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Anxiety, depression, and social skills in girls with fragile X syndrome: Understanding the cycle to improve outcomes

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Abstract

Objective: Females with fragile X syndrome (FXS), a genetic condition associated with a mutation in the *FMR1* gene, are at significantly elevated risk for developing anxiety and depression. This study is designed to better understand these symptoms in school-aged girls, particularly as they relate to age, social skills, and functional outcomes.

Methods: We compared 58 girls ages 6–16 years with FXS to 46 age-, gender-, and developmentally-matched peers without FXS on measures of anxiety, depression, social skills, adaptive behavior, and quality of life.

Results: Girls with FXS 10.5 years and older demonstrated significantly higher levels of depression, withdrawal, and social avoidance than girls younger than 10.5 with FXS (*p's* < .01). Girls in the comparison group did not show any age-related differences on these measures. The older FXS cohort also showed associations between social communication and interaction skills, adaptive behavior, and measures of anxiety and depression (*p's < .05)* not seen in the comparison group, regardless of age.

Conclusion: We found that age appears to play an important role in the development of mood symptoms and that such symptoms are uniquely correlated with social communication and reciprocal social interaction behaviors and adaptive functioning in girls with FXS post-puberty. These data suggest a critical window of intervention for girls with FXS in the improvement of social interaction skills and the prevention of social avoidance and symptoms of anxiety and depression, with the ultimate goal of improving quality of life and promoting greater independence.

Keywords

fragile X syndrome; females; anxiety; depression; social skills

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Anxiety and depression are two of the most commonly diagnosed mental health disorders world-wide (1). Females, through a combination of genetic, societal, and environmental influences, are more likely than males to experience anxiety and/or depression by early adolescence (2, 3). Puberty, in particular, presents increased risk for social anxiety and depression in girls (4, 5). Intervening early is particularly important given that a history of childhood or adolescent depression and anxiety symptoms strongly predicts the manifestation of clinical diagnoses later in life (6, 7).

Certain genetic conditions such as fragile X syndrome (FXS) are associated with significantly increased risk for the development of anxiety and depressive disorders in females (8). FXS is the leading monogenic cause of autism and intellectual disability affecting 1/7,000–11,000 individuals per the CDC (9). Girls with FXS are at increased risk for mood disorders throughout their lifetime, and anxiety and depressive symptoms are frequently cited as primary concerns (8, 10).

Individuals with FXS also frequently exhibit symptoms of autism spectrum disorder (ASD) including social reticence, social avoidance, and social anxiety. Impaired social behaviors appear to relate more significantly to increased anxiety and reduced independence in females with FXS than females with idiopathic ASD (11) suggesting other factors, such as underlying anxiety, social phobia, or mood symptoms, may play a role in the manifestation of symptoms associated with ASD.

Females with FXS demonstrate deficits in adaptive behavior and independent living skills that may significantly impact their quality of life and long-term independence (12, 13). Symptoms of anxiety and/or depression, along with social skills, predict level of independence in adulthood and appear to impact overall quality of life (14) (13). Further, reduced quality of life has been shown to significantly correlate with lower social functioning and aberrant social skills (15) and research shows that children and adolescents with FXS have fewer social relationships than their typically developing peers (16). Collectively, these studies emphasize the importance of better understanding the development of social-emotional symptoms in females with FXS to inform the design of optimally timed, targeted therapeutic and behavioral interventions necessary for successful independent living.

This study was designed to better understand the symptoms of anxiety and depression in school-aged girls with FXS as well as the association between these symptoms and social skills, functional outcomes, and quality of life. We predicted that girls with FXS would demonstrate higher levels of mood disorder symptomatology than the comparison group, particularly in the early adolescent timeframe. We further hypothesized that the level of mood disorder symptoms would be associated with social and adaptive skills and overall quality of life.

METHODS

Participants

Participants were 58 girls (ages 6–16 years) with a confirmed diagnosis of FXS (>200 CGG repeats within the *FMR1* gene and evidence of hypermethylation) and 46 age- and developmentally-matched girls with a variety of learning and developmental challenges (See Table 1). Comparison group participants exhibited a range of idiopathic developmental delays, intellectual disabilities, or learning disabilities. Participants were excluded per parent report for very preterm birth (<32 weeks), significant visual or hearing impairment such that they could not complete the study protocol, and uncontrolled seizure disorder, psychosis, bipolar disorder, or head trauma with loss of consciousness. We did not exclude participants in either group if they reported a diagnosis of ADHD, anxiety disorder, depression, specific learning disorder, or autism spectrum disorder. All participants were part of a longitudinal study examining the developmental trajectory of anxiety, arousal, and avoidance in young females. Participants with FXS were recruited from North America through FXS communities such as the National Fragile X Foundation and the Fragile X Clinical and Research Consortium. Comparison group participants were recruited through school districts, agencies, parent organizations, and social media sites targeting the desired patient population. All child participants spoke English as their primary language. Parents provided informed consent and participants provided assent as appropriate based on developmental level. The study protocol was approved by the study site Institutional Review Board, and all protocols were carried out in accordance with the Declaration of Helsinki. All assessments were carried out before the onset of the COVID-19 pandemic.

Materials

Measures were chosen based on their wide usage in the FXS population, clinical expertise, and/or recommendations in the field (17–19). Parent report measures and interviews were completed by a primary caregiver as determined by each family. Interviews were conducted by either a PhD level clinician or research assistant trained to reliability with the PhD level clinicians.

Anxiety and Depression.—Parents reported on their child's mood and related behavior using the Anxiety, Depression, and Mood Scale (ADAMS; 20), the Child Behavior Checklist School-Age Form (CBCL; 21), and the Pediatric Anxiety Rating Scale – Revised (PARS-R; 22). The ADAMS questionnaire assesses mood disorder symptoms in individuals with intellectual disability. Domains of the ADAMS and total possible scores (score at 50th percentile) for each domain are as follows: Manic/Hyperactive - 15 (5.5), Depressed Mood - 21 (3), Social Avoidance - 21 (4), General Anxiety - 21 (5), and Compulsive Behavior - 9 (2). The CBCL evaluates a range of externalizing and internalizing behaviors in children 6–18 years old. T scores of 65 or above are considered clinically relevant. Parents and children were interviewed about current (past month) anxiety symptoms using the PARS-R. The PARS-R reviews a broad list of symptoms associated with anxiety disorders with a primary caregiver and the child and is scored by the interviewer for presence or absence of each symptom. The interviewer then assigns a final rating for each item based on the answers from the parent and child. Once the interview is complete, the interviewer rates

seven summary items on a 0–5 scale for number of symptoms, frequency of symptoms, severity of anxiety feelings, severity of physical symptoms, overall avoidance of anxiety-provoking situations, interference with family relationships/home, interference with peer/adult relationships outside of the home. The Severity Score combines the scores from these summary items and a score of 18 or higher represents significant anxiety (18). Based on evaluation of the domains comprising these measures, specific scores were chosen to represent the constructs of anxiety and depression in our analyses: (1) for Anxiety – ADAMS General Anxiety, CBCL Anxious/Depressed, and PARS-R Severity Score; (2) for Depression – ADAMS Depressed Mood and CBCL Withdrawn/Depressed.

Social Behavior.—Social behavior was evaluated using the Autism Diagnostic Observation Schedule-Second Edition (ADOS-2; 23), the ADAMS Social Avoidance, and CBCL Social Problems scales (ADAMS and CBCL described above). The ADOS-2 is a semi-structured, interactive behavioral observation administered to the participant by a research reliable, trained examiner. It assesses social, communicative, play, and ritualistic/repetitive behaviors commonly seen in ASD. Scores are tabulated using an algorithm providing totals for Social Affect (social communication and reciprocal social interaction), Restricted and Repetitive Behavior, and Overall Total where an Overall Total of 7 or above indicates a level of symptoms consistent with the autism spectrum. The majority of participants were evaluated with the Module 3 (for verbally fluent children/young adolescents) of the ADOS-2. One participant in the FXS group received Module 1 (for children who do not consistently use phrase speech).

Quality of Life.—Parents reported on perceived quality of life using the Pediatric Quality of Life Inventory (Peds-QL; 24). The Peds-QL evaluates children across four domains: physical, emotional, social, and school. The domains combine into the total score (scale from 0–100; higher scores indicate better quality of life) used for analyses.

Developmental Characteristics.—To assess the developmental characteristics of the two groups, parents participated in the survey interview version of the Vineland Adaptive Behavior Scales, Third Edition (Vineland-3; 25). The Vineland-3 captures a child's functional day to day skills in the areas of Communication, Daily Living, and Socialization. Interview responses compile into an Adaptive Behavior Composite (Vineland-3 ABC) standard score used in the analyses for this study to capture functioning across all domains. Verbal abilities and academic level were evaluated for each participant using the Verbal Ability domain of the Differential Abilities Scale, Second Edition (DAS-II Verbal; 26) and the Brief Achievement Composite of the Kaufman Test of Educational Achievement, Third Edition – Brief Form (KTEA-3 BAC; 27).

Analyses

One-way ANOVAs were run using SPSS, Version 26, to evaluate for group differences in developmental characteristics including age, verbal abilities, academic level, and adaptive behavior level. Multivariate analysis of variance (MANOVA) was used to test our a priori hypotheses of group differences in anxiety, depression, social behavior, and quality of life (see Table 1 for variable groupings). Planned follow-up tests with one-way ANOVAs

were conducted to examine between-group differences on specific areas measured within categories if the omnibus (Wilks' Lambda) F was significant for the overall MANOVA.

To identify the potential differences across groups and symptom severity as a function of age, the participants were divided into two cohorts: younger and older. Age cohorts were determined in accordance with definitions of pubertal onset in current research (28). For this study sample, parent-reported Tanner staging was used to assess pubertal development for thelarche (breast development) and pubarche (pubic hair development). Clinician-determined Tanner staging was not available; however, clinician and parent report are very highly correlated (29). Pubertal onset was determined based on whether the participant had reached at least the second stage in either category. This was then compared to chronological age to account for the social, academic, and environmental influences, which may play a role in the outcomes of interest irrespective of puberty. Girls were grouped (Younger/Older) using 10.5 years as the cutoff at which Tanner stage accurately corresponded to age for 93% of girls in the study. Seven girls had Tanner stage scores that that were either just above or just below the prescribed cutoff corresponding to age. Given the variables of interest for this study and the external factors that may also play a role, these girls were grouped with their Tanner-based age cohort, rather than directly with their Tanner staging. We then conducted MANOVAs to test the interaction between participant group (FXS/Comparison) and age (Younger/Older) using the same categorical groupings described above. Finally, we explored relationships among the variables of interest within each group and by age using Pearson bivariate correlations.

RESULTS

Group comparisons on developmental characteristics, anxiety, depression, social behavior, and quality of life are presented in Table 1. There were no significant group differences for age, $F(1, 102) = .04$, $p = .85$, academic level (KTEA-3 BAC), $F(1, 100) = 1.63$, $p = .21$, or adaptive behavior (Vineland-3 ABC), $F(1, 102) = 1.17$, $p = .28$. The two groups differed on verbal abilities (DAS-II Verbal), $F(1, 102) = 4.25$, $p = .04$ (Comparison > FXS). There were no significant differences between groups on the MANOVAs examining anxiety, $F(3, 94) = 0.53$, $p = .66$, or depression, $F(2, 97) = 0.69$, $p = .51$. The MANOVA for social behavior showed a significant main effect, $F(3, 95) = 6.58$, $p < .001$. Follow-up ANOVAs indicated girls with FXS had higher scores than the girls in the comparison group for the ADOS-2 Social Affect domain, $F(1, 101) = 5.46$, $p = .02$ while the girls in the comparison group demonstrated higher scores than the FXS group on CBCL Social Problems, $F(1, 98) = 5.17$, $p = .03$ (fig 1). There was no group difference for ADAMS Social Avoidance, $F(1, 102) = 2.83$, $p = .10$. A one-way ANOVA indicated the FXS group had significantly higher scores on the Peds-QL Total, $F(1, 95) = 7.63$, $p = .01$

A statistically significant interaction effect (group × age) was found for the MANOVA for depression, $F(2, 95) = 5.15$, $p = .01$, and social behavior, $F(3, 93) = 3.53$, $p = .02$. Follow-up tests showed that for ADAMS Depressed Mood, CBCL Withdrawn/Depressed, and ADAMS Social Avoidance, the FXS group demonstrated significantly higher scores in the older cohort relative to the younger cohort (p's < .01) whereas there were no significant differences between the age cohorts in these domains for the control group (fig 1). The

group × age interaction was not significant for anxiety, $F(3, 92) = 1.67$, $p = .18$. While the interaction between group and age was not significant for the Peds-QL, $F(1, 93) = 0.72$, $p = .40$, there was an overall trend for decreased quality of life scores in the older cohort, particularly for the FXS group, $p = .06$ (fig 1).

Finally, we explored associations among the variables of interest within each group. Bivariate correlations revealed significant associations within the FXS group for the ADOS-2 Social Affect domain and depression (ADAMS Depressed Mood, CBCL Withdrawn/Depressed), anxiety (ADAMS General Anxiety, CBCL Anxious/Depressed, PARS-R Severity), social behavior (ADAMS Social Avoidance, CBCL Social Problems), adaptive behavior (Vineland-3 Composite), and quality of life (Peds-QL Total). Specifically, girls with FXS showed significant negative correlations between ADOS-2 Social Affect score (higher scores indicate more impairment) and Vineland-3 Composite, and Peds-QL Total such that higher scores for Social Affect correlated with lower (worse) scores on the Vineland-3 and Peds-QL. The ADOS-2 Social Affect domain had significant positive correlations with PARS-R Severity, ADAMS General Anxiety, Social Avoidance, and Depressed Mood, and CBCL Withdrawn/Depressed and Anxious/Depressed indicating associations between poorer social skills and higher levels of anxiety and depression. These same associations were not significant for the comparison group with the exception of Vineland-3 Composite, which showed a similar negative correlation with ADOS-2 Social Affect as for the girls with FXS. (See Table 2).

To further examine the impact of age within each group, correlation analyses were performed for each age cohort within the FXS and comparison groups. Within the FXS group, the correlations between social behavior, mood, and quality of life remained significant for the older cohort, but not the younger cohort with the exception of adaptive behavior (Vineland-3 Composite), for which the significant negative correlation remained in both age blocks. For the comparison group, the correlations were not significant for either age cohort with the exception of ADAMS Social Avoidance, for which the comparison group showed a significant positive correlation with social behavior (ADOS-2 Social Affect) in the older cohort but not the younger, and functional skills (Vineland-3 Composite) which remained negatively correlated regardless of age (see Table 2). Between group differences in correlations (fisher's r to z) with the ADOS-2 Social Affect were significant for ADAMS Depressed Mood (p=.03) and CBCL Withdrawn/Depressed (p=.05). Overall adaptive behavior as measured by the Vineland-3 Composite was significantly negatively correlated with CBCL Withdrawn/Depressed and Social Problems, ADAMS Depressed Mood, Social Avoidance, and General Anxiety, PARS-R Severity, and Peds-QL Total for the FXS group such that higher adaptive behavior scores were associated with fewer symptoms of anxiety and depression and better quality of life (See Table 3). For the comparison group, this association was only observed for the Peds-QL Total and CBCL Social Problems. Again, within the FXS group, the older cohort drove the relationships between adaptive behavior and depression, anxiety, and quality of life, while the comparison group did not demonstrate this pattern with the exception of CBCL Social Problems for which the older cohort demonstrated an association with Vineland-3 Composite whereas the younger cohort did not.

DISCUSSION

We investigated whether girls with FXS differed from age- and developmentally-matched girls on measures of anxiety, depression, social behavior, adaptive behavior, and quality of life. We further explored associations among these variables within each group and as a function of age. We found that age appears to play an important role in the development of mood symptoms and that such symptoms are uniquely correlated with social communication and reciprocal social interaction behaviors and adaptive functioning in girls with FXS.

Overall, the groups displayed similar levels of anxiety, social avoidance, withdrawal, and depression when examining the sample irrespective of age. Further, parents of the girls with FXS reported better quality of life than parents for the comparison group. However, for our sample, age appears to play an important role in the manifestation of anxiety and depression symptoms. Consistent with our hypotheses, levels of withdrawal, depression, and social avoidance appear to worsen as girls with FXS enter puberty. When considering age on a cross-sectional basis, we discovered unique patterns across the groups and age cohorts. Girls with FXS 10.5 years of age and older demonstrated significantly higher rates of withdrawal, depression, and social avoidance than their younger counterparts. Girls in the older cohort of the comparison group reported similar or decreasing symptoms compared to their younger counterparts (fig 1). This trend for increasing symptoms of depression and anxiety in the older age group is particularly concerning, given that a higher proportion of girls in the older FXS group were receiving medication for anxiety (41% in the older cohort compared to 21% in the younger cohort) than in the comparison cohort (17% in the older cohort compared to 13% in the younger cohort). This suggests that, though girls with FXS are being targeted and treated for anxiety, their symptoms may not be alleviated by traditional treatments, which warrants further longitudinal investigation. While the interaction effect was not significant for overall quality of life, a trend emerged for both groups suggesting a pattern of decreasing quality of life as girls get older.

The two groups did not differ significantly on levels of adaptive functioning. However, distinct patterns of associations between adaptive function and mood emerged for the two groups. Adaptive function was significantly negatively correlated with symptoms of depression, anxiety, social avoidance, and withdrawal for the FXS group but not for the comparison group. Adaptive function was significantly positively correlated with quality of life for both groups. For the FXS group, these relationships appear driven by the girls in the older cohort. This finding indicates that mood/affect should be a particularly important clinical domain for assessment in girls with FXS as they age. Additionally, understanding and managing emotions and working to counteract social withdrawal, could serve as key targets for intervention in the school-age years with the goal of preventing worsening symptoms and, in turn, facilitating long-term independence and quality of life.

Consistent with previous literature (30), our data demonstrated significant differences between the two groups on symptoms of autism. Similar to previous work suggesting that the profile of ASD behaviors is different for children with FXS than for children with idiopathic ASD (31), the elevated rate of ASD symptoms in girls with FXS in the current sample was seen only in the Social Affect (SA) domain. The SA domain

evaluates social communication and reciprocal social interaction skills in an interactive and observational manner. In our sample, more atypical social behavior as observed on the SA domain of the ADOS significantly correlated with higher levels of depression, anxiety, social avoidance, and overall quality of life for the FXS group but *not* the comparison group. More specifically, these correlations were unique to the girls with FXS in the older cohort. These data suggest that aberrant social skills of the type measured by the ADOS are disproportionately associated with increased anxiety, depression, and withdrawal in girls with FXS as they reach adolescence compared to developmentally matched girls with a heterogeneous mixture of learning and developmental disorders. Conversely, girls in the comparison group demonstrated higher levels of social problems as measured by the parent report CBCL than the girls in the FXS group. The nature of these social problems suggest that these girls have more trouble getting along with peers, are more frequently teased, tend to prefer younger peers, seem lonely, feel jealous, and rely more on adults both pre- and post-puberty. Social problems were also related to anxiety, depression, and quality of life, especially for the older age group when withdrawal and adaptive behavior additionally related to social problems. These associations with mood/affect, functional outcomes, and quality of life suggest that the potentially chronic social challenges become increasingly impactful as girls in the comparison group enter puberty. The FXS group also showed relationships between this type of social problems and the various behaviors measured in the study in both age cohorts. Taken together, these data suggest that girls in the FXS group demonstrate a differentiated pattern of social challenges than those in the comparison group. The CBCL and ADOS SA domain capture different components of social behavior, with the behaviors measured by the ADOS reflecting the reciprocal social interactions that appear more challenging for girls with FXS. The additional compound of aberrant social communication and reciprocal interactions seen in the FXS group may put them at significantly greater risk for increasing problems post-puberty while also providing a unique window for intervention and prevention in the pre-puberty timeframe.

Parents of girls with FXS reported higher quality of life for their daughters than the comparison group. While this finding is somewhat unexpected, it is possible that the cohesion of the FXS population through networks specific to FXS differentially supports families and children with this genetic diagnosis better than for families who do not have genetic diagnoses, particularly at a younger age which may be related to initial diagnosis. More critical, however, is the trend seen in both groups for a possible decline in quality of life as girls age, providing additional evidence for the importance of early intervention and warranting further study.

The current study assessed school-aged girls with FXS compared to a heterogeneous group of age-matched girls with a similar developmental level of functioning. Therefore, conclusions can only be drawn about the genetic component of FXS compared to developmentally similar girls, but not as compared to a typically developing population or girls with other specific genetic conditions. Additionally, the study considers age cross-sectionally and cannot assess the developmental trajectory at this time. However, longitudinal data are currently being collected enabling future analyses addressing the longitudinal nature of patterns shown here. Despite these limitations, this study addresses an important set of intervention targets for girls with FXS.

CONCLUSION

Girls with FXS were shown to have significantly poorer social communication and reciprocal interaction skills than girls in the comparison group, and these aberrant skills were positively correlated with anxiety and depressive symptoms and inversely correlated with quality of life for girls with FXS 10.5 years and older. These relationships were not shown by the girls in the comparison group. Girls aged 10.5 years and older with FXS also exhibited elevated levels of depressive symptoms and social avoidance that were not seen in the comparison group or for the younger cohort with FXS. By addressing critical social interaction skills and mood early (pre-puberty), downstream impacts such as peer rejection and increased anxiety or depression may be ameliorated resulting in improved quality of life for females with FXS.

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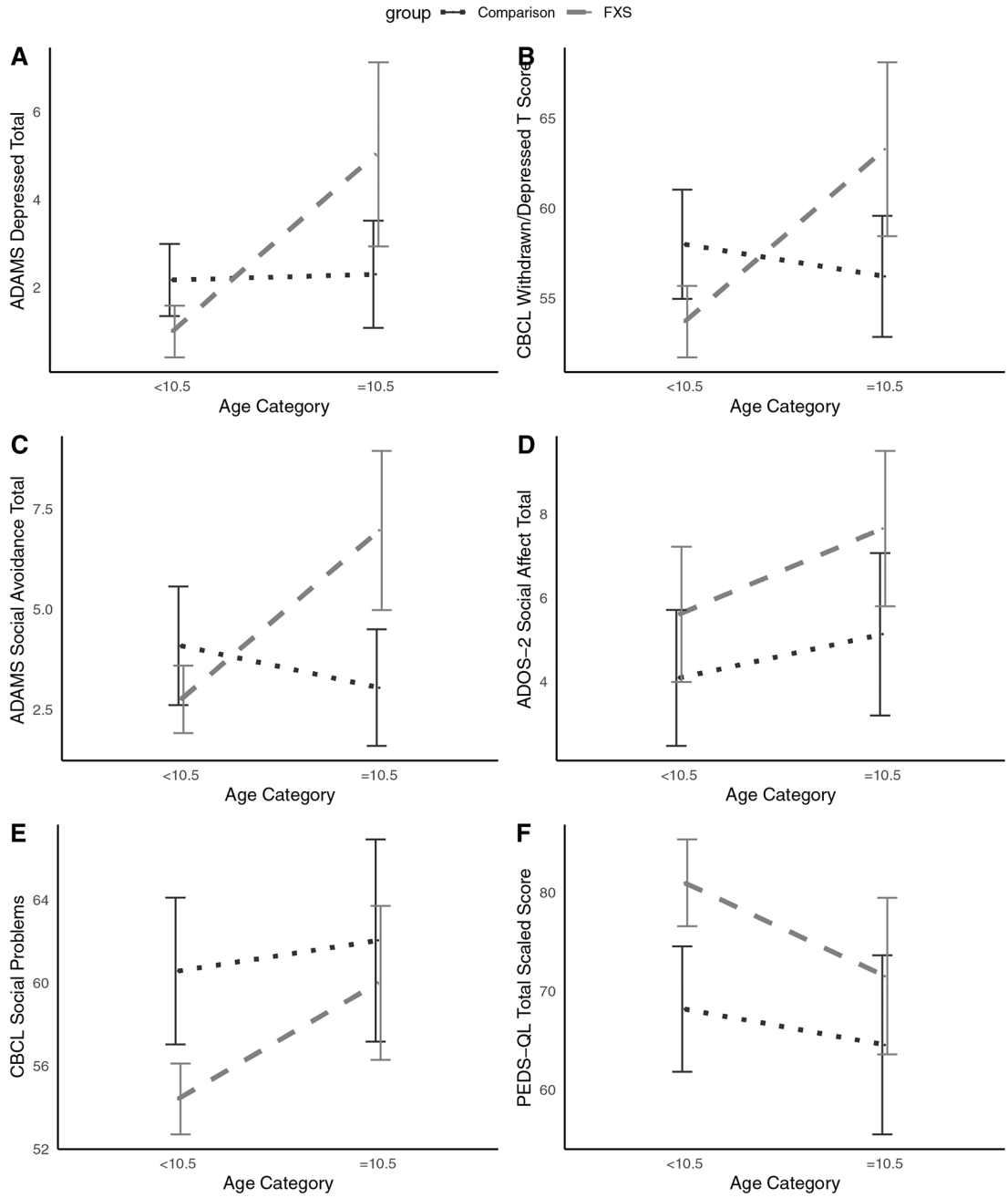

Figure 1.

Interaction between age category and group: A. ADAMS Depression Total Score B. CBCL Withdrawn/Depressed T Score C. ADAMS Social Avoidance Total Score D. ADOS-2 Social Affect Total E. CBCL Social Problems T Score F. PEDS-QL Total Scaled Score

Table 1.

Group Comparisons: Age, Mood, Social Behavior, Adaptive Behavior, Quality of Life

	FXS (n=58)		Comparison (n=46)		
Outcome Variable	**Mean**	**SD**	**Mean**	**SD**	**P**
Developmental Characteristics					
Age	10.58	2.98	10.49	2.35	.85
Vineland-3 Composite	80.64	11.96	78.22	10.50	.28
DAS-II Verbal Abilities	81.93	17.50	88.89	16.60	**.04**
KTEA-3 Brief Composite	78.97	18.71	83.59	17.31	.21
Anxiety					
ADAMS General Anxiety	5.67	4.31	5.13	3.96	.51
CBCL Anxious/Depressed	58.73	10.33	59.07	8.71	.86
PARS-R Severity Score	16.84	7.69	16.98	7.00	.93
Depression					
ADAMS Depressed Mood	3.09	4.61	2.24	2.38	.26
CBCL Withdrawn/Depressed	58.66	10.82	57.07	7.24	.40
Social Behavior					
ADAMS Social Avoidance	4.93	4.60	3.57	3.40	.10
ADOS-2 Social Affect	6.65	4.62	4.61	4.12	**.02**
CBCL Social Problems	57.30	8.07	61.34	9.67	**.03**
Quality of Life					
Peds-QL Total Score	76.16	17.38	66.55	16.09	**.01**

Table 2.

Correlations with ADOS-2 Social Affect by Group and Age Cohort

	Fragile X			Comparison		
Outcome Variable	**All Ages (n=58)**	**<10.5 (n=28)**	**≥ 10.5 (n=30)**	**All Ages (n=46)**	**<10.5 (n=23)**	**≥ 10.5 (n=23)**
ADAMS Depressed Mood	0.47***	−0.13	0.61***	0.07	−0.08	0.16
ADAMS General Anxiety	0.47***	−0.31	0.49**	0.14	0.11	0.15
ADAMS Social Avoidance	0.39**	−0.11	0.51**	0.27	0.12	0.45*
PARS-R Severity Score	0.31*	0.06	0.40*	0.10	−0.11	0.25
CBCL Withdrawn/Depressed	0.40**	−0.02	0.49**	0.03	0.04	0.08
CBCL Anxious/Depressed	0.30*	−0.11	0.44*	0.16	−0.01	0.16
CBCL Social Problems	0.32*	−0.10	0.42*	0.19	0.19	0.18
Vineland-3 Composite	−0.48***	−0.42*	−0.48**	−0.55***	−0.57**	−0.53**
Peds-QL Total Score	−0.39**	−0.26	−0.41*	−0.12	−0.10	−0.11

*** p<.001;

** p<.01;

p*<.05

Table 3.

Correlations with Vineland-3 Adaptive Behavior Composite by Group and Age Cohort

	Fragile X			Comparison		
Outcome Variable	All Ages (n=58)	<10.5 (n=28)	≥ 10.5 (n=30)	All Ages (n=46)	<10.5 (n=23)	≥ 10.5 (n=23)
ADAMS Depressed Mood	−0.44**	−0.01	−0.55**	−0.10	0.19	−0.21
ADAMS General Anxiety	−0.33*	−0.06	−0.40*	−0.27	0.04	−0.41
ADAMS Social Avoidance	−0.35**	−0.02	−0.43*	−0.08	0.17	−0.27
PARS-R Severity Score	−0.26*	−0.14	−0.21	−0.23	0.11	−0.42
CBCL Withdrawn/Depressed	−0.45**	−0.18	−0.55**	−0.15	−0.14	−0.19
CBCL Anxious/Depressed	−0.24	0.06	−0.34	−0.28	0.11	−0.36
CBCL Social Problems	−0.33*	−0.11	−0.40*	−0.48**	−0.18	−0.59**
Peds-QL Total Score	0.51***	0.20	0.66***	0.39*	0.27	0.46

*** p<.001;

** p<.01;

p*<.05