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Anxiety in Angelman Syndrome

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Abstract:	<p>Angelman Syndrome (AS) is a neurodevelopmental disorder most commonly caused by the impaired expression of the maternal UBE3A gene on chromosome 15. Though anxiety has been identified as a frequently present characteristic in AS, there are limited studies examining anxiety in this population. Studies of anxiety in other neurodevelopmental disorders have found disorder specific symptoms of anxiety and age specific displays of anxiety symptoms. However, there is a consistent challenge in identifying anxiety in individuals with neurodevelopmental disorders given the lack of measurement instruments specifically designed for this population. Given the limited information about AS and anxiety, the aims of the current project were to a) examine symptoms of anxiety in children with AS and b) determine the correlates of anxiety in children with AS. Participants included 42 adult caregivers of youth with AS in the AS Natural History study who completed the Developmental Behavior Checklist. The results found that 26% of the sample demonstrated elevated symptoms of anxiety and established a relationship between elevated anxiety in youth with AS and higher levels of irritability, hyperactivity, self-absorbed behaviors, and disruptive/antisocial behaviors. Findings from this research provide a foundation for tailoring evidence-based assessments and treatments for youth with AS and anxiety.</p>

Abstract

Angelman Syndrome (AS) is a neurodevelopmental disorder most commonly caused by the impaired expression of the maternal *UBE3A* gene on chromosome 15. Though anxiety has been identified as a frequently present characteristic in AS, there are limited studies examining anxiety in this population. Studies of anxiety in other neurodevelopmental disorders have found disorder specific symptoms of anxiety and age specific displays of anxiety symptoms. However, there is a consistent challenge in identifying anxiety in individuals with neurodevelopmental disorders given the lack of measurement instruments specifically designed for this population. Given the limited information about AS and anxiety, the aims of the current project were to a) examine symptoms of anxiety in children with AS and b) determine the correlates of anxiety in children with AS. Participants included 42 adult caregivers of youth with AS in the AS Natural History study who completed the Developmental Behavior Checklist. The results found that 26% of the sample demonstrated elevated symptoms of anxiety and established a relationship between elevated anxiety in youth with AS and higher levels of irritability, hyperactivity, self-absorbed behaviors, and disruptive/antisocial behaviors. Findings from this research provide a foundation for tailoring evidence-based assessments and treatments for youth with AS and anxiety.

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Anxiety in Angelman Syndrome

Angelman Syndrome (AS) is a neurodevelopmental disorder caused by the impaired expression of the maternal UBE3A gene on chromosome 15 in neurons (Albrecht et al., 1997; Tan & Bird, 2016). The molecular etiology of AS can be categorized into two main groups, “deletion-positive” and “deletion-negative.” Individuals with a “deletion-positive” etiology are those with a deletion on chromosome 15 within the AS critical region 15q11.2–q13 (Dagli, Buiting, & Williams, 2012), whereas those with a “deletion-negative” etiology have other causes such as a pathogenic variant in UBE3A, paternal uniparental disomy, or an imprinting defect (Lossie et al., 2001). AS is characterized by the lifelong consistent features of intellectual disability, motor dysfunction, lack of speech, and behavioral uniqueness, which includes any combination of frequent laughter/smiling, apparent happy demeanor, and an easily excitable personality (Margolis et al., 2015; Williams et al., 2006). Seizures, sleep difficulties, and other behavioral features (e.g., hyperactivity, aggression, anxiety) have also been reported as frequently present (Wheeler et al., 2017).

Information on anxiety in AS is limited compared to other developmental disorders such as intellectual disability (Bailey, 2007; Pruijssers et al., 2014), autism spectrum disorder (Mattila et al., 2010; van Steensel & Heeman, 2017; White et al., 2009), cerebral palsy (McDougall & Wright, 2017; Smith et al., 2019), and other genetic syndromes such as Fragile X (Woodcock et al., 2009; Ezell et al., 2019) and Prader-Willi syndromes (van Lieshout et al., 1998). Anxiety within these disorders has been most strongly associated with social situations, crowded places, new environments, and changes in routine (McDougall & Wright, 2017; Pruijssers et al., 2014; Woodcock et al., 2009). Biological markers of anxiety such as cortisol levels and atypical

hypothalamic-pituitary-adrenal (HPA) axis functioning have also been identified (Hardiman & Bratt, 2016; Matherly et al., 2018).

Previous studies have described how anxiety symptoms can be identified across neurodevelopmental conditions. A meta-analysis by Royston et al. (2017) concluded that individuals with Williams Syndrome (WS) are prone to have Generalized Anxiety Disorder and phobias related to the phenotypic and neurological traits of WS (e.g., sensitivity to loud noises and neural structural differences that increase sensitivity to threat stimuli). Kerns et al. (2014), reported that anxiety symptoms among children with ASD may manifest itself in typical (i.e., similar to neurotypical individuals, like specific phobias, somatic symptoms, and distress or worries about separating from a caregiver) and atypical (i.e., symptoms associated with autistic characteristics, such as fears related to uncertainty, social discomfort, and idiosyncratic phobias) ways. Crawford et al. (2017), compared anxiety profiles among Fragile X, Cornelia de Lange, and Rubinstein-Taybi Syndrome groups and used a symptom-based approach to better understand anxiety presentations. This approach identified the presence and severity of distress caused by anxiety and potentially overlapping neurodevelopmental symptoms to pinpoint areas for symptom-specific interventions to reduce anxiety (Crawford et al., 2017). Overall, these studies distinguished clinically significant anxiety symptoms to encompass both typical and atypical presentations that may overlap or resemble traits of the individual's neurodevelopmental condition. Based on previous findings, anxiety symptoms in neurodevelopmental populations can be defined as those that are captured by DSM criteria, indicate anticipatory worry, reactivity to/fear of unpleasant stimuli, result in behavioral inhibition, and in physical responses.

Anxiety occurs across the lifespan within these populations, with some disorders showing an increase in anxiety symptoms with age (McDougall & Wright, 2017; van Lieshout et al., 1998).

Moreover, anxiety within these disorders has been associated with particularly high levels of psychological distress and physical responses such as repetitive and self-injurious behaviors (Pruijssers et al., 2014; Woodcock et al., 2009). These studies highlight the importance of ensuring that standardized measures and diagnostic tools accurately capture anxiety within populations with developmental disorders (Pruijssers et al., 2014; Woodcock et al., 2009).

In a previous study, a review of 53 medical records of individuals between the ages of 16 to 43 years old with molecularly-confirmed AS found anxiety was present in 57% of the sample, with incidence of anxiety being greater in patients over the age of 26 years (71% of sample). Separation from a caregiver or encountering an unfamiliar environment were frequently-endorsed triggers of anxiety, with behavioral responses including avoidance, head banging or slapping, pacing, cyclic vomiting, and behavioral outbursts (Prasad et al., 2018). Though anxiety has been identified as a frequently present characteristic in AS (Larson et al., 2015), there are limited studies which examine the prevalence and features of anxiety in this population. Furthermore, there are challenges associated with assessing anxiety in individuals with AS, including the lack of existing measures normed on this population, limited self-reporting, and a reliance on caregiver reports of behavior. Given that many anxiety studies among individuals with neurodevelopmental conditions are limited by the aforementioned factors, results should be interpreted with caution.

Parents of children with AS have reported higher levels of parenting stress related to child factors including intellectual abilities, physical abilities and mood characteristics (Miodrag & Peters, 2015). When examining caregiver perceptions of individuals with AS, anxiety was identified as one of the primary clinical manifestations of the disorder. One hundred and ten caregivers completed standardized medical history questions about the adolescent or adult with

AS, and 46% (n = 48) of the caregivers reported that the individual with AS had shown some signs of anxiety (Larson et al., 2015). In another study of caregiver reports (n = 100), when assessed using a clinician-developed questionnaire, anxiety concerns were reported in 40% of individuals with AS (ages 10-56 years), with over 50% displaying distress when separated from their preferred caregiver (Wheeler et al., 2019). Contrary to the aforementioned studies, one study found that the social avoidance, generalized anxiety, and obsessive-compulsive behavior subscales were not elevated in a sample of 12 individuals with AS when measured by the Anxiety, Depression, and Mood Scale (ADAMS) (Wink et al., 2015). While this existing literature suggests that anxiety is elevated in AS, it has generally been assessed without standardized assessments, and few studies have reported on correlates or factors that may differentiate those with AS with and without anxiety.

The impact of AS is significant and lifelong for both the diagnosed individual and their caregivers. However, there is still limited information about the correlates and prevalence of anxiety in individuals with AS. Additionally, the clinical characteristics of individuals with AS and anxiety needs to be further studied to help identify anxiety-specific symptoms within this population. These symptoms may not be fully captured in the anxiety diagnostic criteria or typical measurement tools used to assess anxiety. Having a better understanding of this information represents an initial step towards improving both the assessment of and intervention for anxiety in AS.

The aims of the current project were to examine anxiety symptom prevalence in children with AS and how it relates to other clinical characteristics and identify potential factors that drive these associations. Our first aim was to explore what proportion of youth with AS (ages 1 – 19 years) exhibited symptoms of anxiety reported by their caregiver, as measured by the

Developmental Behavior Checklist-Primary Carer Anxiety subscale. Based on previous findings (Larson et al., 2015; Wheeler et al., 2019), we anticipated a substantial portion would report elevated symptoms of anxiety. Secondly, we aimed to identify what significant factors were associated with elevated anxiety (i.e., age, behavior/cognitive functioning, molecular diagnosis, etc.) in children with AS. Given that there are few data pertaining to the second aim, data from studies in other developmental disabilities were used to glean hypotheses. It was hypothesized that anxiety in individuals with AS would be positively associated with age, developmental level (neurocognitive functioning), adaptive functioning, and behavior problems. This paper is an important initial step in describing anxiety symptom prevalence and identifying anxiety correlates in AS groups. We hope that this paper will provide insight on the understudied anxiety symptoms in individuals with AS and help contribute to improving anxiety prognosis within this population.

Methods

Participants

As part of the AS Natural History study (ClinicalTrials.gov identifier: NCT00296764) conducted under the National Institutes of Health Rare Diseases Clinical Research Network, participants were recruited from one of six urban hospital study sites across the United States from January 2006 to July 2014. Each participant attended a baseline session at one of the study sites, and then approximately annual visits for developmental, behavioral, and medical assessments. The DBC was introduced as a measure in the study only at the beginning of 2014. Hence only a limited number of families with AS were administered the DBC. Data for the current study were taken from the first visit with a completed Developmental Behavior Checklist-Primary Carer (DBC-P). Forty-two adult caregivers of youth with AS in the AS

Natural History study completed the DBC-P, the key variable of interest in this analysis.

Additional child inclusion criteria included 1) a molecular diagnosis of AS, 2) absence of comorbid disorders that might confound or distort AS phenotype, and 3) age between 1 and 19 years. Child exclusion criteria included 1) not meeting diagnostic criteria for a molecular diagnosis of AS, 2) presence of comorbid medical or genetic disorders, and 3) extreme prematurity (i.e., born before 26 weeks gestation). Information regarding child demographics can be seen in Table 1 below.

Measures

In addition to direct testing with the individual with AS, multiple measures were used to gather information regarding caregiver perspectives of their child's behavioral and developmental functioning. All of the measures were administered on the same day. The neurodevelopmental measures were administered by doctoral-level child or developmental psychologists and the remaining measures were completed by the parents. Participants also completed an initial evaluation form, which included demographic information in addition to a family data form, which focused on family and social history.

Behavioral Measures

Aberrant Behavior Checklist-Community Version. The Aberrant Behavior Checklist-Community Version (ABC-C; Aman et al., 1985) is a 58-item questionnaire, which measures maladaptive behaviors in individuals with intellectual disabilities. It has previously been used in outcome studies examining problem behaviors in individuals with developmental disabilities (Freund & Reiss, 1991; Sansone et al., 2012). The ABC-C is scored on a 4-point scale (0-3) with higher scores indicating greater problem behavior. Four of the five scales on the ABC-C were used: Irritability (15 items), Hyperactivity (16 items), Lethargy (16 items), and Stereotypy (7

items) (Aman et al., 1985). The Inappropriate Speech (4 items) scale was excluded because the majority of individuals with AS are nonverbal.

Developmental Behavior Checklist-Primary Carer Version. The Developmental Behavior Checklist-Primary Carer Version (DBC-P; Einfeld & Tonge, 2002), is a 96-item questionnaire used to assess behavior and emotional problems in youth ages 4-18 years with developmental and intellectual disabilities. Items are scored on 3-point scale (0-2) with 0 indicating the behavior is not true and 2 indicating it is very/often true. It includes 5 subscales: Disruptive/Antisocial (27 items), Self-Absorbed (31 items), Communication Disturbance (13 items), Anxiety (9 items), and Social Relating (10 items), and an overall Total Problem Behavior score (Einfeld & Tonge, 2002). Specifically, the anxiety items reflect symptoms commonly seen in anxious individuals with intellectual disabilities, such as distress about being alone, shy, or fearing particular situations which are related to numerous anxiety presentations (e.g., social, separation, etc.)

Developmental Measures

Bayley Scales of Infant and Toddler Development, Third Edition. Neurodevelopment was assessed at each visit with the Bayley Scales of Infant and Toddler Development, Third Edition (Bayley-III; Bayley, 2005). The Bayley-III is a standardized measure for children up to 42 months and provides assessment of cognitive, receptive and expressive language, and fine and gross motor functioning (Bayley, 2005). It has been used in individuals outside of the normative chronological age range whose abilities fall within the developmental age range of 0-42 months. The developmental quotient (DQ), which has been recommended over scaled scores for individuals with intellectual disabilities, generally refers to a child's performance on a set of tasks compared to other children their age (Dykens et al., 1994). The DQ is calculated by

dividing the child's developmental age by chronological age, then multiplying the quotient by 100; this has been used in prior AS studies to identify, compare, and monitor levels of the child's development across same-aged groups (Gentile et al., 2010).

Vineland Adaptive Behavior Scales, 2nd Edition. The Vineland Adaptive Behavior Scales, 2nd Edition (Vineland-2; Sparrow et al., 2005) is a measure of personal and social skills for individuals from birth to 90 years. The overall adaptive functioning standard score (ABC, Adaptive Behavior Composite) was used in this study.

Data Analysis

To evaluate the proportion of youth with AS with elevated symptoms of anxiety, the frequency of individuals above and below a raw score of 4 on the DBC-P-anxiety subscale was presented, corresponding with a T-score of 60, which is consistent with the clinical cutoff for the total score (an anxiety subscale cutoff has not been evaluated; Einfeld & Tonge, 2002). The proportion of participants above a T-score of 70 (raw score of 5) was also examined, as this clinical significance cutoff is often used in other standardized rating scales (e.g., Achenbach & Rescorla, 2001).

Bivariate correlations were conducted between the DBC-P-Anxiety subscales and the following variables: Bayley-III subscales (Cognitive, Receptive, Expressive, Fine Motor, and Gross Motor), ABC subscales (Irritability, Lethargy, Stereotypy, and Hyperactivity), other DBC-P subscales (Disruptive/Antisocial, Self-Absorbed, Communication Disturbance, and Social Relating), the Vineland composite adaptive behavior score, and age in months. Finally, the DBC-P-Anxiety subscale scores were compared across genotypes (i.e., deletion-positive vs. deletion-negative), as deletion-positive individuals have been noted to show lower adaptive and cognitive functioning, and thus were anticipated to experience lower anxiety (Godavarthi, Dey,

Maheshwari, & Ranjan Jana, 2012). Anxiety was expected to be positively associated with age, developmental level (neurocognitive functioning), adaptive functioning, and behavior problems. Effect size interpretation followed Cohen's (1992) recommendations.

Of the 42 participants in this study, data on the Vineland ABC standard score was missing for 2 (4.7%) participants. Because of the low proportion of missing data for these measures, case wise deletion was used for the two participants who had incomplete Vineland data. Regarding normality, a threshold of -2 to +2 for skewness or kurtosis was used to assess significant deviations from a normal distribution (Hair et al., 1998).

Results

Demographics

The mean age of completion for participants was 118.8 months (~9 years old). Participation was nearly equal between males and females with 57% of the sample (n = 24) being male. Sixty-seven percent (n = 28) of participants were in the deletion-positive genotypic subgroup. All participants were at least 2 standard deviations below the mean in terms of adaptive functioning measured by the Vineland adaptive behavior composite standard score, indicating all participants had significant deficits in adaptive functioning. No child in this sample reached the ceiling for any Bayley-III subtest (the highest age-equivalent score was one child whose age equivalent was at 41 months on the fine motor subscale).

Aim 1: What proportion of youth with AS exhibit elevated symptoms of anxiety?

Twenty-six percent of the sample (n = 11) was classified as experiencing elevated anxiety corresponding with a DBC-P-Anxiety subscale raw score of 4 (Einfeld & Tonge, 2002). The mean score for the sample was 3.

Aim 2: What factors are associated with elevated anxiety symptoms in children with AS?

Significant moderate positive correlations were found between the DBC-P-Anxiety and the DBC-P-Disruptive-Antisocial subscale, $r = .42$, $p = .005$, the DBC-P-Self-Absorbed subscale, $r = .41$, $p = .008$, and the ABC-Hyperactivity subscale, $r = .35$, $p = .025$. A large association between DBC-P-Anxiety and ABC-Irritability was also found, $r = .58$, $p < .001$. Significant associations with the other emotional-behavioral measures, the Vineland, and the Bayley-III domain scores were not found. See Table 2 for a summary.

Finally, the DPC-Anxiety subscale was compared across genotypic subgroups. Deletion-positive individuals did not differ from deletion negative on the DPC-Anxiety subscale, $M (SD)_{\text{deletion-positive}} = 2.21 (2.01)$, $M (SD)_{\text{deletion-negative}} = 3.50 (2.85)$, $t (44) = 1.66$, $d = .54$.

Discussion

Based on previous studies on anxiety symptoms in AS populations, we hypothesized that a substantial portion of our sample would exhibit elevated anxiety symptoms based on caregiver report. As measured by the DBC-P-Anxiety subscale, only 26% of the sample was classified as experiencing elevated symptoms of anxiety. This is slightly lower than previous studies reporting anxiety symptoms in 40-57% of individuals with AS (Wheeler et al., 2019; Prasad et al., 2018). Differences in anxiety symptom rates could be due to the age ranges of the participants in the studies. In previous research, anxiety symptoms were more common in older individuals (26+ years of age) (Prasad et al., 2018). Our participants were predominantly in a younger age range (average age of just under 10-years-old). Thus, it is possible the lower rate of anxiety symptoms we found is explained by anxiety being less common in younger individuals with AS, or because symptoms of anxiety may be easier for caregivers to identify in older individuals. Differences in anxiety symptom rates could also be due to the use of different measures to identify anxiety symptoms in our study compared to prior studies. Given that anxiety symptoms in AS may

present differently from anxiety criteria used for the neurotypical population or those with higher levels of cognitive functioning, current anxiety measures may not fully capture anxiety symptoms within this specific population. Future studies should investigate anxiety characteristics in individuals with AS taking into account cognitive abilities and across a wider age range with multiple assessment tools, to compare prevalence and correlates and the influence of cognitive functioning and/or age on anxiety symptoms within this population.

In this study, “elevated” was operationalized as above the 60th percentile; thus, approximately 40% of any developmental disability population would be expected to experience elevated symptoms using this definition. Finding that 26% of this sample was above this cutoff suggests that anxiety symptoms may not be more of an issue in AS than any other developmental disability population, at least in the age range sampled in our study. Although clinical cutoffs have not been established for the DBC-P-Anxiety subscale, we find this cutoff score justified given that an Anxiety subscale cutoff has not yet been evaluated for this measure, and it is consistent with the validated clinical cutoff for the total score on the DBC-P. This approach utilizes more psychometrically-supported score information to identify symptoms of anxiety when compared to previous studies utilizing clinician-developed questionnaires (Prasad et al., 2018) and review of medical records (Larson et al., 2015). The use of established measures (e.g., Anxiety Disorders Interview Schedule, Pediatric Anxiety Rating Scale, Anxiety, Depression, and Mood Scale, etc.) (March, Parker, Sullivan, Stallings, & Conners, 1997; Reynolds & Richmond, 1978) to examine the reliability of anxiety symptoms in AS should be explored in future research. Given that these measures were developed for neurotypical individuals, and our current sample demonstrated overall low DQ for individuals with AS, there may be a need to develop an entirely new tool (or modify an existing tool) to capture anxiety symptoms in AS and other

disorders with intellectual disability. Measurement of possible biomarkers for anxiety within AS could also be examined to reduce the heavy reliance on parental/caregiver reports and potential for misidentifying observable behaviors as something else other than anxiety.

Our hypothesis that maladaptive behavior severity would correlate with anxiety presentations in individuals with AS was supported. Positive correlations were found between the DBC-P-Anxiety and the ABC-Irritability scale, the DBC-P-Self-Absorbed subscale, and the DBC-P-Disruptive-Antisocial subscale. Caregivers of children with AS and elevated anxiety symptoms endorsed higher levels of disruptive and antisocial behaviors compared to parents of children without elevated anxiety symptoms. Because disruptive/antisocial behavioral characteristics were significantly correlated with anxiety symptoms, anxiety treatment may be more effective if paired with interventions to target disruptive/antisocial behaviors.

Regarding our second aim, developmental level (measured by the Bayley-III and Vineland-2), and maladaptive behavior severity (measured by the ABC-C) characteristics were not found to be significantly correlated with anxiety symptoms. Future studies with larger samples should explore whether cognitive and adaptive functioning are associated with anxiety when evaluating these variables.

While we recognize the small sample size of our study as a limitation, it is important to note that AS is a rare neurogenetic disorder (Buiting et al., 2016), so achieving well-powered samples may often present as a challenge in research. As noted, some analyses approached medium effect sizes, including relationships between anxiety and adaptive behavior, fine motor functioning, and genotypic subtype, that may have reached statistical significance with a larger sample. Thus, future research is needed in well-powered samples to explore a wide range of

anxiety correlates, as well as interrogate differences among the non-deletion genotypes (paternal uniparental disomy, imprinting defect, and UBE3A mutation).

Similar to other studies of anxiety in AS, another limitation of this study is the use of parent-reports of anxiety symptoms and anxiety measures not specifically normed for individuals with AS. However, the anxiety measures utilized were created to assess behavioral and emotional problems among individuals with developmental and intellectual disabilities. Additionally, although parent reports were helpful in determining manifestations of anxiety, we should consider that there is a high overlap between anxiety and syndrome-specific traits. Nonetheless, exploration of these anxiety symptoms will hopefully reduce diagnostic overshadowing where clinicians interpret certain behaviors to be attributed solely to the syndrome rather than co-occurring anxiety. Significant correlations across parent-report measures may have also reflected informant effects; future research should use multi-informant, multi-method approaches. Lastly, item level data were not collected for the DBC-P or ABC. Given the limited information known about the anxiety symptom profiles for AS, future studies utilizing item level information could provide more descriptive information on how anxiety is operationalized within this population.

Given that anxiety symptoms in youth with AS are understudied, future research should explore if these disruptive, antisocial, or irritable behaviors are possible expressions of anxiety within the AS population. Anxiety in AS samples is predominately identified and measured through symptom-specific factors, thus, having a better understanding of anxiety correlates and manifestations can help with distinguishing anxiety from AS and potentially overlapping symptoms. This data could prove to be useful in developing interventions to reduce behavioral issues and co-occurring anxiety.

Conclusion

The present study examines caregiver reports of elevated anxiety symptoms using standardized measures and correlates in a relatively young group of individuals with AS. Anxiety symptoms frequently occur in individuals with AS, yet limited studies examine the characteristics and correlates of this co-occurrence. The sparsity of research in this area limits our understanding on how to effectively identify and treat anxiety symptoms among individuals with AS. Findings from this research provide a foundation for tailoring evidence-based assessments and treatments for youth with AS and anxiety.

Our study suggested a relationship between elevated anxiety symptoms in youth with AS and higher levels of challenging behaviors, such as irritability, self-absorbed behaviors, hyperactivity and disruptive/antisocial behaviors. Treatment recommendations targeting the manifestations of anxiety for individuals with AS, may benefit from behavioral and/or pharmacological interventions that target these behavioral issues. Given that maladaptive behaviors in children with AS (such as hyperactivity, irritability and aggression) have an adverse effect on parent stress and quality of life (Sadhvani et al., 2019), future studies should examine how these behaviors affect interpersonal factors and how these relate to anxiety in large cohorts of individuals with AS across genotypes and age groups. Additionally, future research on anxiety presentations in AS individuals should consider selecting anxiety measures that are appropriate for the participant's developmental level, rather than the participant's age. Since AS is a developmental disorder, developmental delays are anticipated. Thus, looking at development level and functional performance may be more meaningful than looking at chronological age. Lastly, caregivers of individuals with AS could be examined separately to see how their child's AS impacts their own stress and anxiety. Recognition and treatment of a wide range of emotional

and behavioral challenges for youth with AS may therefore improve functioning both for them and their caregivers.

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Table 1. Child Demographics

Male sex N (%)	24 (57%)
Female sex N (%)	18 (43%)
Age in months M (range)	118.8 (50.1-223.9)
Age range N (%)	
0-2 years-old	3 (7%)
3-6 years-old	14 (30%)
7-11 years-old	18 (39%)
12-17 years-old	9 (20%)
18-years-old+	2 (4%)
Vineland adaptive behavior standard scores M (SD)	48.4 (10.7)
Bayley age equivalents in months M (SD)	
Cognitive	18.4 (6.8)
Receptive language	14.2 (6.3)
Expressive language	8.8 (3.0)
Fine motor	18.2 (9.3)
Gross motor	16.2 (4.2)
Race N (%) ^a	
White	34 (81%)
Asian	7 (17%)
African-American/Black	6 (14%)
Genotypic subgroups	
Deletion-positive	28 (67%)
Deletion-negative	14 (33%)

^a Participants could select more than one race and thus the tally adds up to greater than 100%

Table 2

Correlates of anxiety in youth with AS

Variable	Cognitive, developmental, and adaptive functioning						
	Bayley-III					Vineland ABC	Age
	Cognitive	Receptive language	Expressive language	Fine motor	Gross motor		
DBC-P- Anxiety	-.131	.058	-.152	.038	-.029	.15	-.035

Variable	Behavioral and emotional functioning							
	ABC				DBC-P			
	Irritability	Lethargy	Stereotypy	Hyper- activity	Disruptive- Antisocial	Self- absorbed	Communi- cation	Social Relating
DBC-P- Anxiety	.58***	.19	.16	.35*	.42**	.41**	.20	.23

* $p < .05$ ** $p < .01$; *** $p < .001$ Note: Above are r coefficients. ABC = Aberrant Behavior Checklist DBC-P = Developmental Behavior Checklist-Primary Carer Version