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ORIGINAL PAPER

Sex Differences in Internalizing Problems During Adolescence in Autism Spectrum Disorder

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Abstract We hypothesized that the double hit conferred by sex and diagnosis increases the risk for internalizing disorders in adolescent females with autism spectrum disorder (ASD). In a sample of 32 adolescents with ASD and 32 controls, we examined the effects of sex, diagnostic factors, and developmental stages on depression and anxiety. A 3-way interaction revealed that females with ASD exhibited greater depressive symptoms than males with ASD and female controls particularly during early adolescence; therefore, females with ASD might have a unique combination of genetic, hormonal, and psychosocial vulnerabilities that heighten their risk for depression during early adolescence. Additionally, the ASD group reported high levels of separation anxiety and panic in late adolescence, possibly indicating atypical development of independence.

Keywords Autism · Sex differences · Adolescence · Depression · Anxiety

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Introduction

Autism spectrum disorder (ASD) has an estimated prevalence of 1 in 68, and is almost 5 times more common among boys (1 in 42) than among girls (1 in 189) (CDC 2014). The overrepresentation of males in the ASD population has motivated a narrowing research focus on the clinical presentation of ASD in boys. Enhancing the understanding of the ASD profile in females has critical implications for issues of equity, as well as diagnosis, treatment, and research. This has been underscored by the federal Interagency Autism Coordinating Committee (IACC), which states in their Strategic Plan for ASD Research that there is a "pressing need to conduct research aimed at understanding all aspects of ASD (genes, brain, and behavior) in females with ASD" (IACC 2012). One research area that may be particularly critical to the study of sex differences in ASD is internalizing psychopathologies, such as depression and anxiety. Within the typically developing population, a strong sex difference emerges during adolescence, with females experiencing higher rates of depression and anxiety than males (Angold and Rutter 1992; van Oort et al. 2009). Further, research indicates that individuals with ASD are at a heightened risk for developing depression and anxiety (Mayes et al. 2011; Simonoff et al. 2008). Thus, it has been suggested that females with ASD might be at an especially high risk for developing

internalizing disorders because of the "double hit" conferred by sex and diagnostic factors (Solomon et al. 2012).

Sex Differences in Depression and Anxiety within the General Population

Convergent findings from extensive research on the general population indicate that depression increases in both males and females during adolescence, however, the prevalence rate is nearly twice as high for females than males during adolescence and adulthood (Angold and Rutter 1992; Culbertson 1997; Kessler et al. 1994; Nolen-Hoeksema and Girgus 1994; Saluja et al. 2004). In particular, during early adolescence the sex difference is minimal or non-existent, but by late adolescence a strong sex difference in depression emerges once the majority of adolescents have undergone puberty (Essau et al. 2000; Hankin et al. 1998).

Similar to the developmental pattern found for depression, levels of anxiety appear to dramatically increase for females compared to males during adolescence (Angst and Dobler-Mikola 1985; Bruce et al. 2005; Regier et al. 1990; Spitzer et al. 2006). Van Oort et al. (2009) have conducted one of the only large-scale studies on the developmental progression of anxiety across preadolescence to late adolescence and found a general pattern for both males and females across all subtypes of anxiety (i.e., Generalized Anxiety Disorder, Social Phobia, Separation Anxiety Disorder, Panic Disorder, and Obsessive Compulsive Disorder), such that anxiety symptoms first decreased during early adolescence and subsequently increased during later adolescence. Adolescent females, however, experienced overall higher anxiety levels than males across all anxiety subtypes except Obsessive Compulsive Disorder.

Depression and Anxiety in ASD

Depression and anxiety are two of the most common comorbidities found in individuals with ASD (Gadow et al. 2012; Ghaziuddin et al. 2002; Kim et al. 2000; Szatmari et al. 1989; White et al. 2009). Comorbidity rates of ASD and depression range from 4 to 57 % (Ghaziuddin et al. 2002; Lainhart 1999; White et al. 2009), while those for anxiety disorders range from 7 to 84 %, with the majority of anxiety studies suggesting a comorbidity rate between 40 and 50 % (White et al. 2009). Most ASD research has focused on assessing overall anxiety or social anxiety levels. A limited number of studies, however, have explored specific types of anxiety and have found that higher functioning children and adolescents with ASD have significantly higher levels of Physical Symptoms, Social Anxiety, Separation/Panic, Obsessive Compulsive Disorder, and Total Anxiety compared to controls (Bellini 2004; Gillott et al. 2001; Hammond and Hoffman 2014).

Sex Differences in Depression and Anxiety in ASD

Research on sex differences in depression and anxiety in ASD is limited and, to date, findings have been inconsistent. A large-scale study of internalizing problems in children and adolescents with ASD revealed that maternal ratings of anxiety and depression were not related to sex of the child (Mayes et al. 2011). Similarly, Kuusikko et al. (2008) assessed anxiety in 52 higher functioning individuals with autism or Asperger's ages eight to 15 years (40 males; 12 females) using both self-report and parent-report measures, but no sex differences in anxiety were revealed. The one study that explored sex differences in anxiety and depression specifically within a sample of *adolescents* with ASD (ranging from 12 to 18 years of age) found marginally significant parent-reported sex differences in 10 male and 10 female adolescents with ASD, such that females compared to males presented higher levels of anxiety but not depression (Solomon et al. 2012). Prior research on the general population has found that the developmental stage of adolescence, *early* adolescence (12–14 years of age) versus *late* adolescence (15–17 years of age), affects the risk for internalizing problems in both sexes, but more strongly for females (Hankin et al. 1998; van Oort et al. 2009). To our knowledge, no study has empirically tested whether females with ASD compared to males with ASD are at a particularly high risk for depression and anxiety during different developmental stages of adolescence. Instead, studies that have examined the effect of age on depression and anxiety in the ASD population span a wide age range and do not examine sex effects. These studies have found age-related increases in depression and anxiety in ASD (Mayes et al. 2011; Brereton et al. 2006; Ghaziuddin and Greden 1998; Vickerstaff et al. 2007; Weisbrot et al. 2005), with some exceptions (Strang et al. 2012; Sukhodolsky et al. 2008).

ASD Severity and IQ in Relation to Depression and Anxiety

In order to expand our understanding of depression and anxiety in the ASD population, it is crucial to examine an array of possible risk factors for internalizing problems, such as ASD severity and IQ, in addition to sex and developmental stage. Research examining whether greater ASD severity and higher IQ places individuals with ASD at an increased risk for depression and anxiety has provided mixed results. Many studies have found that internalizing problems in ASD are positively correlated with ASD severity and IQ (Brereton et al. 2006; Ghaziuddin and Greden 1998; Kanne et al. 2009; Vickerstaff et al. 2007), but other studies have not found this relation (Mazurek and

Kanne 2010; Simonoff et al. 2008; Strang et al. 2012; Sukhodolsky et al. 2008). One of the largest studies to address this question included a sample size of 627 mothers of children with ASD ranging in age (1–17 years) and IQ (16–146) and found that the best combined predictors of depression and anxiety were increasing ASD severity, verbal IQ, and age, explaining close to 25 % of the variance (Mayes et al. 2011).

Rationale for Current Study

This is the first study to examine the effects in ASD of sex and developmental stage of adolescence on internalizing symptomatology compared to typically developing (TYP) controls. We tested three primary hypotheses drawn from the existing literature: (1) that the ASD group would have significantly greater depressive and anxiety symptoms than the TYP group, (2) that adolescent females with ASD would be at a significantly greater risk for developing depression and anxiety than adolescent ASD or TYP males, and (3) that both ASD severity and IQ would positively correlate with depression and anxiety across the ASD group.

The study goal also provides the first data on potential 3-way interactions of diagnostic group by both sex and developmental stage of adolescence. We had no specific hypotheses as there is a lack of previous data addressing this topic.

We utilized both parent- and adolescent self-reports of depressive and anxiety symptoms. This allowed examination of both parent and adolescent perspectives. Parent and child report measures of anxiety were selected that contained several anxiety subscales which allowed characterization of the specific anxiety issues in this group.

Methods

Participants

Forty-three participants with ASD and 61 participants with TYP development were recruited into a larger study that took place in Eugene, Oregon. Participants came from four sources: the University of Oregon Psychology Department's Developmental Database, fliers in the community, a participant database developed by the researchers from prior studies, and autism agencies in Eugene, Oregon, and Portland, Oregon. To be enrolled in the study, participants with ASD needed a community diagnosis of ASD made by a medical doctor (e.g., psychiatrist, developmental pediatrician), clinical psychologist, or a multidisciplinary team (two prospective ASD participants were screened out at this step). TYP participants were screened for a variety of neurological and developmental disorders, including ADHD and ASD, before being accepted into the study (one prospective TYP participant was screened out at this step). The present study used a subset of the participants from this larger study. Eleven participants with ASD were screened out of the present study because they did not meet the following inclusion criteria, which was specific to the current study: age ranging from 12 to 17 years, composite IQ $\geq$75, a standard cut-off score $\geq$30 on the Autism-Spectrum Quotient (AQ) Adolescent Version (Baron-Cohen et al. 2006), and a cut-off score $\geq$90 on the Asperger's Syndrome Diagnostic Scale (ASDS; Myles et al. 2001). A one-to-one matching of participants with ASD to the TYP controls on gender and composite IQ was next conducted. At this step, 29 TYP participants were excluded. The criterion used for IQ matching consisted of the control participant's composite IQ falling within the 90 % confidence interval for the composite IQ of the participant with ASD. If there was more than one TYP participant who met this criterion, then the TYP participant who had verbal and nonverbal IQ scores closest to the participant with ASD was selected. Additionally, the number of males and females with ASD grouped into early and late adolescence was matched by the same number of male and female controls. The final sample for the current study consisted of 64 adolescents between the ages of 12.0 and 17.9 years ($M = 14.80$, $SD = 1.69$). Participants included 32 higher functioning adolescents with ASD (18 male; 14 female) and 32 TYP adolescents (18 male; 14 female). Additional demographic data are represented in Table 1. One parent of each adolescent also participated in the study (59 mothers; 2 female guardians; 3 fathers). All parent and adolescent participants gave informed consent or assent. The study was approved by the University of Oregon Institutional Review Board.

Inclusion Measures

To screen for IQ, the Kaufman Brief Intelligence Test-2nd Edition. (KBIT-2; Kaufman and Kaufman 1990) was used. This test provides a standardized measure of Verbal IQ, indexed by verbal knowledge and riddles, and Nonverbal IQ, indexed by matrices, as well as a composite IQ.

To assess autism spectrum disorder specifically in higher functioning youth, we used the Autism-Spectrum Quotient—Adolescent Version (AQ-Adolescent Version; Baron-Cohen et al. 2006) and the Asperger's Syndrome Diagnostic Scale (ASDS; Myles et al. 2001). The AQ-Adolescent Version is a parent-report instrument that measures ASD traits in adolescents on a 4-point Likert scale from "definitely agree" to "definitely disagree". It is comprised of 50 questions, assessing 5 different domains: social skills, attention switching, attention to detail,

Table 1 Participant characteristics

	TYP			ASD			Group effect	
	Males ($n = 18$) M (SD)	Females ($n = 14$) M (SD)	Total ($n = 32$) M (SD)	Males ($n = 18$) M (SD)	Females ($n = 14$) M (SD)	Total ($n = 32$) M (SD)	F	
Age	14.69 (1.97)	14.94 (1.65)	14.80 (1.82)	14.67 (1.49)	15.09 (1.81)	14.86 (1.62)	0.02	<0.01
VIQ	108.72 (10.54)	111.36 (18.11)	109.87 (14.15)	105.44 (12.76)	105.29 (17.81)	105.38 (14.91)	1.58	0.03
NVIQ	109.00 (11.24)	103.64 (14.68)	106.66 (12.92)	115.06 (9.46)	107.79 (15.59)	111.88 (12.82)	2.55	0.04
FSIQ	110.61 (10.60)	108.79 (16.80)	109.81 (13.44)	112.11 (11.67)	107.64 (18.13)	110.16 (14.75)	<0.01	<0.01
ASDS	45.33 (11.00)	43.07 (10.82)	44.34 (10.81)	119.44 (14.23)	118.00 (13.81)	118.81 (13.84)	552.20***	0.90
AQ	13.57 (6.41)	10.41 (3.92)	12.19 (5.61)	36.72 (5.49)	33.29 (5.74)	35.22 (5.78)	271.93***	0.82
SES	4.13 (1.02)	3.95 (1.10)	4.05 (1.04)	3.88 (1.24)	4.29 (1.28)	4.06 (1.25)	0.02	<0.01

There were no group differences in age, NVIQ, VIQ, FSIQ, or SES. SES represents a composite of maternal education, paternal education, and household income. All groups fell within the upper middle class range on SES

TYP typically developing, *ASD* autism spectrum disorder, *VIQ* verbal IQ, *NVIQ* nonverbal IQ, *FSIQ* composite IQ, *ASDS* Asperger's Syndrome Diagnostic Scale, *AQ* Autism-Spectrum Quotient—Adolescent Version, *SES* socio-economic status

communication, and imagination. Using a cut-off of ≥30 on the AQ, Baron-Cohen et al. (2006) found that 100 % of higher functioning girls with ASD and 86.8 % higher functioning boys with ASD were correctly classified, and no controls were incorrectly classified, suggesting strong sensitivity and specificity. Further, Baron-Cohen et al. (2006) reported good internal consistency ($\alpha = 0.79$) for the AQ-Adolescent Version Total scale. The second measure used to screen for autism traits in higher functioning youth, the ASDS, is a yes–no 50-item norm-referenced instrument that indexes five behavioral areas: behavior, cognitive, maladaptive, social and sensorimotor. A cut-off of ≥90 on the ASDS indicates a "likely" to "very likely" probability of Asperger Syndrome. The test manual reported good internal consistency for the ASDS Total scale ($\alpha = 0.83$), and evidence of criterion validity as the total score correctly identified 85 % of children across five classifications.

Parent Report Measure of Anxiety and Depression

The Revised Child Anxiety and Depression Scale—Parent Version (RCADS-P; Chorpita et al. 2000) is a 47-item parent report measure that indicates on a four-point Likert scale how often a symptom of anxiety or depression is present from "never" to "always". The measure includes a Major Depressive Disorder scale and a Total Anxiety scale. The Total Anxiety scale consists of the following five subscales: Separation Anxiety Disorder, Social Phobia, Generalized Anxiety Disorder, Panic Disorder, and Obsessive Compulsive Disorder. Ebesutani et al. (2010) found excellent internal consistency for the anxiety total scale ($\alpha = 0.94$) and good internal consistency for all subscales (α's > 0.80). Further, all RCADS-P scales indicated strong discriminant validity, successfully discriminating youth with and without disorders corresponding to the RCADS-P subscales. Sterling et al. (2015) found acceptable internal consistency of the RCADS in a sample of 67 youth with ASD. In the current study, internal consistency for the RCADS Total Anxiety scale was excellent in both groups (ASD, $\alpha = 0.96$; TYP, $\alpha = 0.92$), and in the ASD group for the Social Phobia scale ($\alpha = 0.92$) and Panic Disorder scale ($\alpha = 0.90$). In the present study, internal consistency was good in both groups for the Generalized Anxiety Disorder scale (ASD, $\alpha = 0.89$; TYP, $\alpha = 0.82$), and Obsessive Compulsive Disorder scale (ASD, $\alpha = 0.83$; TYP, $\alpha = 0.83$). Further, internal consistency was good in the ASD group for the Major Depressive Disorder scale ($\alpha = 0.85$), and in the TYP group for the Separation Anxiety Disorder scale ($\alpha = 0.81$) and the Social Phobia scale ($\alpha = 0.84$). Internal consistency was acceptable in the TYP group for the Major Depressive Disorder scale ($\alpha = 0.75$) and in the ASD group for the Separation Anxiety Disorder scale ($\alpha = 0.74$). Internal consistency was questionable in the TYP group for the Panic Disorder scale ($\alpha = 0.69$).

Adolescent Measures of Anxiety and Depression

The Multidimensional Anxiety Scale for Children (MASC; March et al. 1997) is a 39-item self-report instrument that assesses four major domains of anxiety in children: (1) *Physical Symptoms,* consisting of items on tense/restless and somatic/autonomic, (2) *Harm Avoidance* consisting of items on perfectionism and anxious coping, (3) *Social Anxiety* comprised of items on humiliation/rejection and performance fear, and (4) *Separation/Panic* consisting of items assessing separation anxiety and panic and phobia symptoms. Additionally, a MASC standardized total score is provided. Items are rated using a four-point Likert scale

of the occurrence of the behavior from "never true about me" to "often true about me". Standardized scores are calculated based on age and sex of the respondent. Based on a study of the general population (March et al. 1997), internal consistency was good for the Total Anxiety scale ($\alpha = 0.87$), and acceptable for the four major subscales (α's = 0.72–0.80). March et al. (1999) found the discriminant validity of the MASC to be satisfactory, with an overall classification rate of 71 %. In the current study, internal consistency for the MASC Total scale was excellent for the ASD group ($\alpha = 0.90$). Further, in the current study, internal consistency was good for the Social Anxiety scale (ASD, $\alpha = 0.82$; TYP, $\alpha = 0.84$), as well as the Physical Symptoms scale for the ASD group ($\alpha = 0.85$), MASC Total scale for the TYP group ($\alpha = 0.81$). Internal consistency was acceptable for the Separation/Panic scale (ASD, $\alpha = 0.71$; TYP, $\alpha = 0.72$), Physical Symptoms scale for the TYP group ($\alpha = 0.78$). The internal consistency was questionable for the Harm Avoidance scale for the ASD group ($\alpha = 0.64$) and unacceptable for the Harm Avoidance scale for the TYP group ($\alpha = 0.44$).

The Center for Epidemiologic Studies Depression Scale (CES-D; Radloff 1977) is a 20-item self-report that measures on a 4-point Likert scale, from "rarely or none of the time" to "most or all of the time", how frequently a respondent has felt depressive feelings in the past week. The CES-D has good internal consistency for adolescent populations ($\alpha > 0.87$ for all subgroups; Roberts et al. 1990). Further, it was found to discriminate well between psychiatric inpatient and general population samples, identifying 73 % of the patients with Major Depressive Disorder. In the current study, internal consistency of the CES-D was questionable for the ASD group ($\alpha = 0.68$) and the TYP group ($\alpha = 0.65$).

Procedure

Adolescent participants completed their self-report measures and IQ testing in a quiet testing room with one experimenter. The parents completed their questionnaires in an adjoining video monitor room. Data was collected as part of a larger behavioral study involving social and cognitive measures.

Data Analytic Plan

To evaluate Hypotheses 1 and 2, analysis of covariance (ANCOVA) was used, except in cases where the dependent variables were correlated and then multivariate analysis of covariance (MANCOVA) was used. The dependent variables were parent-rated and child-reported depression and anxiety, and the independent variables were group, sex, and developmental stage (early vs. late adolescence). Composite IQ was included as a covariate. Full models, consisting of all main effects and 2-way and 3-way interactions, were tested for significance. Significant interactions were followed up with post hoc testing using one-way ANCOVAs with Dunn-Sidak correction (Sidak) to all possible pairwise comparisons. We elected to use Sidak because it is considered to be more powerful than the traditional Bonferroni correction (Dunn 1964). To address Hypothesis 3, we examined the correlations among internalizing problems, ASD severity, and IQ. In order to reduce the influence of outliers, we utilized a winsorization procedure, which is a robust accommodation technique that preserves the sample size while pulling the mean toward the middle of the distribution (Dixon and Tukey 1968). We winsorized the data by setting the outliers on the upper extreme to a value corresponding to the 95th percentile and setting the outliers on the lower extreme to a value corresponding to the 5th percentile. Examination of the distribution of residuals revealed no substantial deviations from normality, confirming the assumption of normal distribution of error terms was satisfied.

Results

Parent Report of Depression and Anxiety

The Total Anxiety scale and Depression scale on the RCADS parent report were correlated in both the ASD group and TYP group (see Table 2), confirming that a MANCOVA was warranted. We conducted a $2 \times 2 \times 2$ MANCOVA with Group (TYP vs. ASD), Sex (male vs. female), and Developmental Stage (early vs. late adolescence) as fixed factors, and the Total Anxiety and Major Depressive Disorder subscales from the RCADS parent-report measure as dependent variables, covarying for composite IQ. Consistent with Hypothesis 1, this analysis revealed a multivariate main effect of group, Wilks' $\Lambda = 0.67$, $F(2, 54) = 13.27$, $p < 0.001$, $\eta^2 = 0.33$. Univariate results revealed that parents reported significantly greater anxiety symptoms in the ASD group ($M = 30.20$, $SD = 18.37$) in comparison to the TYP group ($M = 13.99$, $SD = 8.79$), $F(1, 55) = 20.87$, $p < 0.001$, $\eta^2 = 0.28$. Similarly, parents also reported significantly higher depressive symptoms in the ASD group ($M = 8.70$, $SD = 4.63$) relative to the TYP group ($M = 3.92$, $SD = 2.79$), $F(1, 55) = 26.33$, $p < 0.001$, $\eta^2 = 0.32$. Counter to Hypothesis 2, the parent report data did not reveal a significant 2-way interaction that supported the double hit theory of females with ASD. However, a 3-way interaction of sex, developmental stage of adolescence, and group, provided a more complex picture of the double hit theory of females with ASD. The parent report revealed a

Table 2 Pearson correlations among IQ, ASD severity, and parent report of depression and anxiety (RCADS-P) in adolescents with ASD or TYP

	1	2	3	4	5	6	7	8	9	10
1. FSIQ	–	0.124	0.413*	0.141	−0.054	0.125	0.094	0.027	−0.355*	0.082
2. AQ	0.055	–	0.421*	0.480**	0.393*	0.507**	0.368*	0.324	0.268	0.349
3. ASDS	0.335	0.540**	–	0.650**	0.440*	0.443*	0.477**	0.404*	0.293	0.382*
4. MDD	0.169	0.324	0.622**	–	0.798**	0.699**	0.720**	0.700**	0.695**	0.658**
5. Total Anx.	0.070	0.501**	0.569**	0.714**	–	0.861**	0.863**	0.893**	0.893**	0.837**
6. SAD	0.037	0.352*	0.482**	0.625**	0.819**	–	0.760**	0.706**	0.663**	0.696**
7. GAD	0.062	0.186	0.311	0.610**	0.838**	0.676**	–	0.712**	0.688**	0.631**
8. PD	0.112	0.378*	0.382*	0.429*	0.569**	0.603**	0.338	–	0.725**	0.761**
9. SP	0.199	0.591**	0.659**	0.612**	0.875**	0.544**	0.627**	0.336	–	0.671**
10. OCD	−0.289	0.338	0.194	0.410*	0.666**	0.363*	0.581**	−0.022	0.631**	–

Correlations for the ASD group ($n = 32$) are shown above the diagonal. Correlations for the TYP group ($n = 32$) are shown below the diagonal

ASD autism spectrum disorder, *TYP* typical development, *FSIQ* composite IQ, *AQ* Autism-Spectrum Quotient—Adolescent Version, *ASDS* Asperger's Syndrome Diagnostic Scale. *RCADS-P* Revised Child Anxiety and Depression Scale—Parent Version contains the following scales, *MDD* Major Depressive Disorder, *Total Anx.* Total Anxiety, *SAD* Separation Anxiety Disorder, *GAD* Generalized Anxiety Disorder, *PD* Panic Disorder, *SP* Social Phobia, *OCD* Obsessive Compulsive Disorder

* $p \leq 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$

significant 3-way interaction, Wilks' $\Lambda = 0.89$, $F(2, 54) = 3.30$, $p = 0.04$, $\eta^2 = 0.11$. Univariate tests indicated that the 3-way interaction was mainly driven by differences in depression ($F(1, 55) = 5.06$, $p = 0.03$, $\eta^2 = 0.08$). To further examine this 3-way interaction, we used follow-up tests and corrected for multiple comparisons with the Sidak correction. These tests revealed that the females with ASD tended to exhibit greater depressive symptoms than the males with ASD (Sidak, $p < 0.10$) and the TYP females ($p = 0.001$) during early adolescence, whereas by late adolescence ASD females and ASD males were at similarly high levels (see Fig. 1a). Further, males with ASD tended to present greater depressive symptoms in late adolescence compared to early adolescence ($p = 0.08$), whereas there was no developmental effect for the females with ASD or the TYP females or males.

Next, we conducted a MANCOVA with the five anxiety subscales of the RCADS parent-report as the dependent variables (i.e., Separation Anxiety Disorder, Social Phobia, Generalized Anxiety Disorder, Panic Disorder, Obsessive Compulsive Disorder), and Group, Sex, and Developmental Stage as fixed factors, covarying for composite IQ. In line with Hypothesis 1, we found a significant multivariate effect of group, Wilks' $\Lambda = 0.66$, $F(5, 51) = 5.17$, $p < 0.001$, $\eta^2 = 0.34$. Thus, we followed up by examining the univariate tests (see Table 3) and found a significant Group effect of all five anxiety subscales, (p's ≤ 0.01), such that the ASD group showed greater anxiety symptoms across the five anxiety disorders compared to the TYP group. There was also a marginally significant multivariate interaction of group × developmental stage, Wilks' $\Lambda = 0.82$, $F(5, 51) = 2.23$, $p = 0.07$, $\eta^2 = 0.18$. Univariate tests indicated that the group × developmental stage interaction was being driven by the Generalized Anxiety Disorder subscale ($F(1, 55) = 3.62$, $p = 0.06$, $\eta^2 = 0.06$). Follow up tests revealed that older adolescents with ASD relative to the younger adolescents with ASD exhibited greater symptoms of Generalized Anxiety Disorder (Sidak, $p = 0.04$), whereas there was no difference between older and younger TYP adolescents ($p = 0.52$; see Fig. 2).

Adolescent Self-Reports of Depression and Anxiety

The MASC Total Anxiety scale and CES-D Depression scale from the adolescent self-reports were correlated in the ASD group but not the TYP group (see Table 4). For this reason, we conducted an ANCOVA for the CESD-D and a separate ANCOVA for the MASC Total Anxiety scale, controlling for composite IQ. For both analyses, we used a 2 × 2 × 2 design, with Group (TYP vs. ASD), Sex (male vs. female), and Developmental Stage (early vs. late adolescence) as fixed factors. Consistent with Hypothesis 1, the ANCOVA revealed that the ASD group reported significantly higher depressive symptoms ($M = 16.61$, $SD = 8.77$) relative to the TYP group ($M = 11.29$, $SD = 6.68$), $F(1, 55) = 7.54$, $p < 0.01$, $\eta^2 = 0.12$. Similarly, the ANCOVA revealed that the ASD group reported significantly greater Total Anxiety symptoms ($M = 57.40$, $SD = 10.63$) than the TYP group ($M = 52.92$, $SD = 7.94$), $F(1, 54) = 5.05$, $p < 0.05$, $\eta^2 = 0.09$. Regarding Hypothesis 2, the adolescent report data did not

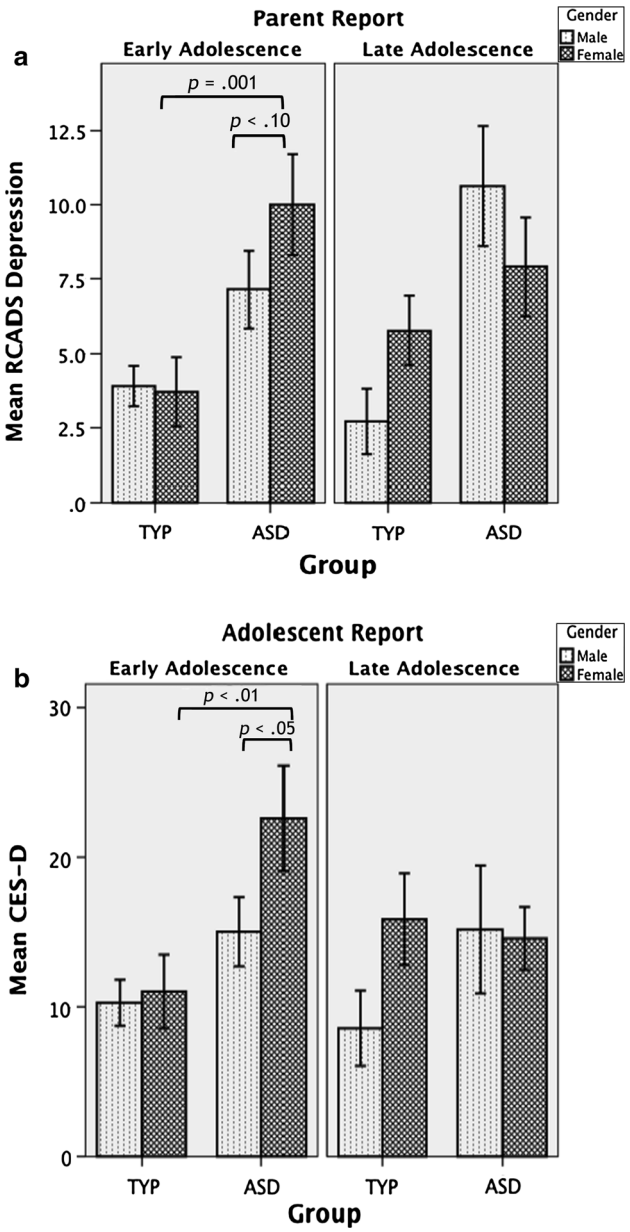

Fig. 1 **a** Represents parent report data from the RCADS-P Total Depression scale, indicating that during early adolescence females with ASD exhibited greater depressive symptoms than males with ASD or TYP females and males. **b** Represents adolescent report data from the CES-D scale, indicating a pattern consistent with the parent report findings on depression. Sample size per subgroup ranged from 7 to 11. *Error bars* represent ±1 standard error of the mean

reveal a significant 2-way interaction that supported the double hit theory of females with ASD. However, the ANCOVA revealed a marginally significant 3-way interaction for adolescent reported depression, $F(1, 55) = 3.79$, $p = 0.06$, $\eta^2 = 0.06$. As can be seen in Fig. 1b, Sidak post hoc tests revealed that in early adolescence the ASD females reported significantly higher depression than the TYP females ($p < 0.01$) and ASD males ($p < 0.05$), in line with our parent findings.

We next conducted a MANCOVA with the four major domains of the MASC (i.e., Physical Symptoms, Harm Avoidance, Social Anxiety, and Separation/Panic) as the dependent variables and Group, Sex, and Developmental Stage as fixed factors, controlling for composite IQ. Although we did not find a significant multivariate effect of Group, Wilks' $\Lambda = 0.88$, $F(4, 51) = 1.68$, $p = 0.17$, $\eta^2 = 0.12$, based on Hypothesis 1 we expected group effects and so we examined the univariate test for each anxiety subscale. Univariate tests revealed a significant Group effect for the Physical Symptoms domain, $F(1, 54) = 5.47$, $p = 0.02$, $\eta^2 = 0.09$, and for the Separation/Panic domain, $F(1, 54) = 4.61$, $p = 0.04$, $\eta^2 = 0.08$. Specifically, adolescents with ASD reported greater physical symptoms and separation anxiety and panic symptoms relative to the TYP group (see Table 3). A goal of our study was to explore potential 3-way interactions, and we found a marginally significant multivariate 3-way interaction of group × sex × developmental stage, Wilks' $\Lambda = 0.86$, $F(4, 51) = 2.17$, $p = 0.09$, $\eta^2 = 0.15$. Univariate tests revealed that the group × sex × developmental stage interaction was driven by differences in the Separation/Panic domain, $F(1, 54) = 6.75$, $p = 0.01$, $\eta^2 = 0.11$. To elucidate this significant 3-way interaction, we employed post hoc tests using one-way ANCOVAs with Sidak correction. Notably, in early adolescence the TYP males and ASD females were reporting higher levels of separation anxiety and panic than the TYP females or ASD males, but by late adolescence ASD males and females tended to report higher levels of separation anxiety and panic than TYP males and females (see Fig. 3).

Correlations Among ASD Severity, IQ, Depression, and Anxiety

Lastly, to test Hypothesis 3, we examined whether ASD severity, as measured by the AQ Total Scale and ASDS Total Scale, and composite IQ correlated with parent report of depression and anxiety (RCADS Depression and Total Anxiety Scales) and adolescent report of depression and anxiety (CES-D and MASC Total Anxiety). Consistent with Hypothesis 3, based on parent-report, we found that ASD severity was positively correlated with anxiety and depression in both adolescent groups, such that increases in anxiety and depression were associated with increases in ASD symptoms (see Table 2). Similarly, based on adolescent self-report, the MASC Total Anxiety scale was marginally correlated with ASD severity in both the TYP and ASD groups (see Table 4), but no correlations between depression and ASD severity were found. Composite IQ was only correlated with parent reported Total Anxiety in the TYP group (see Table 2).

Table 3 Group differences in anxiety based on parent and adolescent report

Measure	Group		*F*	η
	TYP *M (SD)*	ASD *M (SD)*		
Parent report (RCADS-P)				
Separation Anxiety Disorder	1.94 (2.27)	4.49 (3.23)	13.06***	0.18
Generalized Anxiety Disorder	2.69 (2.24)	6.43 (3.78)	22.83***	0.27
Panic Disorder	1.39 (1.47)	4.15 (4.47)	10.74**	0.15
Social Phobia	7.61 (3.72)	11.63 (6.19)	10.19**	0.14
Obsessive Compulsive Disorder	0.74 (1.34)	3.40 (3.24)	18.05***	0.23
Total Anxiety	13.99 (8.79)	30.20 (18.37)	20.87***	0.28
Adolescent Report (MASC)				
Physical Symptoms	48.62 (8.16)	53.57 (10.39)	4.39*	0.07
Harm Avoidance	52.50 (7.10)	54.15 (8.82)	0.66	0.01
Social Anxiety	55.01 (10.19)	57.39 (10.57)	0.79	0.01
Separation/Panic	54.21 (10.75)	57.67 (11.21)	1.50	0.02
Total Anxiety	52.92 (7.94)	57.40 (10.63)	3.51†	0.06

The table represents ANCOVA results of group effects for the anxiety scales of the RCADS-P parent report ($n = 32$ TYP; $n = 32$ ASD) and MASC adolescent report ($n = 31$ TYP; $n = 32$ ASD)

TYP typically developing, *ASD* autism spectrum disorder, *RCADS-P* Revised Child Anxiety and Depression Scale—Parent Version, *MASC* Multidimensional Anxiety Scale for Children

† $p \leq 0.10$; * $p \leq 0.05$; *** $p \leq 0.001$

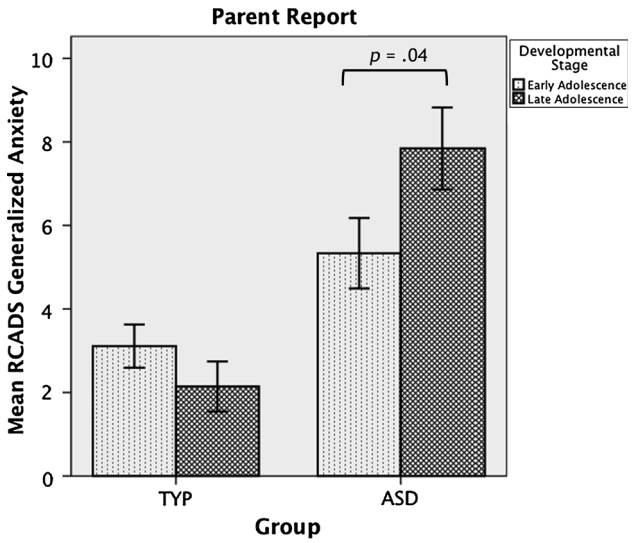

Fig. 2 The *bar graph* represents a group × developmental stage interaction of the means of Generalized Anxiety Disorder, as reported by parents on the RCADS-P. In particular, the older adolescents with ASD relative to the younger adolescents with ASD exhibited greater symptoms of Generalized Anxiety Disorder. Sample size per subgroup ranged from 14 to 18. *Error bars* represent ±1 standard error of the mean

Discussion

In the current study, we investigated whether sex, developmental stage of adolescence, ASD severity, and IQ influenced the presentation of anxiety and depressive symptoms in higher functioning adolescents with ASD relative to TYP adolescent controls. Consistent with *Hypothesis 1*, we found that parent-report and adolescent self-report indicated that the ASD group had greater symptoms of depression and Total Anxiety than the TYP group, replicating prior research (Gadow et al. 2012; Ghaziuddin et al. 2002; Kim et al. 2000; Szatmari et al. 1989; White et al. 2009). As a further test of Hypothesis 1, we examined whether there were group differences within specific anxiety disorders. Parent-report revealed that the ASD group compared to the TYP group exhibited more anxiety symptoms in all five categories assessed by the RCADS-P (i.e., Separation Anxiety Disorder, Social Phobia, Generalized Anxiety Disorder, Panic Disorder, and Obsessive Compulsive Disorder). Adolescent report of anxiety dimensions, revealed that the ASD group exhibited greater symptoms than the TYP group on the Physical Symptoms and Separation/Panic MASC subscales, consistent with Bellini (2004). Counter to *Hypothesis 2*, we did not find a 2-way interaction to support the double-hit hypothesis (Solomon et al. 2012) that females with ASD might be at a particularly heightened risk for developing internalizing disorders. Finally, our data partially supported *Hypothesis 3*. Parent- and adolescent self-reports indicated that greater ASD severity was associated with higher anxiety levels, but only parent report further indicated that greater ASD severity was associated with higher depression levels. We did not find significant correlations with IQ and depression or anxiety in the ASD group, which may be the result of

Table 4 Pearson correlations among IQ, ASD severity, and self report of depression (CES-D) and anxiety (MASC) in adolescents with ASD or TYP

	1	2	3	4	5	6	7	8	9
1. FSIQ	–	0.124	0.413*	−0.072	0.000	0.082	−0.212	−0.102	0.080
2. AQ	0.055	–	0.421*	−0.004	0.307	0.282	0.100	0.339	0.273
3. ASDS	0.335	0.540**	–	0.057	0.080	0.077	−0.212	0.209	0.131
4. Depression	0.072	0.151	0.075	–	0.420*	0.402*	0.158	0.311	0.402*
5. Total Anxiety	0.525**	0.207	0.393*	0.226	–	0.897**	0.600**	0.771**	0.781**
6. Physical Symptoms	0.493**	−0.089	0.192	0.190	0.678**	–	0.430*	0.572**	0.637**
7. Harm Avoidance	0.256	0.134	0.281	−0.319	0.296	−0.107	–	0.270	0.450**
8. Social Anxiety	0.267	0.365*	0.236	0.448*	0.766**	0.335	−0.094	–	0.429*
9. Separation/Panic	0.273	0.006	0.270	−0.033	0.754**	0.357*	0.475**	0.396*	–

Correlations for the ASD group ($n = 32$) are shown above the diagonal. Correlations for the TYP group ($n = 32$) are shown below the diagonal

ASD autism spectrum disorder, *TYP* typical development, *CES-D* Center for Epidemiologic Studies Depression Scale, *MASC* Multidimensional Anxiety Scale for Children, *FSIQ* composite IQ, *AQ* Autism-Spectrum Quotient—Adolescent Version, *ASDS* Asperger's Syndrome Diagnostic Scale

* $p \leq 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$

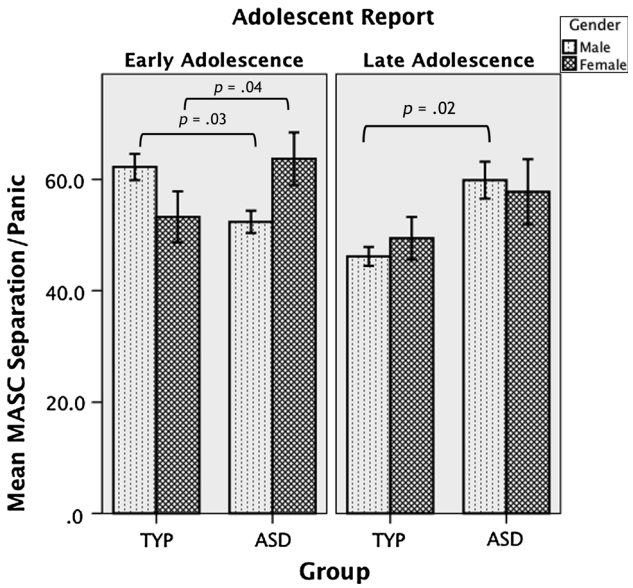

Fig. 3 Represents the means of the Separation/Panic scale as reported by adolescents on the MASC. The *left panel* reflects Separation/Panic in early adolescence, whereas the *right panel* reflects Separation/Panic in late adolescence. The *graph* indicates that males and females with ASD tend to have higher levels of separation anxiety and panic than TYP males and females in late adolescence. Sample size per subgroup ranged from 7 to 11. *Error bars* represent ±1 standard error of the mean

constraining the range of IQs by including only higher functioning youth in our sample (e.g., Strang et al. 2012).

Although we did not find evidence supporting the double-hit theory that was the subject of Hypothesis 2, we did find a significant 3-way interaction suggesting that the risk for internalizing problems in adolescent females with ASD might be more complex than specified in this theory. A pattern borne out by both parent-report and adolescent self-report indicated that females with ASD had greater depressive symptoms specifically during *early adolescence* compared to TYP females and males with ASD. By late adolescence, females with ASD were more similar in depression levels to TYP females and males with ASD. Prior research on the general population has investigated various vulnerability factors to explain the emergence of sex differences in depression during adolescence, including: pubertal maturation (Angold et al. 1998, 1999), lack of quality friendships (Pedersen et al. 2007), greater physiological reaction to social rejection (Ladd 2006; Stroud et al. 2002), and negative cognitive style and rumination (Alloy et al. 2000; Robinson and Alloy 2003). Young adolescent females with ASD might have a unique combination of genetic, hormonal, and psychosocial vulnerabilities that place them at higher risk for depression during early adolescence. An earlier onset of pubertal maturation for females than males (e.g., Velez et al. 1989), greater rumination (Crane et al. 2013; Gotham et al. 2014), and lack of quality friendships (Chamberlain et al. 2007; Mazurek and Kanne 2010) characteristic of ASD, combined with a female predisposition toward greater physiological stress responsivity to social rejection (Stroud et al. 2002), might contribute additively (Ladd 2006) to the risk for depression specifically during early adolescence for females with ASD. Follow-up studies investigating the relations among pubertal status and timing, psychosocial stressors, physiological stress responsivity, and rumination in adolescent females and males with ASD are warranted.

Another notable significant 3-way interaction involved child-reported separation anxiety and panic. In early adolescence, there were sex differences amongst the groups, such that females with ASD and TYP males had significantly higher levels of separation anxiety and panic than males with ASD or TYP females. By late adolescence, the pattern suggested that males and females with ASD had higher levels of separation anxiety and panic than the male and female TYPs. Prior research on the TYP population has found that both sexes tend to decrease in separation anxiety and panic during adolescence (Cohen et al. 1993), paralleling the changes in independence that emerge during this developmental phase. In our data, the TYP males but not females followed this typical pattern of decreasing levels of separation anxiety and panic symptoms over adolescence. Our limited sample suggests that males and females with ASD may experience high levels of separation anxiety and panic during late adolescence, indicating that the development of independence in ASD may be atypical. Follow-up studies to examine the developmental trajectory of separation anxiety, panic and autonomy in ASD may be important to understanding adult outcomes for this population. Research indicates that higher functioning adults with ASD overall have poor adult outcomes, relying heavily upon others for support in living, employment, and relationships (Howlin et al. 2004). Findings from a nationally representative study on youth with disabilities indicated that only 17 % of young adults with ASD lived independently (Newman et al. 2011). Training on self-determination, including decision-making, goal-setting and attainment, and self-advocacy, has been found to effectively scaffold the development of goal-directed behavior and autonomous adult functioning in individuals with certain disabilities and, therefore, may help promote autonomy in transition-age youth with ASD (Wehmeyer et al. 2010). Cognitive behavioral therapy (CBT) also has been found to be an effective treatment for anxiety in ASD (McGillivray and Evert 2014; Russell et al. 2013; Storch et al. 2014; Wood et al. 2009, 2015) and may compliment interventions on self-determination. Combination therapy with these two elements represents a promising intervention approach.

To our knowledge, our study is the first to investigate the prevalence of internalizing symptoms during early versus late adolescence in ASD. Both parent and child reports suggested that anxiety increases over adolescence in individuals with ASD. We found a two-way interaction between group and developmental stage for generalized anxiety disorder, such that parents reported that older adolescents with ASD exhibited greater generalized anxiety disorder symptoms compared to younger adolescents with ASD, consistent with Wing's theory (1981) that older adolescents with ASD develop painful awareness of their own deficits, which may trigger internalizing problems.

Finally, it is noteworthy that there were few differences between parent and adolescent reports. A growing number of studies have addressed the important problem of parent-child reporting discrepancies in high functioning children and adolescents with ASD (e.g., Johnson et al. 2009; Lerner et al. 2012; Ozsivadjian et al. 2014; Sterling et al. 2015; Vickerstaff et al. 2007), and their results have been mixed. Given that it is highly plausible that reduced self-awareness of one's own social impairments within the ASD population leads to underreporting of anxiety symptoms relevant to social contexts, as might be measured by Social Anxiety or Harm Avoidance scales, it is not surprising that several studies have found parent-child discrepancies in reports of social functioning impairments, with parents reporting poorer functioning (Johnson et al. 2009; Lerner et al. 2012; McMahon and Solomon 2015; Vickerstaff et al. 2007). However, a recent meta-analysis examining agreement in children with ASD and those with intellectual disability found moderate levels of agreement between parents and children for internalizing symptoms (Stratis and Lecavalier 2015). Furthermore, other studies suggest it is valuable to obtain self-reports of depression in verbally skilled ASD populations (Gotham et al. 2014), and that self-ratings of anxiety by boys with ASD correlate with physiological markers of their anxiety (Bitsika et al. 2014). The current study is consistent with the perspective that the reports of high functioning children with ASD and their parents are generally concordant. Future studies that use parent and adolescent self-report versions of the same internalizing measure would allow for direct comparisons between parent and adolescent informants through discrepancy analysis.

One major limitation of this study was small sample size. This limited the power to detect significant 3-way interactions. Further, given that we used a cross-sectional design, a next step would be to examine whether these interactions are replicated in a prospective longitudinal study. A further limitation was the lack of a semi-structured interview to confirm diagnosis and reliance on cut-off scores from parent report measures of ASD symptomology. Regarding a statistical limitation, there is always some level of uncertainty when using ordinary least squares about whether the assumption has been met that all variables have been accounted for in the model. Regarding another statistical limitation, there was a small number of scales that had low reliability, however our findings confirmed that reliability was acceptable for most of the depression and anxiety measures in both groups. Although we found no differences in socio-economic status (SES) between the ASD and TYP groups, both groups fell within the upper middle class range. Given the use of self-selected case and control groups and bias toward higher SES, our study may be limited in its generalizability.

Strengths of the study included recruitment of a community sample, which may be more representative of the ASD population than a clinic-referred sample. Clinic samples may have disproportionate rates of severe comorbidities that have led to a clinic referral. Another strength is that we used one-to-one matching of participants with ASD to control participants on both IQ and sex. Relative to matching at the group level, matching at the subject level enhances the power to detect significant differences, which is especially useful for smaller sample sizes.

Conclusions

This study has replicated earlier findings of significantly greater internalizing problems (specifically depression and anxiety) during adolescence in those with ASD compared to TYP controls. ASD severity was found to be positively correlated with depression and anxiety in both the ASD and TYP groups, suggesting that greater ASD symptoms are associated with an increased risk of developing internalizing disorders. Our data also suggest that the "double hit" hypothesis of internalizing problems for females with ASD may need to be revised to account for our data on developmental stages of adolescence. We found that depression peaks during early adolescence in females with ASD, whereas males with ASD reach these higher levels of depression during late adolescence.

We suggest that especially during periods of pubertal growth, adolescents with ASD be closely monitored for depressive and anxiety symptoms and receive therapeutic interventions, such as cognitive behavioral therapy, to reduce internalizing symptoms. We found that both females and males with ASD had high levels of separation panic in late adolescence, possibly indicating atypical development of independence. Training on self-determination to increase autonomous and goal-oriented behavior may be crucial in promoting independence and successful transitions to adulthood for youth with ASD.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

References

Alloy, L. B., Abramson, L. Y., Hogan, M. E., Whitehouse, W. G., Rose, D. T., Robinson, M. S., & Joanna, B. (2000). The temple-Wisconsin cognitive vulnerability to depression project: Lifetime history of Axis I psychopathology in individuals at high and low cognitive risk for depression. *Journal of Abnormal Psychology, 109*, 403–418.

Angold, A., Costello, E. J., Erkanl, A., & Worthman, C. M. (1999). Pubertal changes in hormone levels and depression in girls. *Psychological Medicine, 29*, 1043–1053.

Angold, A., Costello, E. J., & Worthman, C. M. (1998). Puberty and depression: The roles of age, pubertal status and pubertal timing. *Psychological Medicine, 28*, 51–61.

Angold, A., & Rutter, M. (1992). Effects of age and pubertal status on depression in a large clinical sample. *Development and Psychopathology, 4*, 5–28.

Angst, J., & Dobler-Mikola, A. (1985). The Zurich study: VI. A continuum from depression to anxiety disorders? *European Archives of Psychiatry & Neurological Sciences, 235*(3), 179–186.

Baron-Cohen, S., Hoekstra, R. A., Knickmeyer, R., & Wheelwright, S. (2006). The autism-spectrum quotient (AQ)—Adolescent version. *Journal of Autism and Developmental Disorders, 36*(3), 343–350.

Bellini, S. (2004). Social skills and anxiety in higher functioning adolescents with autism spectrum disorders. *Focus on Autism and Other Developmental Disabilities, 19*(3), 78–86.

Bitsika, V., Sharpley, C. F., Sweeney, J. A., & McFarlane, J. R. (2014). HPA and SAM axis responses as correlates of self-vs parental ratings of anxiety in boys with an Autistic Disorder. *Physiology & Behavior, 127*, 1–7.

Brereton, A. V., Tonge, B. J., & Einfeld, S. L. (2006). Psychopathology in children and adolescents with autism compared to young people with intellectual disability. *Journal of Autism and Developmental Disorders, 36*(7), 863–870.

Bruce, S. E., Yonkers, K. A., Otto, M. W., Eisen, J. L., Weisberg, R. B., Pagano, M., & Keller, M. B. (2005). Influence of psychiatric comorbidity on recovery and recurrence in generalized anxiety disorder, social phobia, and panic disorder: A 12-year prospective study. *American Journal of Psychiatry, 162*(6), 1179–1187.

CDC. (2014). Prevalence of autism spectrum disorder among children aged 8 years—Autism and developmental disabilities monitoring network, 11 sites, United States, 2010. *MMWR Surveill Summ, 63*, 1–21.

Chamberlain, B., Kasari, C., & Rotheram-Fuller, E. (2007). Involvement or isolation? The social networks of children with autism in regular classrooms. *Journal of Autism and Developmental Disorders, 37*(2), 230–242.

Chorpita, B. F., Yim, L., Moffitt, C., Umemoto, L. A., & Francis, S. E. (2000). Assessment of symptoms of DSM-IV anxiety and depression in children: A revised child anxiety and depression scale. *Behavior Research and Therapy, 38*, 835–855.

Cohen, P., Cohen, J., Kasen, S., Johnson, J., Rojas, M., Brook, J., et al. (1993). An epidemiological study of disorders in late childhood and adolescence: Age- and gender-specific

prevalence. *The Journal of Child Psychology and Psychiatry, 34*(6), 851–867.

Crane, L., Goddard, L., & Pring, L. (2013). Autobiographical memory in adults with autism spectrum disorder: The role of depressed mood, rumination, working memory and theory of mind. *Autism, 17*(2), 205–219.

Culbertson, F. M. (1997). Depression and gender: An international review. *American Psychologist, 52*(1), 25–31.

Dixon, W. J., & Tukey, J. W. (1968). Approximate behavior of the distribution of Winsorized t (Trimming/Winsorization 2). *Technometrics, 10*, 83–98.

Dunn, O. J. (1964). Multiple comparisons using rank sums. *Technometrics, 6*, 241–252.

Ebesutani, C., Bernstein, A., Nakamura, B. J., Chorpita, B. F., Weisz, J. R., & Research Network on Youth Mental Health. (2010). A psychometric analysis of the revised child anxiety and depression scale—Parent version in a clinical sample. *Journal of Abnormal Child Psychology, 38*(2), 249–260.

Essau, C. A., Conradt, J., & Petermann, F. (2000). Frequency, comorbidity, and psychosocial impairment of anxiety disorders in German adolescents. *Journal of Anxiety Disorders, 14*(3), 263–279.

Gadow, K. D., Guttmann-Steinmetz, S., Rieffe, C., & DeVincent, C. J. (2012). Depression symptoms in boys with autism spectrum disorder and comparison samples. *Journal of Autism and Developmental Disorders, 42*(7), 1353–1363.

Ghaziuddin, M., Ghaziuddin, N., & Greden, J. (2002). Depression in persons with autism: Implications for research and clinical care. *Journal of Autism and Developmental Disorders, 34*(2), 299–306.

Ghaziuddin, M., & Greden, J. (1998). Depression in children with autism/pervasive developmental disorders: A case–control family history study. *Journal of Autism and Developmental Disorders, 28*(2), 111–115.

Gillott, A., Furniss, F., & Walter, A. (2001). Anxiety in high-functioning children with autism. *Autism, 5*(3), 277–286.

Gotham, K., Bishop, S. L., Brunwasser, S., & Lord, C. (2014). Rumination and perceived impairment associated with depressive symptoms in a verbal adolescent–adult ASD sample. *Autism Research, 7*(3), 381–391.

Hammond, R. K., & Hoffman, J. M. (2014). Adolescents with high-functioning autism: An investigation of comorbid anxiety and depression. *Journal of Mental Health Research in Intellectual Disabilities, 7*(3), 246–263.

Hankin, B. L., Abramson, L. Y., Moffitt, T. E., Silva, P. A., McGee, R., & Angell, K. E. (1998). Development of depression from preadolescence to young adulthood: Emerging gender differences in a 10-year longitudinal study. *Journal of Abnormal Psychology, 107*(1), 128–140.

Howlin, P., Goode, S., Hutton, J., & Rutter, M. (2004). Adult outcome for children with autism. *Journal of Child Psychology and Psychiatry, 45*(2), 212–229.

Interagency Autism Coordinating Committee (IACC). (2012). *ACC strategic plan for autism spectrum disorder (ASD) research—2012 update*.

Johnson, S. A., Filliter, J. H., & Murphy, R. R. (2009). Discrepancies between self-and parent-perceptions of autistic traits and empathy in high functioning children and adolescents on the autism spectrum. *Journal of Autism and Developmental Disorders, 39*(12), 1706–1714.

Kanne, S. M., Christ, S. E., & Reiersen, A. M. (2009). Psychiatric symptoms and psychosocial difficulties in young adults with autistic traits. *Journal of Autism and Developmental Disorders, 39*(6), 827–833.

Kaufman, A. S., & Kaufman, N. L. (1990). *Kaufman brief intelligence test manual*. Circle Pines, MN: American Guidance Service.

Kessler, R. C., McGonagle, K. A., Nelson, C. B., Hughes, M., Swartz, M., & Blazer, D. G. (1994). Sex and depression in the national comorbidity survey. II: Cohort effects. *Journal of Affective Disorders, 30*(1), 15–26.

Kim, J. A., Szatmari, P., Bryson, S. E., Streiner, D. L., & Wilson, F. J. (2000). The prevalence of anxiety and mood problems among children with autism and Asperger syndrome. *Autism, 4*(2), 117–132.

Kuusikko, S., Pollock-Wurman, R., Jussila, K., Carter, A. S., Mattila, M. L., Ebeling, H., & Moilanen, I. (2008). Social anxiety in high-functioning children and adolescents with autism and Asperger syndrome. *Journal of Autism and Developmental Disorders, 38*(9), 1697–1709.

Ladd, G. W. (2006). Peer rejection, aggressive or withdrawn behavior, and psychological maladjustment from ages 5 to 12: An examination of four predictive models. *Child Development, 77*(4), 822–846.

Lainhart, J. E. (1999). Psychiatric problems in individuals with autism, their parents and siblings. *International Review of Psychiatry, 11*(4), 278–298.

Lerner, M. D., Calhoun, C. D., Mikami, A. Y., & De Los Reyes, A. (2012). Understanding parent–child social informant discrepancy in youth with high functioning autism spectrum disorders. *Journal of Autism and Developmental Disorders, 42*(12), 2680–2692.

March, J. S., Parker, J., Sullivan, K., Stallings, P., & Conners, C. K. (1997). The Multidimensional Scale for Children (MASC): Factor structure, reliability, and validity. *Journal of the American Academy of Child and Adolescent Psychiatry, 36*, 554–565.

March, J. S., Sullivan, K., & Parker, J. (1999). Test–retest reliability of the Multidimensional Anxiety Scale for children. *Journal of Anxiety Disorders, 13*(4), 349–358.

Mayes, S. D., Calhoun, S. L., Murray, M. J., Ahuja, M., & Smith, L. A. (2011). Anxiety, depression, and irritability in children with autism relative to other neuropsychiatric disorders and typical development. *Research in Autism Spectrum Disorders, 5*(1), 474–485.

Mazurek, M. O., & Kanne, S. M. (2010). Friendship and internalizing symptoms among children and adolescents with ASD. *Journal of Autism and Developmental Disorders, 40*(12), 1512–1520.

McGillivray, J. A., & Evert, H. T. (2014). Group cognitive behavioural therapy program shows potential in reducing symptoms of depression and stress among young people with ASD. *Journal of Autism and Developmental Disorders, 44*(8), 2041–2051.

McMahon, C. M., & Solomon, M. (2015). Brief report: Parent–adolescent informant discrepancies of social skill importance and social skill engagement for higher-functioning adolescents with autism spectrum disorder. *Journal of Autism and Developmental Disorders, 45*(10), 3369–3403.

Myles, B. S., Bock, S. J., & Simpson, R. L. (2001). *Asperger syndrome diagnostic scale*. Austin, TX: Pro-ed.

Newman, L., Wagner, M., Knokey, A. M., Marder, C., Nagle, K., Shaver, D., et al. (2011). *The post-high school outcomes of young adults with disabilities up to 8 years after high school: A report from the National Longitudinal Transition Study-2 (NLTS2)*. NCSER 2011-3005. National Center for Special Education Research.

Nolen-Hoeksema, S., & Girgus, J. S. (1994). The emergence of gender differences in depression during adolescence. *Psychological Bulletin, 115*(3), 424.

Ozsivadjian, A., Hibberd, C., & Hollocks, M. J. (2014). Brief report: The use of self-report measures in young people with autism spectrum disorder to access symptoms of anxiety, depression and negative thoughts. *Journal of Autism and Developmental Disorders, 44*(4), 969–974.

Pedersen, S., Vitaro, F., Barker, E. D., & Borge, A. I. H. (2007). The timing of middle-childhood peer rejection and friendship: Linking early behavior to early-adolescent adjustment. *Child Development, 78*, 1037–1051.

Radloff, L. S. (1977). The CES-D scale: A self-report depression scale for research in the general population. *Applied Psychological Measurement, 1*, 385–401.

Regier, D. A., Narrow, W. E., & Rae, D. S. (1990). The epidemiology of anxiety disorders: The epidemiologic catchment area (ECA) experience. *Journal of Psychiatric Research, 24*(2), 3–14.

Roberts, R. E., Andrews, J. A., Lewinsohn, P. M., & Hops, H. (1990). Assessment of depression in adolescents using the center for epidemiologic studies depression scale. *Psychological Assessment: A Journal of Consulting and Clinical Psychology, 2*(2), 122–128.

Robinson, M. S., & Alloy, L. B. (2003). Negative cognitive styles and stress-reactive rumination interact to predict depression: A prospective study. *Cognitive Therapy and Research, 27*(3), 275–291.

Russell, A. J., Jassi, A., Fullana, M. A., Mack, H., Johnston, K., Heyman, I., & Mataix-Cols, D. (2013). Cognitive behavior therapy for comorbid obsessive–compulsive disorder in high-functioning autism spectrum disorders: A randomized controlled trial. *Depression and Anxiety, 30*(8), 697–708.

Saluja, G., Iachan, R., Scheidt, P. C., Overpeck, M. D., Sun, W., & Giedd, J. N. (2004). Prevalence of and risk factors for depressive symptoms among young adolescents. *Archives of Pediatrics and Adolescent Medicine, 158*(8), 760–765.

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 and Adolescent Psychiatry, 47*(8), 921–929.

Solomon, M., Miller, M., Taylor, S. L., Hinshaw, S. P., & Carter, C. S. (2012). Autism symptoms in internalizing psychopathology in girls and boys with autism spectrum disorders. *Journal of Autism Developmental Disorders, 42*(1), 48–59.

Spitzer, R. L., Kroenke, K., Williams, J. B., & Löwe, B. (2006). A brief measure for assessing generalized anxiety disorder: The GAD-7. *Archives of Internal Medicine, 166*(10), 1092–1097.

Sterling, L., Renno, P., Storch, E. A., Ehrenreich-May, J., Lewin, A. B., Arnold, E., & Wood, J. (2015). Validity of the Revised Children's Anxiety and Depression Scale for youth with autism spectrum disorders. *Autism, 19*(1), 113–117.

Storch, E. A., Lewin, A. B., Collier, A. B., Arnold, E., De Nadai, A. S., Dane, B. F., & Murphy, T. K. (2014). A randomized controlled trial of cognitive-behavioral therapy versus treatment as usual for adolescents with autism spectrum disorders and comorbid anxiety. *Depression and Anxiety, 32*(3), 174–181.

Strang, J. F., Kenworthy, L., Daniolos, P., Case, L., Wills, M. C., Martin, A., & Wallace, G. L. (2012). Depression and anxiety symptoms in children and adolescents with autism spectrum disorders without intellectual disability. *Research in Autism Spectrum Disorders, 6*(1), 406–412.

Stratis, E. A., & Lecavalier, L. (2015). Informant agreement for youth with autism spectrum disorder or intellectual disability: A meta-analysis. *Journal of Autism and Developmental Disorders, 45*(4), 1026–1041.

Stroud, L. R., Salovey, P., & Epel, E. S. (2002). Sex differences in stress responses: Social rejection versus achievement stress. *Biological Psychiatry, 52*(4), 318–327.

Sukhodolsky, D. G., Scahill, L., Gadow, K. D., Arnold, L. E., Aman, M. G., McDougle, C. J., & Vitiello, B. (2008). Parent-rated anxiety symptoms in children with pervasive developmental disorders: Frequency and association with core autism symptoms and cognitive functioning. *Journal of Abnormal Child Psychology, 36*(1), 117–128.

Szatmari, S., Bartolucci, G., Bremner, R., Bond, S., & Rich, S. (1989). A follow-up study of high-functioning autistic children. *Journal of Autism and Developmental Disorders, 19*(2), 213–225.

Van Oort, F., Greaves-Lord, K., Verhulst, F., Ormel, J., & Huizink, A. (2009). The developmental course of anxiety symptoms during adolescence: The TRAILS study. *The Journal of Child Psychology and Psychiatry, 50*(10), 1209–1217.

Velez, C. N., Johnson, J., & Cohen, P. (1989). A longitudinal analysis of selected risk factors for childhood psychopathology. *Journal of the American Academy of Child and Adolescent Psychiatry, 28*(6), 861–864.

Vickerstaff, S., Heriot, S., Wong, M., Lopes, A., & Dossetor, D. (2007). Intellectual ability, self-perceived social competence, and depressive symptomatology in children with high-functioning autistic spectrum disorders. *Journal of Autism and Developmental Disorders, 37*(9), 1647–1664.

Wehmeyer, M. L., Shogren, K. A., Zager, D., Smith, T. C., & Simpson, R. (2010). Research-based principles and practices for educating students with autism: Self-determination and social interactions. *Education And Training In Autism And Developmental Disabilities, 45*(4), 475–486.

Weisbrot, D. M., Gadow, K. D., DeVincent, C. J., & Pomeroy, J. (2005). The presentation of anxiety in children with pervasive developmental disorders. *Journal of Child & Adolescent Psychopharmacology, 15*(3), 477–496.

White, S. W., Oswald, D., Ollendick, T., & Scahill, L. (2009). Anxiety in children and adolescents with autism spectrum disorders. *Clinical Psychology Review, 29*(3), 216–229.

Wing, L. (1981). Asperger's syndrome: A clinical account. *Psychological Medicine, 11*(01), 115–129.

Wood, J. J., Drahota, A., Sze, K., Har, K., Chiu, A., & Langer, D. A. (2009). Cognitive behavioral therapy for anxiety in children with autism spectrum disorders: A randomized, controlled trial. *Journal of Child Psychology and Psychiatry, 50*, 224–234.

Wood, J. J., Ehrenreich-May, J., Alessandri, M., Fujii, C., Renno, P., Laugeson, E., & Storch, E. A. (2015). Cognitive behavioral therapy for early adolescents with autism spectrum disorders and clinical anxiety: A randomized, controlled trial. *Behavior Therapy, 46*(1), 7–19.