J Autism Dev Disord (2018) 48:3702–3710
DOI 10.1007/s10803-017-3180-7

S.I. : AUTISM INPATIENT COLLECTION - STUDYING THE SEVERELY AFFECTED

Talking About Death or Suicide: Prevalence and Clinical Correlates in Youth with Autism Spectrum Disorder in the Psychiatric Inpatient Setting

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Published online: 17 June 2017

Abstract Little is known about suicidal ideation in youth with autism spectrum disorder (ASD), making it difficult to identify those at heightened risk. This study describes the prevalence of thoughts about death and suicide in 107 verbal youth with ASD with non-verbal IQ >55, assessed during inpatient psychiatric admission. Per parent report, 22% of youth with ASD had several day periods when they talked about death or suicide "often," or "very often." Clinical correlates included the presence of a comorbid mood (OR 2.71, 95% CI 1.12–6.55) or anxiety disorder (OR 2.32, 95% CI 1.10–4.93). The results suggest a need for developmentally appropriate suicide risk screening measures in ASD. Reliable detection of suicidal thoughts in this high-risk population will inform suicide prevention strategies.

Keywords Autism spectrum disorder · Suicide · Inpatient · Suicidal ideation · Psychiatric patients · Screening · Autism Inpatient Collection (AIC)

Introduction

Suicide is an international public health crisis and the second leading cause of death for youth aged 10–24 years (Centers for Disease Control and Prevention 2015; World Health Organization 2014). While individuals with a variety of psychiatric diagnoses are at heightened risk for suicide, recent studies suggest that youth with autism spectrum disorder (ASD) are at elevated risk (Bennett 2016; Mayes et al. 2013). Several factors may contribute to this increased risk, including comorbid psychiatric disorders and social challenges. Yet there is a dearth of research on suicide risk in youth with ASD. An understanding of how suicidal thoughts and behaviors develop, are expressed and can be reliably detected in youth with ASD is critical for reducing morbidity and mortality in this population.

Detecting suicidal ideation and behavior in youth has become a national priority. In 2012, the United States Surgeon General and the National Institute of Mental Health in conjunction with the National Action Alliance for Suicide Prevention issued the National Strategy for Suicide Prevention, which recommended the development and implementation of suicide risk screening as a method of suicide prevention in the general population (Office of the Surgeon General & National Action Alliance for Suicide Prevention 2012). However, youth with ASD [as well as those with intellectual disability (ID)] have typically been either systematically or functionally excluded from suicide risk screening studies due to cognitive limitations, the lack of screening measures validated for the population,

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and challenges in accessing large ASD samples. Currently, while there have been advances in the development and validation of suicide risk measures for typically developing youth in medical settings (Horowitz et al. 2012), there are no suicide risk screening instruments designed or validated specifically for the ASD or ID populations. Thus, youth with ASD or ID will likely pass through the U.S. healthcare system with undetected suicidal thoughts and behaviors, placing them at greater risk for suicide.

Although suicide was recently determined to significantly contribute to increased premature mortality in ASD (Hirvikoski et al. 2016), very few data are available to provide estimates of suicidal ideation or behavior in ASD. One study of adults in a clinic setting indicated that 66% reported previous suicidal ideation or behavior (Cassidy et al. 2014) and one study of youth in a research setting indicated a combined rate of 11% (Storch et al. 2013). As a reference, 18% of youth in the general population reported past year suicidal ideation and 9% reported suicidal behavior (Centers for Disease Control and Prevention 2015; Kann et al. 2016). The few studies on suicidal ideation or behavior in ASD have been limited by small sample sizes, variations in methods, or a frequent focus on adults and those with Asperger Disorder (Balfe and Tantam 2010; Cassidy et al. 2014; Mandell et al. 2005; Raja et al. 2011; Shtayermman 2007) (see Table 1).

A significant barrier to accurately detecting suicide risk in ASD is the gap in our knowledge of how suicidal thoughts are expressed in this population and how they may vary from that of the typically developing youth population (Hannon and Taylor 2013). It is unknown how difficulties associated with ASD, such as identifying and communicating self-states, understanding abstract concepts of death and dying, and the use of idiosyncratic or stereotyped language, as well as circumscribed interests that may include morbid topics, affect attempts to measure suicide risk. Although research in youth in general indicates that relying on parent report can result in underestimates of suicidal ideation (Klimes-Dougan 1998), parent report may be more sensitive in ASD given these self-report challenges (Mazefsky et al. 2011). With a lack of population-specific screening instruments to identify those at risk for suicide, there is very sparse empirical evidence to guide our understanding of suicide risk in youth with ASD.

The current report describes a sub-analysis of data from a large, multisite study of youth with ASD admitted to six specialized inpatient psychiatry units (The Autism Inpatient Collection; AIC; Siegel et al. 2015). Our goal was to obtain a prevalence estimate of thoughts of death or suicide in youth with ASD utilizing a sample of psychiatric inpatients. We used the only indicator that included suicidal thoughts in this multi-measure study—a single parent reported item from the Child and Adolescent Symptom Inventory-5 (CASI-5; Gadow and Sprafkin 2013), inquiring whether the youth "has periods lasting at least several days where he/she… talks about death or suicide." We also assessed individual characteristics associated with talking about suicide or death in this sample, including intellectual ability and co-morbid psychiatric diagnoses, to inform suicide prevention.

Methods

Participant Population

This is a sub-analysis of a large multisite study designed to produce a collection of phenotypic and genetic data on youth with ASD that includes the full range of intelligence, verbal ability, adaptive functioning and problem behaviors seen in ASD. Participants were aged 4–20 years, inclusive, and were offered serial study enrollment at admission to six U.S. specialized inpatient psychiatry units for youth with ASD and other developmental disorders (see Siegel et al. 2015 for details of the AIC methods). Briefly, children with a score of ≥12 on the Social Communication Questionnaire (SCQ; Rutter et al. 2003), or who scored <12 but were referred by the inpatient hospital team due to high suspicion of ASD, were eligible. Exclusion criteria included caregiver lack of proficiency in English and youth having prisoner status. Legal guardians provided informed consent within 7 days of admission. All retained participants met criteria for ASD based on the Autism Diagnostic Observation Schedule-Second Edition (ADOS-2; Lord et al. 2012), administered during the inpatient stay by a research-reliable examiner. The Aberrant Behavior Checklist—Irritability Subscale (ABC-I), was used to capture physical aggression, self-injurious behavior, and tantrums, within 7 days of admission. For the current analyses, which included a report item that required fluent verbal ability, the sample was restricted to those who were aged 10 years or older (the age of development when youth begin to understand the concept of death) (Mishara 1999; Pfeffer 1981), used sentences to communicate (i.e., received ADOS-2 module 3 or 4), had a measured non-verbal IQ of 55 (the conventional lower limit of the mild range of ID) or greater (using the Leiter-3), and had a parent response to the Child and Adolescent Symptom Inventory—item 86 (see below). Age and IQ inclusion criteria were chosen to be consistent with other research studies of suicide risk and ASD.

Measures

Child and Adolescent Symptom Inventory-5 (CASI-5; Gadow and Sprafkin 2013)

This is a behavior rating scale based on the Diagnostic and Statistical Manual for Mental Disorders, fifth edition

Table 1 Studies since 2000 including suicidal thoughts or behavior in ASD

Study (author, year)	Population (diagnosis) and sample size	Setting	Suicidal thoughts or behavior assessed and question asked	Prevalence
Balfe and Tantam (2010)	Adolescents and adults with Asperger syndrome N = 42	Community sample	Suicidal ideation and suicide attempt via self-report questionnaire (included questions about behavior) Question(s): not specified	Suicidal ideation: 40% Suicide attempt: 15%
Cassidy et al. (2014)	Adults with Asperger disorder N = 374	Outpatient diagnostic clinic	Suicidal ideation, suicide planning or attempt via—a self-report questionnaire (not validated; plans and attempts collapsed into one item) Question(s): "Have you ever felt suicidal?" "If yes, have you ever planned or attempted suicide?"	Suicidal ideation: 66% (243/367) Suicide plans or attempts: 35% (127/365)
Mandell et al. (2005)	Youth with Autism Spectrum Disorder or Asperger disorder N = 156	Several community samples	Suicide attempt (examined in relation to history of physical or sexual abuse) via structured interview with the parent/caregiver Question(s): not specified	Suicide attempt: 31.6% in sub-sample of children physically abused (n = 22); 39.1% in sub-sample of children sexually abused (n = 26); 7–8.5% in children without a history of abuse
Mayes et al. (2013)	Children with autism spectrum disorders N = 791	Psychiatric diagnostic clinic	Suicidal ideation and suicide attempt via parent/caregiver ratings on the pediatric behavior scale (PBS) Question(s): "talks about harming or killing self"; "Deliberately harms self or attempts suicide" with frequency rating	Suicidal ideation: 10.9% Suicide attempt: 7.2%
Raja et al. (2011)	Adults psychiatric patients with autism spectrum disorders N = 26	(1) Psychiatric intensive care unit of general hospital (2) Private practice	Retrospective chart review of recent (last month suicidal ideation, suicide planning, or suicide attempt) Question(s): "thought about suicide in general"; "thought about methods for possible suicide"; "attempted suicide or self-harmed in anyway"	Suicide completion: 7.7% (2/26) Suicide attempt: 3.8% (1/26) Suicidal ideation: 30.8% (8/26)
Shtayermman (2007)	Adolescents and young adults with Asperger syndrome N = 10	Community sample	Suicidal ideation, suicidal thoughts assessed via self-report questionnaire Question(s): Suicide Ideation Questionnaire—30 items with Likert responses assessing suicidal ideation in the past month using	Suicidal ideation: 50%

Table 1 (continued)

Study (author, year)	Population (diagnosis) and sample size	Setting	Suicidal thoughts or behavior assessed and question asked	Prevalence
Storch et al. (2013)	Youth with autism spectrum disorder and co-occurring anxiety problems N = 102	Clinical research setting	Suicidal ideation, suicide planning, or suicide attempt, via Anxiety Disorder Interview Schedule—child and parent versions (structured interviewed) conducted independently with parent/caregiver and child)	Total suicidal thoughts and behavior (including past attempts) 11% Parent-reported suicide ideation (SI): 4% Parent-reported suicide planning (SP): 5% Parent-reported suicide attempt (SA): 1% Child-reported SI: 5% Child-reported SP: 9% Child-reported SA: 1%
Current study	Youth with autism spectrum disorder, verbally-fluent, NVIQ > 55 N = 107	Specialized inpatient psychiatry units	Suicidal ideation via parent-report measure of psychiatric symptoms (child and adolescent symptom inventory-5) Question(s): "talks about death or suicide" Parent/caregiver rated their child on this item using a 4-point likert scale (choices: "never"; "sometimes"; "often"; "very often")	Talks about suicide or death: Often: 16% (17/107) Very often: 7% (7/107)

(DSM-5; American Psychiatric Association 2013)-defined emotional and behavioral disorders in youth. The parent/caregiver report version of the CASI-5 (173 items) was used for this study. It requests a current report from parents and is a measure intended to assess whether a youth has the prerequisite symptoms and clinically significant impairment necessary to meet criteria for a DSM-5 disorder. Item number 86 of the CASI-5, the question of interest for this study, asks the parent or guardian to report the frequency with which their child has had periods lasting several days where he or she "talks about death or suicide" using a 4-point Likert scale with answer choices of "never," "sometimes," "often," and "very often."

Vineland Adaptive Behavior Scales Parent/Caregiver Survey, Second Edition (VABS-II; Sparrow et al. 2005)

This is a caregiver report measure designed to evaluate adaptive functioning in four domains: Communication, Daily Living Skills, Socialization, and Motor Skills. Standard scores with a mean of 100 ± 15 are provided for each domain and for an overall Adaptive Behavior Composite.

Leiter International Performance Scale, Third Edition (Leiter-3; Roid et al. 2013)

The Leiter-3 is a measure of nonverbal cognitive ability, designed specifically to accommodate individuals with language limitations, such as those with ASD. It provides a standard score with a mean of 100 ± 15 for individuals age 3–75 years that served as a measure of nonverbal intelligence (NVIQ).

Procedure

During the hospital stay the parent or guardian completed the CASI-5 and VABS-II and the youth was administered the Leiter-3 by a trained research assistant or psychologist. Consensus diagnosis for co-morbid psychiatric disorders in the youth were made by an expert child psychiatrist and unit clinician (psychologist or social worker) at discharge based on extensive inpatient observation and all available data. Based on this information, variables were created to denote the presence or absence of a mood disorder (Bipolar 1, Unspecified Bipolar, Major Depressive Disorder, and Unspecified Depression), anxiety disorder (phobias, separation anxiety, generalized anxiety, Post-traumatic Stress Disorder; PTSD), disruptive behavior disorder (DBD; oppositional defiant disorder, conduct disorder, disruptive mood dysregulation disorder), and attention deficit hyperactivity disorder (ADHD).

Analysis

Prior to analysis, the Spearman correlation matrix of all predictors was examined for potential sources of collinearity. A series of ordered logistic regressions were used to explore predictors of the outcome measure, CASI-5 item 86 (talks about death or suicide). The first model included only demographic variables [sex, race, age, non-verbal IQ (NVIQ)]. All subsequent models retained these demographic variables. The second model included co-morbid mood disorder, anxiety disorder, DBD, and ADHD as independent variables.

In the ordered logistic regression model, probabilities are cumulated over lower values, such that the obtained odds ratio estimate is for the odds of membership in the higher value ("Very often or Often") versus the odds of membership in the lower values ("Sometimes" and "Never"). Missing data on independent variables was handled with listwise deletion. SAS Version 9.3 was used for all analyses. The proportional odds model of assumption was confirmed using the Score Test for Proportion Odds criterion of $p > .05$.

Results

Of the 895 patients eligible for enrollment, 495 (55%) enrolled, and 350 were confirmed to have ASD. Of these 350, 107 participants met inclusion criteria for the current analyses. See Table 2 for characteristics of the study sample. The mean age at enrollment was 13.63 years (SD = 2.26). The majority of the sample was male (77%) and white (91%). The mean nonverbal IQ score was 95.48 (SD = 20.56); 27 (25%) participants had mild intellectual disability.

Parent/guardian respondents endorsed periods lasting several days where their child "talks about death or suicide" "often" for 17 (16%) or "very often" for 7 (7%) of the participants, with "sometimes" reported most frequently (n = 43, 40%). "Never" was endorsed for 40 (37%) of the patients. It should be noted that for the models below "often" and "very often" responses were collapsed. Results are found in Table 3.

Model 1: Demographic Variables

None of the demographic variables (sex, race, age, or IQ) were related to response on the item of interest, "talks about death or suicide". Still, these expected control variables were retained for the remaining analyses, as it is best practice to still control for variables that were expected to be related to the response when evaluating hypothesized predictors.

Model 2: Comorbid Diagnoses

Composite variables reflecting the presence of a mood disorder (n = 31, 29%), anxiety disorder (n = 45, 42%), ADHD (n = 43, 40%), and/or a DBD (n = 42, 39%) were entered simultaneously in the model. Of the 91 (85%) participants with a diagnosis in at least one of these categories, most had one (n = 34) or two (n = 44). About half of participants with each of the other diagnoses also had ADHD (anxiety, 48%; mood, 38%; DBD, 43%). Controlling for the other diagnostic groups, the presence of an anxiety disorder (OR 2.32, 95% CI 1.10–4.93) or a mood disorder (OR 2.71, 95%

Table 2 Participant characteristics

	Talks about death never or sometimes ($n = 83$)		Talks about death often or very often ($n = 24$)		Full sample ($n = 107$)	
	n (%)	M±SD	*n* (%)	M±SD	*n* (%)	M±SD
Age		13.57 ± 2.28		13.82 ± 2.24		13.63 ± 2.26
10–12 years	36 (43%)		9 (38%)		45 (42%)	
13–18 years	47 (57%)		15 (63%)		62 (58%)	
Male	62 (75%)		20 (83%)		82 (77%)	
White	75 (90%)		22 (92%)		97 (91%)	
NVIQ		94.65 ± 20.70		98.33 ± 20.23		95.48 ± 20.56
<70	8 (10%)		2 (8%)		10 (9%)	
70–84	22 (27%)		4 (20%)		26 (24%)	
85+	53 (64%)		18 (75%)		71 (66%)	
Mood disorder	21 (25%)		10 (42%)		31 (29%)	
Anxiety disorder	31 (38%)		14 (58%)		45 (42%)	
DBD	34 (41%)		8 (33%)		42 (39%)	
ADHD	36 (43%)		7 (29%)		43 (40%)	

Table 3 Results of ordered logistic regression predicting response of "often or very often" on CASI item 86, "Talks about death or suicide"

	OR	95% confidence interval
Model 1: demographic variables		
Sex (male)	1.11	(0.48–2.57)
Race (white)	1.20	(0.33–4.27)
Age	1.05	(0.89–1.23)
NVIQ	1.01	(0.99–1.02)
Model 2: comorbid diagnoses		
Sex (male)	0.86	(0.36–2.06)
Race (white)	0.94	(0.25–3.53)
Age	1.04	(0.88–1.23)
NVIQ	1.00	(0.99–1.02)
Mood disorder diagnosis	2.71	(1.12–6.55)
Anxiety disorder diagnosis	2.30	(1.08–4.91)
ADHD	0.45	(0.21–0.96)
DBD diagnosis	1.69	(0.74–3.88)

CI 1.12–6.55) was significantly and positively related to talking about death or suicide. ADHD was negatively and significantly related to talking about death or suicide (OR 0.48, 95% CI 0.21–0.96).

Discussion

This multisite study reveals that 22% of verbally fluent youth with ASD hospitalized in an inpatient psychiatric unit were reported by a parent or guardian to exhibit frequent periods lasting several days where they talked about suicide or death. These results are both consistent with and vary from other limited research on suicidality in ASD. For example, this rate is somewhat lower than a rate obtained from an outpatient sample of adults diagnosed with Asperger Disorder detected by clinical interview (Cassidy et al. 2014), but is notably higher than outpatient studies of youth with ASD with anxiety (11%, Storch et al. 2013) and without (11%, Mayes et al. 2013) (see Table 1 for a comparison of current findings with previous studies). Our analysis is the first report to focus on suicidal thoughts in inpatient youth who were rigorously diagnosed with ASD, including those with mild Intellectual Disability.

Demographic factors, including NVIQ, sex, race, and age, did not play a role in the frequency of talking about death or suicide in this sample. In the general youth population, it has been found that the prevalence of suicidal thoughts increases dramatically in adolescence (Cash and Bridge 2009; Nock et al. 2008). Our data reveal that there was no age difference in the frequency of youth with ASD who talked about death or suicide. Though our contrary finding may be related to selection bias generated by using a psychiatric inpatient sample, the possibility of equally high prevalence among younger and older adolescents in ASD merits further exploration in larger inpatient and outpatient samples.

Participants with an anxiety disorder or mood disorder were more than twice as likely to have a parent report that they talked often or very often about death or suicide. While it is well established in youth in general that comorbid affective or anxiety disorders increase suicide risk (Nock et al. 2010), our data provide some information on a potential association in a large sample of youth with ASD. Interestingly, participants with ADHD were less likely to talk frequently about death or suicide, which was similar to the finding of the Storch et al. 2013 study of youth with ASD (Storch et al. 2013). Whether the presence of comorbid ADHD in the context of ASD may in some way inhibit thoughts of death or suicide will need to be explored in future studies.

The best means for reliably detecting suicide risk in individuals with ASD is not well established. In our study we utilized the results of a single question of interest which contained an "or," meaning that the parent was reporting on the frequency that the child talks about death *or* suicide; therefore, these responses are not necessarily an indication solely of suicidal ideation. In addition, youth with ASD can have restricted interests in a variety of narrow topics, such as heaven, death, and violent cartoons or video games. The tendency to talk about these topics, paired with deficits in social pragmatics, can lead to repeated statements about death and dying without an awareness of how these statements could be interpreted by others. These factors intrinsic to ASD make studying this population uniquely challenging and could lead to falsely inflating the positive screen rate in this study, because the question under study includes the phrase "talks about death." While theoretically imperfect, other studies of this population have used the same approach of coding parent endorsements of their children talking about death as suicidal ideation (Storch et al. 2013). We utilized the approach of detecting potential suicidal ideation with a question in an existing measure, recognizing that the most sensitive and specific question phrasing, as well as the most accurate reporter, for detecting suicidality in ASD are unclear.

It is important to consider the current findings in the context of the Joint Commission issuance of a Sentinel Event Alert in February of 2016, recommending that all patients be screened for suicide risk in all medical settings, both inpatient and outpatient (The Joint Commission 2016). Clinicians require setting-specific and population-specific tools to screen effectively. The pediatric ASD population presents unique challenges for the medical system,

as differences in the cognitive ability, social communication, restricted interests, language and abstract reasoning generally seen in youth with ASD have limited the amount and validity of suicide risk screening currently performed. The results of our study, that a significant percentage of inpatient youth with ASD talk about death or suicide often or very often, indicate a critical need to develop valid and reliable suicide screening measures to determine the prevalence of this understudied but concerning phenomenon in both inpatient and outpatient ASD samples. Effective screening methods designed specifically to identify risk in both the ASD and ID populations will need to be developed, so that no one at risk for suicide goes undetected. These methods may need to include both youth and caregiver reports, and should extend further than was possible in the current study by including testing and validation of ASD-specific suicide risk screening measures. Ultimately, tools for youth with ASD will also to need to address the extreme challenge of detecting suicidal thoughts in minimally-verbal youth as well.

These results should be interpreted with the following limitations. The most important limitation is that, suicidal ideation per se was not assessed; instead a proxy, "talking about death or suicide," was utilized. In addition, the youth themselves were not assessed for suicidal ideation as part of the research protocol, which is important, given the potential for lack of correspondence between parent and child regarding endorsement of suicidal ideation seen in one report that used both (Storch et al. 2013), nor is it clear which reporter, or potentially a combination of the two, will prove to be most meaningful and predictive. Future studies should include methodology that allows suicide risk to be determined based on multiple independent questions, for both the caregiver and the individual with ASD or ID directly. It should also include gold standard corroboration by psychiatric clinicians with expertise in evaluating youth with ASD and co-morbid mental health problems. In our study it is also possible that by reporting most of the findings by collapsing the categories of "never" and "sometimes," we are actually under-reporting thoughts of death and suicide. Because it is common for youth to think about death sometimes, we decided to err on the side of under-reporting and examined the "often" and "very often" responses, which are frequencies that may represent emotional distress.

Another limitation is that the sample consisted of psychiatric inpatients, predominately male and white, and did not include those with IQs lower than 55 or a minimally verbal status, and may therefore not be generalizable to the larger population of youth with ASD. Future studies could also include comparisons of other diagnostic inpatient or outpatient groups, to compare rates and predictors using similar methodology. In addition, externalizing behaviors were the near universal reason that youth with ASD were admitted to these settings and thoughts of death or suicide were likely rarely the identified presenting problem. Finally, many factors other than those considered in this report, will be necessary to consider before we can more fully comprehend suicide risk behavior in ASD. While other studies have begun to examine psychiatric and psychosocial risk factors that may place ASD youth at particular risk for suicide (Mandell et al. 2005), (see Hannon and Taylor 2013 for a review) future studies will require large samples and rigorous measurement of both suicide risk and hypothesized risk factors to adequately evaluate relative risk factors. The current study is an exploration of possible contributing psychiatric and demographic clinical correlates, and future research will benefit from including systematic queries about potential stressors to more fully appreciate how they relate to development or maintenance of suicidal thoughts and behaviors in youth with ASD.

Conclusions

In a psychiatric inpatient sample of youth with ASD, we found a high, but not unexpected, rate of thoughts about death or suicide, providing data related to suicidal ideation in this population. This finding is additionally notable because it is most often the case that specialized psychiatric hospitalization of youth with ASD is typically due to other problems, namely externalizing behavior (Siegel et al. 2012). The high rate of thoughts about death or suicide occurred in subjects with and without mild intellectual disability and across the age range from 10 to 20 years old, suggesting that neither mild cognitive impairment nor older age may be related to suicide risk in this inpatient population. Empirically validated suicide risk screening and assessment tools specific to youth with ASD do not exist, but are urgently needed to accurately identify those at risk and reduce the significant costs, morbidity and mortality associated with suicidality. Based on multiple reports of a markedly increased prevalence of suicidal ideation in youth with ASD across settings, developing measures to efficiently and accurately detect their suicidal thoughts and behaviors is a high value strategy to apply to national suicide prevention efforts.

Acknowledgments The ADDIRC is made up of the co-investigators: Matthew Siegel, MD (PI) (Maine Medical Center Research Institute; Tufts University), Craig Erickson, M.D. (Cincinnati Children's Hospital; University of Cincinnati), Robin L. Gabriels, PsyD (Children's Hospital Colorado; University of Colorado), Desmond Kaplan, MD (Sheppard Pratt Health System), Carla Mazefsky, PhD (Western Psychiatric Institute and Clinics; University of Pittsburgh), Eric M. Morrow, MD, PhD (Bradley Hospital; Brown University), Giulia Righi, PhD (Bradley Hospital; Brown University), Susan L Santangelo, ScD (Maine Medical Center Research Institute; Tufts

University), and Logan Wink, MD (Cincinnati Children's Hospital; University of Cincinnati). Collaborating investigators and staff: Jill Benevides, BS, Carol Beresford, MD, Carrie Best, MPH, Katie Bowen, LCSW, Briar Dechant, BS, Tom Flis, BCBA, LCPC, Holly Gastgeb, PhD, Angela Geer, BS, Louis Hagopian, PhD, Benjamin Handen, PhD, BCBA-D, Adam Klever, BS, Martin Lubetsky, MD, Kristen MacKenzie, BS, Zenoa Meservy, MD, John McGonigle, PhD, Kelly McGuire, MD, Faith McNeil, BS, Joshua Montrenes, BS, Tamara Palka, MD, Ernest Pedapati, MD, Kahsi A.Pedersen, PhD, Christine Peura, BA, Joseph Pierri, MD, Christie Rogers, MS, CCC-SLP, Brad Rossman, MA, Jennifer Ruberg, LISW, Elise Sannar, MD, Cathleen Small, PhD, Nicole Stuckey, MSN, RN, Brittany Troen, MA, R-DMT, Barbara Tylenda, PhD, Mary Verdi, MA, Jessica Vezzoli, BS, Deanna Williams, BA, and Diane Williams, PhD, CCC-SLP. We gratefully acknowledge the contributions of the coordinating site advisory group: Donald L. St. Germain, MD and Girard Robinson, MD, and our scientific advisory group: Connie Kasari, PhD., Bryan King, MD, James McCracken, MD, Christopher McDougle, MD, Lawrence Scahill, MSN, PhD, Robert Schultz, PhD and Helen Tager-Flusberg, PhD, the input of the funding organizations and the families and children who participated.

Funding This work was supported by the Intramural Research Program (ZIA MH002914) of the National Institute of Mental Health of the National Institutes of Health. The Autism Inpatient Collection (AIC) phenotypic database and biorepository is supported by a grant from the Simons Foundation Autism Research Initiative and the Nancy Lurie Marks Family Foundation, (SFARI #296318 to M.S.). Dr. Mazefsky was also supported by the National Institute of Child Health and Human Development (R01HD079512; K23HD060601).

Author contribution LMH, AT and MS conceptualized and designed the study, provided input for statistical analyses, wrote the first draft of the manuscript, provided critical review and revision of the manuscript, wrote the final manuscript, and approved the final manuscript as submitted. CF conceptualized and designed the study, conducted statistical analyses of the data, provided critical review and revision of the manuscript, and approved the final manuscript as submitted. EL contributed to conceptualizing the study, prepared the data set for analysis, provided input for statistical analyses, provided critical review and revision of the manuscript, and approved the final manuscript as submitted. RG, JAB, CM, and MP contributed to conceptualizing the study, provided critical review and revision of the manuscript, and approved the final manuscript as submitted.

Compliance with Ethical Standards

Conflict of interest Lisa M. Horowitz, Audrey Thurm, Cristan Farmer, Carla Mazefsky, Elizabeth Lanzillo, Jeffrey A. Bridge, Rachel Greenbaum, Maryland Pao and Matthew Siegel declares that they have no conflict of interests.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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

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