the impact of autistic characteristics on anxiety, such that the association was stronger for males than for females. At low levels of autistic characteristics, females were more anxious than males. However, as levels of autistic traits increased, males' levels of anxiety also increased so they were indistinguishable from females' levels of anxiety. Prior studies have found evidence that restricted repetitive behaviors are associated with elevated anxiety symptoms (Baribeau et al., 2020; Lidstone et al., 2014), and some studies suggest that boys have higher levels of restricted repetitive behaviors than girls (Kreiser & White, 2014; Rivet & Matson, 2011). It may be that, as levels of autistic characteristics increase, so does the presence of restricted repetitive behaviors for males specifically, placing them at elevated risk relative to females for experiencing symptoms of anxiety. Girls and boys may also experience different social consequences, or be perceived differently by their parents and caregivers, as a result of behaviors associated with increased autistic characteristics. A wealth of literature demonstrates that gender stereotypes impact social perception (Eagly & Steffen, 1984; Haines et al., 2016), and that parental attributions regarding the cause of children's behaviors vary by gender (Gretarsson & Gelfand, 1988). As the present study is based on parental report of youth symptoms, it may be that behaviors associated with autistic characteristics in boys are interpreted by parents as reflecting elevated symptoms of anxiety, but that those same behaviors are perceived differently in girls. Future research using child self-reported symptoms of anxiety or anxiety biomarkers is necessary to address this possibility.

Interestingly, youth without cognitive impairment experienced increased levels of anxiety, but not depression, suggesting that higher cognitive abilities may confer specific risk for anxiety symptoms, rather than for internalizing broadly. It has been hypothesized that youth with intact cognitive abilities may have increased insight into their social difficulties, and may also be more likely to engage in the types of cognitive processes theorized to confer risk for anxiety and depression (Mazurek & Kanne, 2010; Rao et al., 2008). Present results suggest that this risk may be specific to anxiety, however. Among autistic youth, it may be that risk for anxiety is conferred by cognitive processes, whereas risk for depression is conferred via interpersonal or social mechanisms, in line with interpersonal theories of depression (Coyne, 1976; Joiner et al., 1999). Consistent with this hypothesis, high levels of autistic characteristics, which include social communication deficits, were more explanatory of depression than cognitive impairment in the present models. Additionally, CBCL items that load onto the Anxiety Problems subscale tend to tap specific cognitions (e.g., "self-conscious or easily embarrassed," "fears they might think or do something bad") whereas many items that load onto the Depressive Problems subscale tap observable behaviors (e.g., "cries a lot," "sleeps less than most kids"). Risk for anxiety was uniquely amplified among autistic females without cognitive impairment. Among non-autistic adults, a wealth of literature demonstrates that women report more intense and frequent worry than men (Olatunji et al., 2010; Robichaud et al., 2003). Similar sex differences in cognitive processes that confer risk for depression, such as worry, may explain the particular vulnerability to anxiety of autistic females with intact cognitive abilities.

The present study demonstrated a number of strengths that advance knowledge regarding risk for internalizing

problems among autistic children and adolescents. In addition to a large national sample, the present study is unique in that included a large number of females ($n = 1837$), enabling us to examine sex as a potential moderator of risk for anxiety and depression. As many samples of autistic children and adolescents are underpowered to examine sex differences due to small numbers of females, the current findings advance our understanding of the role of sex as a factor moderating risk for anxiety among autistic youth. However, it will be important for future work in samples better characterized with regard to gender identity to explore associations between gender differences in risk for internalizing problems among autistic youth. Likewise, our sample comprised youth with diverse cognitive abilities, building upon existing literature that has at times limited ranges of intellectual functioning represented. Our ability to differentiate between symptoms of anxiety and depression, rather than using a composite measure of internalizing symptoms, represents another strength. As current results support differential associations of cognitive impairment with internalizing outcomes, it will be important for future work to continue to separate symptoms of anxiety from depression to better understand associations of particular risk factors with specific domains of psychopathology among autistic youth.

These findings should be interpreted in light of several limitations that represent important areas for future research. First, as the data in the present study are cross-sectional, causal inferences about these associations cannot be drawn. Future longitudinal work is needed to establish the temporal precedence of these and other risk factors for anxiety and depression in autistic youth in order to establish causality and identify potential mediators of these associations. Second, the present findings are based on a dimensional measure of caregiver-reported child symptoms, which may be biased in systematic ways. It will be important for additional studies to replicate these findings using child self-report, particularly on measures of internalizing symptoms, and to utilize diagnostic interviews to capture youth whose levels of anxiety and depression reach diagnostic thresholds. The use of diagnostic interviews and/or measures of daily functioning would also provide additional information to support the clinical significance of current findings. Additionally, while the present study does find evidence that autistic characteristics, cognitive impairment, and sex are significantly associated with internalizing outcomes, the models account for a small proportion of the variance in symptoms of anxiety and depression. Future work is needed to elucidate predictors of internalizing outcomes among autistic youth (e.g., social marginalization, stigma, stressful life events) that may have greater predictive power in explaining variance in symptoms.

Further, while the CBCL has been shown to be a reliable and valid measure for the assessment of emotional and behavioral problems in autistic youth (Magyar & Pandolfi, 2017; Pandolfi et al., 2012), it was not developed for use in this population. Although youth with cognitive impairment were included in these validation samples, most had an FSIQ ≥ 70. As symptoms of anxiety and depression may present differently in autistic youth, and especially in those with cognitive impairment, instruments developed for the assessment of non-autistic youth may not be ideally suited for capturing symptoms in this population. Consistent with work by Kerns and colleagues, it is possible that the finding that cognitive impairment was associated with lower levels of parent-reported anxiety reflects poor sensitivity of the CBCL to detect anxiety disorders in autistic children with co-occurring ID (Kerns et al., 2021). Relatedly, some evidence suggests that established factor structure of the CBCL does not fit well in samples of autistic children with intellectual disability (Dovgan et al., 2019). The development of measures that capture the manifestations of internalizing symptoms in autistic children with cognitive impairment represents an important avenue for future work. Finally, the racial composition of the sample does not reflect the demographics of the United States. Specifically, White youth are overrepresented in the present sample, while Black or African American and Asian youth are underrepresented. It will be important for future work to replicate these findings in a more representative sample, especially given evidence supporting racial and ethnic differences in the comorbidity of intellectual disability and autism (Maenner et al., 2023).

Findings from the present study elucidate a number of risk factors associated with elevated symptoms of anxiety and depression in autistic children and adolescents which may be clinically useful. First, results highlight populations that may benefit the most from targeted secondary prevention efforts. Autistic females may benefit from anxiety prevention programs regardless of their level of autistic characteristics, especially those females with intact cognitive abilities. Males on the other hand may be most likely to benefit from anxiety prevention efforts when they have high levels of autistic characteristics. Both males and females with high levels of autistic characteristics may benefit from depression prevention programs. Future longitudinal work will be important to identify specific mechanisms to target, via which autistic characteristics may confer risk for internalizing outcomes.

Results emphasize the importance of autistic characteristics as a risk factor for symptoms of anxiety and depression for autistic youth, regardless of their cognitive abilities. Stronger cognitive abilities, in contrast, were associated specifically with increased anxiety but not depression. The present study also furthers our understanding of sex

differences in anxiety and depression among autistic youth. Overall, findings contribute to a growing literature examining elevated vulnerability for internalizing outcomes among autistic children and adolescents.

Declarations

Conflict of Interest he authors have no conflicts of interest to report.

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