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Psychiatric Symptoms in Youth with a History of Autism and Optimal Outcome

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Abstract Since autism spectrum disorder (ASD) is often comorbid with psychiatric disorders, children who no longer meet criteria for ASD (optimal outcome; OO) may still be at risk for psychiatric disorders. A parent interview for DSM-IV psychiatric disorders (K-SADS-PL) for 33 OO, 42 high-functioning autism (HFA) and 34 typically developing (TD) youth, ages 8–21, showed that OO and HFA groups had elevated current ADHD and specific phobias, with tics in HFA. In the past, the HFA group also had elevated depression and ODD, and the OO group had tics. The HFA group also showed subthreshold symptoms of specific and social phobias, and generalized anxiety. Psychopathology in the OO group abated over time as did their autism, and decreased more than in HFA.

Keywords Autism spectrum disorder · Optimal outcome · Psychiatric functioning · Comorbidity

Introduction

Autism spectrum disorder (ASD) have generally been considered to be lifelong. Recent research, however, indicates that some children with ASD show such improvements in language, cognitive, and social functioning, that they no longer meet criteria for ASD; these so-called optimal outcome (OO) children may have academic (Troyb et al. 2014b) and cognitive and language abilities (Suh et al. 2014; Tyson et al. 2014) comparable to their same-aged peers (Fein et al. 2013). Strict criteria have been proposed to define this form of OO. Specifically, the proposed definition of OO requires that the individual has a well-documented history of ASD, no longer meets criteria for any ASD, and that both IQ and adaptive functioning scores are within the average range (Helt et al. 2008).

There is a significant empirical literature that suggests that ASD presents with high rates of comorbid psychiatric disorders in childhood and adolescence (Canitano and Vivanti 2007; de Bruin et al. 2007; Gadow and DeVincent 2005; Gadow et al. 2004; Gjevik et al. 2011; Joshi et al. 2010; Leyfer et al. 2006; Mattila et al. 2010; Munesue et al. 2008; Muris et al. 1998; Simonoff et al. 2008). The first systematic study of psychiatric comorbidity in ASD found that 70 % of early adolescents met criteria for at least one comorbid psychiatric disorder; 41 % had two or more (Simonoff et al. 2008). Most common were social anxiety, ADHD, and oppositional defiant disorder (ODD). In a more recent study of 8-year-olds with ASD, 21 % had comorbid ADHD and 10 % had other disorders (Levy et al. 2010).

The term comorbidity refers to the presence of two or more symptomatically distinct psychiatric disorders that are present at the same time in an individual. Since ASD has complex and heterogeneous presentations, it may be difficult to distinguish true comorbidity from overlapping

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symptomatology (e.g., ASD versus ADHD). Not only do ASD symptoms overlap behaviorally with other disorders, but ASD and comorbid disorders may be uniquely related through underlying pathophysiology (Gillberg and Billstedt 2000). Psychological disorders may also develop as a reaction to social consequences and stressors (Mazzone et al. 2012). These mechanisms might leave the OO group vulnerable to the same psychiatric conditions as the ASD group.

Anxiety, obsessive–compulsive behavior, tics, and ADHD were reported in high-functioning adults with ASD, some of whom had lost their diagnosis (Burd et al. 2002; Szatmari et al. 1989). Fein et al. (2005) documented a group of children who achieved OOs but had diagnosable ADHD. Zappella (2002) reported that some children who lost their ASD diagnosis exhibited tics and ADHD. Parents reported that children with current ASD were more likely to experience moderate to severe anxiety than children with a past, but not current, ASD diagnosis (Close et al. 2012). Anderson et al. (2014) found that adolescents with very positive outcomes (similar to our OO group) had fewer hyperactivity and depression symptoms compared to high-functioning adolescents who retained their ASD diagnosis. These results support the idea that OO individuals may be vulnerable to some of the same disorders as those with ASD (specifically, ADHD, anxiety, and tics). However, most of these studies did not rigorously define OO using the strict criteria described above or examine psychiatric symptoms comprehensively by looking at all DSM-IV Axis I disorders in the same participants.

We assessed the rates of DSM-IV psychiatric comorbidity in high-functioning, verbal children and adolescents with OO, HFA, and TD. The use of a high-functioning sample was primarily to match the HFA with the OO group, but it also allowed us to assess a wide range of psychiatric disorders, some of which are most easily ascertained in individuals with sufficient cognitive abilities who are better able to communicate their internal states. We expected highest rates of comorbid psychiatric disorders in the HFA group, compared with both the OO and TD groups. In addition, based on previous studies, we anticipated that the OO group would display more symptoms of ADHD, anxiety, and tics than TD youth. Positive relationships were expected between higher ASD symptom severity and psychiatric symptomatology.

Methods

Participants

The current study used the participants and testing procedures described in Fein et al. (2013). Participants were 33 youth with a history of ASD and OO, 42 with HFA, and 34 TD peers. Age ranged from 8 years, 1 month to 21 years, 8 months. Groups did not differ on chronological age, gender, and nonverbal IQ, but differed on verbal IQ (see Table 1). The only requirement was that IQ be higher than 77. However, the OO group had a higher than average mean IQ, which necessitated recruiting high IQ participants in the other two groups as well. The HFA group had poorer adaptive communication and social skills (Vineland) than the other two groups, which did not differ. Participants were predominantly White, with three OO, two HFA, and three TD reporting other races. The data were collected across multiple sites (University of Connecticut, the Institute of Living Hartford Hospital and Queens University, Canada), with approval by their Institutional Review Boards.

Inclusion Criteria

All participants had verbal, nonverbal, and full-scale IQ standard scores greater than 77 (within 1.5 SD of the average of 100). Additional OO criteria were:

1. ASD diagnosis before the age of 5 by a physician or psychologist specializing in autism, in a written report. The report was edited to remove information about diagnosis, summary, and recommendations but leaving descriptions of behavior. One of the co-investigators (MB), an expert in diagnosis of ASD and Director of the University of Connecticut Psychological Services Clinic, reviewed these reports, blind to early diagnosis and current group membership. In addition to potential OO participants, she reviewed 24 "foil" reports for children with non-ASD diagnoses, such as global delay or language disorder. Four potential OO participants were rejected for insufficient early documentation, and were dropped from the study. All 24 foils were correctly rejected.
2. In addition to establishing an early ASD diagnosis, we also required early language delay as an inclusion criteria. Even though an early language delay is not required for an ASD diagnosis, this increased the confidence that the participants truly had an early ASD and not just a personality variation that appeared later in childhood.
3. On the phone screening, parents had to report that the participant had typically developing friends. During evaluation, participants could not meet criteria for any ASD on the Autism Diagnostic Observation Schedule (ADOS; Lord et al. 2000). In addition, the ADOS videotapes of all potential OO cases were reviewed by a clinician with more than 15 years of autism diagnostic experience (IME, MB, or DF) who confirmed

Table 1 Participant characteristics

Mean (SD) range	TD N = 34	OO N = 33	HFA N = 42	F/χ^2	p	Post-hoc
Gender (male: female)	31:3	26:7	38:4	2.97	0.23	
Age	13.9 (2.6)	12.8 (3.5)	13.9 (2.7)	1.60	0.21	
	9.9–21.7	8.1–21.2	8.6–20.0			
WASI-VIQ	112.0 (11.2)	111.9 (13.3)	105.5 (14.7)	3.10	**0.049**	Trend HFA < OO, TD
	93–138	80–137	81–142			
WASI-NVIQ	112.8 (11.3)	110.3 (15.3)	111.0 (12.5)	0.32	0.73	
	89–139	81–142	78–147			
Vineland-communication	93.3 (9.3)	98.2 (12.4)	80.9 (15.0)	18.5	**<0.001**	HFA < OO, TD
	74–119	79–122	42–108			
Vineland-social	101.7 (8.6)	102.2 (8.8)	76.1 (15.1)	62.3	**<0.001**	HFA < OO,TD
	86–120	80–118	46–109			
ADOS-communication	0.41 (0.56)	0.45 (0.62)	3.43 (1.35)	127.0	**<0.001**	OO, TD < HFA
	0–2	0–2	2–7			
ADOS-social	0.50 (0.75)	1.00 (1.23)	6.69 (2.20)	182.9	**<0.001**	OO, TD < HFA
	0–2	0–4	4–13			

Bold indicates $p < 0.05$

that ADOS scores were below ASD thresholds and that, in their expert clinical judgment, an ASD was not present. Five potential OO participants were judged to have social impairments with an autistic quality and were excluded from the study. These five children were borderline cases, as they were judged to have an autistic quality but would not have met criteria for the HFA group.

4. Participants' scores on the Communication and Socialization domains of the Vineland Adaptive Behavior Scales (Vineland; Sparrow et al. 1985) had to be greater than 77 (within 1.5 SDs of the mean of 100).
5. Participants had to be fully included in regular education classrooms with no one-on-one assistance and no special education services to address autism deficits (e.g., no social skills training). However, participants could be receiving limited special education services or psychological support to address impairments not specific to ASD, such as attention or academic difficulties.

To be included in the HFA group:

1. Following Collaborative Programs of Excellence in Autism diagnostic guidelines (Luyster et al. 2005), participants met criteria for ASD on the ADOS (both Social and Communication domains and total score) and according to best estimate clinical judgment.

To be included in the TD group:

1. Participants could not meet criteria for any ASD at any point in their development, by parent report.
2. Participants could not have a first-degree relative with an ASD diagnosis.
3. Participants could not meet current diagnostic criteria for an ASD on the ADOS, or by clinical judgment. There was no attempt to exclude TD children for other learning or psychiatric disorders (but see general exclusion criteria).
4. Scores on the Communication and Socialization domains of the Vineland had to be greater than 77.

Exclusion Criteria

Potential participants for any group were excluded if (1) at the time of the telephone screening they exhibited symptoms of major psychopathology that would impede full participation, (2) they had severe visual or hearing impairments, or (3) they had a seizure disorder, Fragile X syndrome, or significant head trauma with loss of consciousness. Two in the TD group and two in the HFA group were excluded because of possible seizure disorder based on parent report; none were excluded for other reasons.

Measures

The *Wechsler Abbreviated Scale of Intelligence* (WASI) (Wechsler 1999) was used to assess verbal and nonverbal cognitive abilities. The *Vineland Adaptive Behavior Scales* (Sparrow et al. 1985) assessed Communication and Socialization skills. Module 3 or 4 of the *Autism Diagnostic Observation Schedule* (Lord et al. 2000), a

structured play and interview session, was used to assess symptoms of autism.

The Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime version (K-SADS-PL) (Kaufman et al. 1997) assesses symptoms of psychiatric syndromes in children based on the *DSM-IV* criteria. The K-SADS-PL has a *Screen Interview,* an 82-item interview divided into diagnostic areas. Five *Diagnostic Supplements* for (1) Affective Disorders, (2) Psychotic Disorders, (3) Anxiety Disorders, (4) Behavioral Disorders, and (5) Substance Abuse, Eating, and Tic Disorders are administered if the child receives one or more threshold ratings on the screen interview. In the current study, the K-SADS-PL was administered to the parents of study participants. Scoring of the K-SADS-PL involves rating most symptom items from 1 to 3. For ease of interpretation, the scores were converted to a 0–2 scale for the present study, (0 symptom not present, 1 subthreshold symptom, 2 threshold was met). There is significant overlap between ASD and symptoms of many other psychiatric disorders. For the present study, each item was coded as present if the parent's report of the participant's behavior matched the DSM-IV-TR description, which is the basis of the K-SADS-PL questions.

Data Analyses

Fisher Exact tests were used to compare frequencies of individuals meeting criteria for each disorder, separately for past and current time periods. Fisher's exact test assumes that the row and column totals are fixed, or "conditioned", which is not the case in the current study. When one or both of the row or column totals are unconditioned, the Fisher's exact test is not exact. However, it is somewhat conservative, meaning that it is harder to achieve statistical significance. Therefore, although the use of the Fisher's exact test in the current study violated an assumption of the test, the significant findings in the current study were likely accurate. However, we may have failed to detect other significant findings.

Since the goal was to uncover all possible psychiatric tendencies, we wanted an indicator of mild symptoms. Subthreshold reports were noted by parents on the K-SADS Screen Interview. Therefore, an exploratory analysis was conducted to further assess group differences in disorders for which diagnostic criteria may not have been met. The scores for each screening symptom were averaged to create a symptom score for each disorder, separately for current and past, and compared among groups using ANOVAs. When Levene's test for homogeneity of variance was violated, the Games–Howell post hoc test was used; otherwise, the Tukey HSD post hoc test was used. Kruskal–Wallis tests were used to confirm parametric results. G*Power software was used to determine the effect size detectable given the current sample size, with α at 0.05 and power at 0.8. For the ANOVAs, we only had power to detect medium to large effect sizes.

Stepwise discriminant function analysis (DFA) was used to determine which current and past symptoms best predicted group membership. Panic, bipolar, and eating disorders were excluded because no participants in any group met current or past criteria.

Spearman's rho correlations were run between average symptom scores and ADOS communication/social algorithm sum.

In this study, the goal was to elucidate all possible psychiatric symptoms in the OO individuals, rather than prematurely concluding that they had lost not only ASD but other psychiatric symptoms as well; therefore, it was considered most conservative in this case not to correct for multiple comparisons, so that even small to moderate effect sizes would be preserved.

Results

Current Diagnoses

Table 2 shows frequencies meeting criteria for diagnoses, based upon the K-SADS-PL screening and diagnostic supplements. More OO and HFA participants had specific phobias than TD participants; OO and HFA did not differ. More OO and HFA than TD participants met criteria for ADHD; OO and HFA did not differ. Finally, the HFA group had higher rates of tics than the other groups, which had none. See Table 2 for additional results.

Past Diagnoses

Table 3 shows frequencies of individuals who met criteria for past disorders. More OO than TD participants had specific phobias. There was more major depression in HFA than OO or TD groups. More OO and HFA than TD participants met criteria for ADHD. The HFA group showed a trend for more ODD in the past than the other groups. Finally, more HFA and OO than TD participants had tic disorders. See Table 3 for additional results.

Current Symptom Average Scores—Exploratory Analysis

Table 4 shows average current symptom scores; results were confirmed with non-parametric Kruskal–Wallis tests. HFA participants showed more symptoms of specific phobia than TD participants. The HFA group had a higher score for social phobia, generalized anxiety, and major

Table 2 Frequencies [N (%)] and group differences for current psychiatric disorders in TD, OO, and HFA youth based on K-SAD-PL parent interviews

Diagnosis	TD (N = 34)	OO (N = 33)	HFA (N = 42)	Fisher exact *p*	Post-hoc
Anxiety disorders					
Panic disorder	0 (0 %)	0 (0 %)	0 (0 %)	N/A	
Specific phobia	0 (0 %)	5 (15 %)	6 (14 %)	**0.036**	OO, HFA > TD
Separation anxiety disorder	0 (0 %)	0 (0 %)	0 (0 %)	N/A	
Social phobia	0 (0 %)	0 (0 %)	2 (5 %)	0.33	
Generalized anxiety disorder	0 (0 %)	0 (0 %)	2 (5 %)	0.33	
Obsessive–compulsive disorder	1 (3 %)	0 (0 %)	4 (10 %)	0.19	
Posttraumatic stress disorder	0 (0 %)	0 (0 %)	0 (0 %)	N/A	
Mood disorders					
Major depressive disorder	0 (0 %)	1 (3 %)	3 (7 %)	0.31	
Bipolar I or II disorder	0 (0 %)	0 (0 %)	0 (0 %)	N/A	
Externalizing disorders					
ADHD	1 (3 %)	8 (24 %)	14 (33 %)	**0.002**	OO, HFA > TD
Conduct disorder	0 (0 %)	0 (0 %)	2 (5 %)	0.33	
Oppositional defiant disorder	3 (9 %)	1 (3 %)	1 (2 %)	0.51	
Other disorders					
Anorexia nervosa	0 (0 %)	0 (0 %)	0 (0 %)	N/A	
Bulimia nervosa	0 (0 %)	0 (0 %)	0 (0 %)	N/A	
Encopresis	0 (0 %)	0 (0 %)	1 (2 %)	0.99	
Enuresis	0 (0 %)	0 (0 %)	1 (2 %)	0.99	
Tic disorders	0 (0 %)	0 (0 %)	5 (12 %)	**0.012**	HFA > TD, OO

Bold indicates $p < 0.05$

Table 3 Frequencies [N (%)] and group differences for past psychiatric disorders in TD, HFA, and OO youth based on K-SAD-PL parent interviews

Diagnosis	TD (N = 34)	OO (N = 33)	HFA (N = 42)	Fisher exact *p*	Post-hoc
Anxiety disorders					
Panic disorder	0 (0 %)	0 (0 %)	0 (0 %)	N/A	
Specific phobia	2 (6 %)	8 (24 %)	6 (14 %)	0.10	OO > TD
Separation anxiety disorder	0 (0 %)	0 (0 %)	3 (7 %)	0.11	
Social phobia	0 (0 %)	0 (0 %)	2 (5 %)	0.33	
Generalized anxiety disorder	0 (0 %)	0 (0 %)	3 (7 %)	0.11	
Obsessive–compulsive disorder	1 (3 %)	0 (0 %)	4 (10 %)	0.19	
Posttraumatic stress disorder	0 (0 %)	0 (0 %)	2 (5 %)	0.33	
Mood disorders					
Major depressive disorder	1 (3 %)	1 (3 %)	8 (19 %)	**0.028**	HFA > TD, OO
Bipolar I or II disorder	0 (0 %)	0 (0 %)	0 (0 %)	N/A	
Externalizing disorders					
ADHD	1 (3 %)	13 (39 %)	22 (52 %)	**<0.001**	OO, HFA > TD
Conduct disorder	0 (0 %)	0 (0 %)	1 (2 %)	0.99	
Oppositional defiant disorder	2 (6 %)	1 (3 %)	8 (19 %)	0.075	HFA > OO
Other disorders					
Anorexia nervosa	0 (0 %)	0 (0 %)	0 (0 %)	N/A	
Bulimia nervosa	0 (0 %)	0 (0 %)	0 (0 %)	N/A	
Encopresis	0 (0 %)	0 (0 %)	2 (5 %)	0.33	
Enuresis	2 (6 %)	2 (6 %)	4 (10 %)	0.81	
Tic disorders	0 (0 %)	4 (12 %)	7 (17 %)	**0.026**	OO, HFA > TD

Bold indicates $p < 0.05$

Table 4 Average score for each disorder by group for current symptoms

	TD (N = 34)	OO (N = 30)	HFA (N = 34)	F	*p*	Post-Hoc
Anxiety disorders						
Panic disorder	0.06 (0.35)	0.10 (0.31)	0.00 (0.00)	1.21	0.30	
1 item						
Specific phobia	0.16 (0.46)	0.40 (0.66)	0.59 (0.79)	3.71	**0.028**	HFA > TD
2 items						
Separation anxiety disorder	0.04 (0.12)	0.09 (0.17)	0.11 (0.20)	1.69	0.19	
5 items						
Social phobia	0.12 (0.28)	0.23 (0.45)	0.65 (0.72)	9.76	**<0.001**	HFA > OO,TD
2 items						
Generalized anxiety disorder	0.06 (0.14)	0.14 (0.20)	0.34 (0.42)	8.82	**<0.001**	HFA > OO,TD
4 items						
Obsessive–compulsive disorder	0.14 (0.50)	0.08 (0.16)	0.16 (0.37)	0.30	0.74	
2 items						
Posttraumatic stress disorder	0.01 (0.04)	0.01 (0.03)	0.01 (0.05)	0.02	0.98	
11 items						
Mood disorders						
Major depressive disorder	0.02 (0.06)	0.04 (0.07)	0.14 (0.23)	6.97	**0.001**	HFA > OO,TD
8 items						
Bipolar I or II disorder	0.02 (0.06)	0.03 (0.08)	0.04 (0.09)	0.72	0.49	
4 items						
Externalizing disorders						
ADHD	0.27 (0.51)	0.74 (0.74)	0.87 (0.63)	8.32	**<0.001**	OO,HFA > TD
4 items						
Conduct disorder	0.02 (0.08)	0.06 (0.12)	0.08 (0.26)	0.95	0.39	
5 items						
Oppositional defiant disorder	0.27 (0.41)	0.33 (0.51)	0.42 (0.62)	0.69	0.51	
3 items						
Other disorders						
Anorexia nervosa	0.02 (0.09)	0.12 (0.22)	0.02 (0.09)	5.30	**0.007**	OO > HFA,TD
2 items						
Bulimia nervosa	0.00 (0.00)	0.00 (0.00)	0.004 (0.02)	0.94	0.40	
8 items						
Encopresis	0.00 (0.00)	0.07 (0.37)	0.00 (0.00)	1.09	0.34	
3 items						
Enuresis	0.00 (0.00)	0.01 (0.06)	0.05 (0.29)	0.75	0.47	
3 items						
Tic disorders	0.14 (0.46)	0.24 (0.64)	0.12 (0.30)	0.60	0.55	
2 items						

Bold indicates $p < 0.05$

depression symptoms than the other groups. OO and HFA groups had higher symptom scores for current ADHD than the TD group.

Past Symptom Average Scores

Table 5 shows average past symptom scores. HFA participants had more social phobia and generalized anxiety symptoms than TD participants. The HFA group showed more symptoms of major depression than the other groups. Both OO and HFA participants had more symptoms of ADHD and conduct disorders. OO participants had more symptoms of ODD than TD participants.

The same results were found using non-parametric Kruskal–Wallis tests, with one exception: the OO elevation on ODD symptoms was reduced to a trend ($p = 0.058$).

Table 5 Average score for each disorder by group for past symptoms

	TD (N = 34)	OO (N = 30)	HFA (N = 34)	F	*p*	Post-hoc
Anxiety disorders						
Panic disorder	0.12 (0.42)	0.10 (0.31)	0.09 (0.29)	0.08	0.93	
1 item						
Specific phobia	0.26 (0.59)	0.64 (0.83)	0.66 (0.80)	2.90	0.060	
2 items						
Separation anxiety disorder	0.11 (0.15)	0.19 (0.30)	0.24 (0.28)	2.32	0.10	
5 items						
Social phobia	0.13 (0.28)	0.38 (0.58)	0.76 (0.75)	10.17	**<0.001**	HFA > TD
2 items						
Generalized anxiety disorder	0.14 (0.31)	0.16 (0.24)	0.33 (0.39)	3.32	**0.040**	HFA > TD
4 items						
Obsessive–compulsive disorder	0.16 (0.51)	0.27 (0.54)	0.23 (0.42)	0.41	0.67	
2 items						
Posttraumatic stress disorder	0.10 (0.09)	0.10 (0.08)	0.13 (0.11)	0.76	0.47	
11 items						
Mood disorders						
Major depressive disorder	0.08 (0.17)	0.12 (0.14)	0.33 (0.31)	11.7	**<0.001**	HFA > OO, TD
8 items						
Bipolar I or II disorder	0.04 (0.09)	0.04 (0.12)	0.05 (0.10)	0.05	0.95	
4 items						
Externalizing disorders						
ADHD	0.49 (0.68)	1.04 (0.78)	1.02 (0.69)	6.13	**0.003**	OO, HFA > TD
4 items						
Conduct disorder	0.05 (0.11)	0.15 (0.20)	0.18 (0.28)	3.50	**0.034**	OO, HFA > TD
5 items						
Oppositional defiant disorder	0.30 (0.39)	0.68 (0.66)	0.61 (0.68)	3.63	**0.030**	OO > TD
3 items						
Other disorders						
Anorexia nervosa	0.05 (0.20)	0.10 (0.20)	0.00 (0.00)	3.04	0.053	
2 items						
Bulimia nervosa	0.01 (0.04)	0.01 (0.05)	0.004 (0.02)	0.14	0.87	
8 items						
Encopresis	0.00 (0.00)	0.13 (0.51)	0.17 (0.47)	1.65	0.20	
3 items						
Enuresis	0.08 (0.22)	0.11 (0.25)	0.09 (0.33)	0.09	0.92	
3 items						
Tic disorders	0.21 (0.55)	0.59 (0.86)	0.29 (0.62)	2.56	0.082	
2 items						

Bold indicates $p < 0.05$

Discriminant Function Analysis

Current Symptoms

TD Versus HFA The stepwise DFA was significant; social phobia symptoms were the best predictor of group membership, followed by symptoms of ADHD and then depression, Wilks $\lambda = 0.50$, $\chi^2(3) = 38.75$, $p < 0.001$, with a canonical correlation of 0.71. The standardized canonical discrimination coefficient was 0.83 for social phobia, 0.67 for ADHD, and 0.62 for depression. The model predicted 79 % of the group classifications; the HFA group showed more symptoms in each disorder.

OO Versus HFA Results were significant; social phobia symptoms were the best predictor of group membership,

followed by symptoms of depression, Wilks $\lambda = 0.78$, $\chi^2(2) = 14.16, p = 0.001$, with a canonical correlation of 0.47. The coefficients were 0.83 for social phobia and 0.71 for depression. The model predicted 70 % of the group classifications; the HFA group showed more symptoms of both disorders.

OO Versus TD Results were significant; ADHD symptoms were the only significant predictor of group membership, Wilks $\lambda = 0.89$, $\chi^2(1) = 6.37$, $p = 0.012$, with a canonical correlation of 0.33. The standardized canonical discrimination coefficient was 1.00 for ADHD. The model predicted 69 % of the group classifications; the OO group showed more symptoms than the TD group.

Past Symptoms

TD Versus HFA Results were significant; social phobia symptoms were the best predictor, followed by symptoms of depression, and ADHD, Wilks $\lambda = 0.57$, $\chi^2(3) = 33.07$, $p < 0.001$, with a canonical correlation of 0.66. The coefficients were 0.72 for social phobia, 0.56 for depression, and 0.51 for ADHD. The model predicted 77 % of the group classifications; the HFA group showed more symptoms of each disorder.

OO Versus HFA Results were significant; depression symptoms were the only significant predictor, Wilks $\lambda = 0.84$, $\chi^2(1) = 9.72$, $p = 0.002$, with a canonical correlation of 0.40. The coefficient was 1.00 for depression. The model predicted 65 % of the group classifications; the HFA group showed more symptoms.

OO Versus TD Results were significant; ODD symptoms were the best predictor, followed by symptoms of social phobia, tic disorders, and then separation anxiety symptoms, Wilks $\lambda = 0.64$, $\chi^2(4) = 24.0$, $p < 0.001$, with a canonical correlation of 0.60. The coefficients were 0.59 for ODD, 0.64 for social phobia, 0.61 for tic disorder, and 0.54 for separation anxiety disorder. The model predicted 77 % of the group classifications; the OO group showed more symptoms of each disorder.

Autism Severity and Psychiatric Symptoms

Spearman's rho correlations between ADOS Social+Communication scores and symptom averages for each disorder yielded further evidence of the relationship between certain disorders and ASD. There was a significant relationship between higher (more impaired) ADOS scores and higher scores for depression, (current $r = 0.30$, $p = 0.003$, past, $r = 0.32$, $p = 0.002$), social phobia (current, $r = 0.36$, $p < 0.001$, past, $r = 0.39$, $p < 0.001$), generalized anxiety (current: $r = 0.29$, $p = 0.004$, past: $r = 0.21$, $p = 0.04$), and ADHD (current: $r = 0.29$, $p = 0.004$ and past: $r = 0.22$, $p = 0.03$).

Discussion

The current study was designed to investigate comorbid psychiatric symptoms in individuals with a history of an ASD who no longer meet diagnostic criteria in comparison with individuals with a current ASD diagnosis and individuals with typical development. In general, the results were consistent with our hypotheses. The OO group had less current and past comorbidity across all categories than the HFA group, although frequencies were often too low to be significant.

In terms of predictive power, symptoms of disorders that differentiated the HFA group from the TD group did not change over time (social phobia, depression, ADHD), while symptoms of disorders that differentiated the OO group from the TD group diminished from past to present. Finally, as expected, more severe communication and social symptoms were related to more symptoms of depression, social phobia, generalized anxiety, and ADHD. The implications of these results are discussed in detail below.

Comparative Rates of Psychiatric Disorders

As predicted based on previous studies with both OO and HFA participants, we found elevated frequencies of past and current psychiatric symptomatology in the OO and HFA groups, compared to TD, especially specific phobias, ADHD, and tics.

Specific Phobias

The rate of specific phobias in OO suggests that they may be more difficult to remediate than some of the core ASD symptoms, or that intervention for phobias is not implemented as frequently as other interventions. OO youth displayed some phobias that are less common in typical youth, such as crying babies and loud noises. The OO youth both avoided these stimuli and overreacted when exposed to them. These phobias are consistent with the over-reactivity to sensory stimuli that is common in ASD, and could be related to continued sensory sensitivity or early-learned fear of discomfort.

Tic Disorders

Tics were seen in both OO and HFA participants, both currently and in the past. This is consistent with Zappella (2002), which reflects the chronicity of tics into early

adulthood in ASD, compared to the more common transient presentation of tic disorders in the general population (Leckman et al. 1998). It should be noted, however, that questions about tics might have elicited some endorsement based on repetitive behaviors, which can be difficult to differentiate from tics. However, very few repetitive behaviors were noted in the OO participants in another study on the same sample (Troyb et al. 2014a); therefore, the presence of tics was likely not due to that confusion.

ADHD

Consistent with Fein et al. (2005), ADHD was the most frequently seen comorbid disorder in both OO and HFA and included inattention, hyperactivity and impulsivity. Inattention and impulsivity are often part of the ASD presentation, and may be difficult to remediate. This also supports previous suggestions that ADHD and ASD may share common genetic pathways (Ronald et al. 2008; Sinzig et al. 2009). In the OO group, 39 % met criteria for past ADHD, and 24 % continued to meet criteria. Therefore, ADHD symptoms in OO appeared to decrease with age. Similarly, for HFA, ADHD decreased from 52 to 33 %. This is consistent with a typical decrease in ADHD symptoms from childhood to adulthood in the general population (Costello et al. 2011).

ODD and Conduct Disorder (CD)

The increased ODD and CD in the OO and HFA groups shows higher levels of behavioral dysregulation. This may reflect a variety of different factors. Individuals with an autism history often have poor social reciprocity and communication skills, which leads to a decreased ability to interact with others in an appropriate manner, leading to maladaptive behaviors that may be misinterpreted as noncompliance. Furthermore, many children with ASD display cognitive inflexibility, such as insistence on sameness and consistency of routines, and may react in negative ways even to seemingly small changes. Such outbursts may be incorrectly considered a more purposeful, disobedient reaction. In addition, particularly in the past, some of the OO and HFA participants were physically aggressive towards family members and others, when their symptoms of ASD were most severe, which based on criteria alone led to scores in the disruptive behavior disorders category. However, very few in either group met full criteria for ODD or CD and even the mild symptoms abated over time.

Social Phobia

Significant social interaction difficulties are core features of ASD and of social phobia (American Psychiatric Association 2000). Because both ASD and social phobia are defined behaviorally, the overlap between the two disorders may result in misinterpretation of symptoms by clinicians. Significant comorbidity rates, ranging from 12 to 57 % have been reported (e.g., de Bruin et al. 2007; Farrugia and Hudson 2006; Kuusikko et al. 2008; Reaven et al. 2015; Simonoff et al. 2008), primarily in children and adolescents with HFA. Greater capacity for insight in individuals with HFA may contribute to increased awareness of social deficits and thus greater vulnerability to anxiety related to social evaluation (Weisbrot et al. 2005). Research suggests that ASD and social phobia can occur concurrently (de Bruin et al. 2007; Farrugia and Hudson 2006; Gillott et al. 2001; Kim et al. 2000; Simonoff et al. 2008). In ASD, social phobia symptoms of avoidance and social fears are not core features of the disorder. Furthermore, Tyson and Cruess (2012) emphasized that individuals with HFA and individuals with social phobia show some apparent similarities in symptoms that have subtle distinguishing features. For instance, the impaired eye contact and nonverbal behaviors present in HFA are likely due to a profound deficit at the neural level, starting from early in life, while unusual nonverbal behaviors such as averted eye gaze and trembling in social phobia suggest an etiology influenced by temperament and environmental factors. Because past symptoms of social phobia differentiated the OO and TD groups, and symptoms of social phobia were prevalent in the HFA group, future studies should more closely examination the distinction between symptom presentations of ASD and/or social phobia in children and adolescents with a diagnostic history of one or both disorders.

Summary

Optimal outcome (OO) youth showed *more* lifetime psychiatric symptoms and diagnoses than TD youth; however, they evidenced *fewer* lifetime symptoms than HFA youth. These disturbances may represent residual deficits of ASD, such as phobias related to sensory processing. This finding is also consistent with the views of Amaral et al. (2003) that some neuroanatomical findings in autism may reflect the frequent comorbid anxiety rather than core social features. Wood and Gadow (2010) suggested several possible roles of anxiety in youth with ASD: (1) a consequence of ASD symptoms, such as the result of social rejection; (2) a moderator of ASD symptom severity, as core symptoms of ASD may be exacerbated by anxiety; and (3) as a proxy of core ASD symptoms. The results of current study cannot differentiate these roles of anxiety but provide further support for the significant comorbidity of ASD and anxiety.

Also noteworthy are the areas in which OO did *not* differ from TD. Aside from ADHD and specific phobias,

OO youth did not differ from TD youth in other anxiety, mood, or externalizing disorders.

Based on DFA, current attention and impulsivity symptoms were the symptoms that best differentiated OO and HFA from the TD youth. Furthermore, current and past depression and social phobia differentiated HFA from the other two groups. Increased social withdrawal and depressed mood were associated with HFA. These psychiatric symptoms may impede the development of an OO, or the HFA depression might be reactive to the persisting social difficulties (Gotham et al. 2014).

Correlations between ADOS scores and psychiatric disorders support the notion that severe autism symptoms may raise risk for other psychiatric symptoms or that some other factor (such as executive dysfunction) provides a shared risk factor for both ASD and other psychopathology. Alternatively, positive social experiences might provide a buffer that protects against other psychopathology.

Limitations and Future Directions

A significant limitation of the study is that initial ASD diagnosis was assessed retrospectively. Care was taken to obtain documentation of ASD symptoms in early diagnostic reports. In addition, based on the Autism Diagnostic Interview-Revised, there was no difference between the two groups in early communication or repetitive behaviors (Fein et al. 2013). Although the HFA group had significantly more severe social impairments in early childhood than the OO group, both groups were well above the cutoff for autism.

The sample was relatively small and homogeneous in race and SES, and included only high- functioning individuals, who might have more internalizing but less externalizing disorders (Weisbrot et al. 2005), than lower-functioning individuals. Parents were self-selected; perhaps because of this, the TD youth exhibited less psychopathology than would be expected in the general population. Replication with a more heterogeneous sample would be beneficial in interpreting the results of the present study.

Conversely, the age range of participants was quite large (ages 8–21). Although age was balanced across groups, it is possible that age moderated psychiatric presentation in some groups but not others. Unfortunately, the sample was not big enough to allow us to break the sample into groups of latency age, early adolescence, and late adolescence. Such an analysis would be extremely valuable and should be conducted in future studies. Similarly, the sample was too small to examine whether verbal IQ is a moderating variable that accounts for certain psychiatric presentations (e.g., depression or anxiety) in certain age and/or diagnostic groups but not others.

In addition, we deliberately set a low threshold for significant results in order to be able to closely examine all possible psychiatric symptoms in the OO individuals. Thus, we made the decision not to correct for multiple comparisons. However, because a large number of point hypothesis tests were carried out in this paper, including post hoc comparisons, several of the significant findings may be spurious. The current study needs to be replicated in order to increase confidence in the results. Furthermore, it is likely that the statistical tests in the current study were underpowered and could only detect medium to large effect sizes. Thus, the power of the study limits inferences drawn about non-significant results, of which the study had many. Higher powered studies would be beneficial.

The study had only a parent interview to measure psychiatric symptoms. In future studies, use of other measures for validation, such as behavioral observations, interviews, or self-reports, might be useful, since parents may not be as accurate at reporting internalizing disorders in their adolescent children (Cantwell et al. 1997). In addition, the K-SADS is not validated to assess for psychiatric comorbidity in children and adolescents with ASD. Instruments currently used to assess the co-morbidity of ASD and other disorders may not provide valid differential diagnoses. However, the few available instruments that measure co-morbid psychopathology while also accounting for the complex developmental and psychological profile of ASDs have not been extensively validated (e.g., the *Autism Comorbidity Interview-Present and Lifetime Version* (ACI-PL) developed by Leyfer et al. (2006).

Another limitation is that, for past psychiatric symptoms and diagnoses, we were unable to determine whether these reports occurred during the time when the OO children still had their ASD diagnoses or whether the comorbid psychiatric symptoms developed after the ASD symptoms abated. Prospective studies would be ideal in understanding the interrelated course of ASD and psychiatric comorbidity over time. In addition, this type of study would be greatly enhanced by use of an epidemiological sample.

Finally, the current study was unable to carefully differentiate ASD from other disorders, such as autistic inattention versus ADHD, tics versus repetitive behaviors, and sensory avoidance versus phobia. Future studies examining these differentiations might help to clarify some of the comorbidity issues in ASD and OO individuals.

Clinical Implications

The psychiatric vulnerabilities in OO present a strong argument for the importance of carefully diagnosing and treating psychiatric disorders in youth with ASD or OO. The persistence of anxiety, ADHD and tic symptoms suggests that more intervention is needed for HFA individuals. Modified

cognitive behavioral treatments have been shown to be effective for youth with HFA (Chalfant et al. 2007; Reaven et al. 2015). It would be helpful to examine this type of treatment for OO individuals with anxiety, ADHD and/or tic symptoms. In addition, medication studies with OO may provide important information (Santosh et al. 2006). While psychotherapeutic and pharmacologic treatments are likely to be beneficial, it was encouraging that psychiatric symptoms appeared to abate in the OO group over time. Nonetheless, OO should be monitored for co-occurring psychiatric conditions and have subsequent access to providers familiar with the management of neuropsychiatric conditions as needed.

Conclusions

In the present study, the HFA group had high comorbidity rates of many psychiatric disorders, while the OO group had elevated rates of only ADHD, specific phobias, and tics. The TD group had limited comorbidity in the current study. OO youth are at increased risk of lifetime psychiatric symptoms and diagnoses compared to TD youth. HFA youth are at even higher risk. OO and HFA youth should be carefully assessed and treated for psychiatric disorders.

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Conflict of interest There are no conflicts of interest to declare.

Author Contributions D.A.F., M.L.B., I-M.E., E.K., L.N., R.T.S., and M.C.S. designed the larger study from which this data was taken. K.E.T. developed the concept for the current paper. A.O., K.E.T., E.T., M.H., and M.R. collected the data. A.O. analysed the data. A.O., K.E.T., and J.S. wrote sections of the paper. All authors discussed the results and implications and edited the manuscript at all stages.

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