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Change in the Behavioral Phenotype of Adolescents and Adults with FXS: Role of the Family Environment

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Abstract

The present study examined trajectories of adaptive behavior, behavior problems, psychological symptoms, and autism symptoms in adolescents and adults with fragile X syndrome (n=147) over a three-year period. Adaptive behavior significantly improved over time, particularly for adolescents, and the severity of behavior problems decreased over time. Family environmental factors predicted phenotypic variables net of gender, intellectual disability status, and medication use. Maternal warmth was associated with higher levels of adaptive behavior, lower levels of autism symptoms, and decreases in behavior problems over time. Maternal depressive symptoms and criticism were associated with higher levels of psychological symptoms. Implications for interventions are discussed.

Keywords

fragile X syndrome; adaptive behavior; behavior problems; autism symptoms; psychological symptoms; adolescence and adulthood; longitudinal; family environment

Fragile X syndrome (FXS) is the most common inherited cause of intellectual disability (Crawford, Acuna, & Sherman, 2001) and is the result of a mutation in the 5'untranslated region of the *FMR1* gene located on the X chromosome (Brown, 2002). There is a range of phenotypic features associated with FXS including intellectual disability, hyperactivity and inattention, language difficulties, emotional and behavior problems, and autism symptoms (Abbeduto, Brady, & Kover, 2007; Bailey, Hatton, & Skinner, 1998; Bailey et al, 2012; Hessel et al., 2008; Roberts et al., 2011; Sterling & Warren, 2008). Most past research on the FXS behavioral phenotype has focused on childhood and early adolescence (Schneider, Ligsay, & Hagerman, 2013). The present longitudinal study aimed to enhance our understanding of FXS across the life course by examining change over time in key domains (adaptive behavior, behavior problems, psychological symptoms, and autism symptoms) during adolescence and adulthood as well as the impact of the family environment on these aspects of the FXS behavioral phenotype.

In the past two decades, there has been increasing attention in the clinical and research literature in understanding the FXS behavioral phenotype. Notably, most studies of individuals with FXS have focused on children, with little attention given to developmental periods later in the life course. Of the research that has included adolescents and adults, most of the work has been cross-sectional and there is limited knowledge and inconclusive evidence regarding whether there is stability, improvement, or decline in skills and

symptoms as individuals age. For example, findings from cross-sectional studies have suggested age-related differences in adaptive behavior across the life course, with older individuals displaying better adaptive behavior (Bailey et al., 2009; Dykens et al., 1988; Smith et al., 2012). In contrast, emotional and behavioral difficulties and autism symptoms in individuals with FXS appear to be relatively stable (Einfeld et al., 1999; Sabaratnam et al., 2003). Evidence from longitudinal studies suggests that there may be a plateauing and eventual decline in IQ for individuals with FXS (Dykens et al., 1988; Fisch et al., 2002) but, importantly, the sample sizes in these prior longitudinal studies of individuals with FXS were small and focused on a limited range of developmental domains, leaving significant gaps in our understanding of the natural history of the FXS behavioral phenotype as well as the factors that may optimize development for these adolescents and adults.

The family environment has long been recognized as a critical context for development for children without disabilities, with various family factors such as parenting behavior (Borkowski, Ramey, & Bristol-Powers, 2002), home environment (Totsika & Sylva, 2004), and parental well-being (Natsuaki et al., 2014) all exerting influence across childhood and into adulthood. Family factors likewise has been demonstrated to be an important predictor of life course outcomes for children with intellectual and developmental disabilities (IDD; for reviews see Hatton & Emerson, 2003; Warren & Brady, 2007). For example, in a 22-year longitudinal study of 75 adults with Down syndrome, Esbensen and colleagues found that earlier levels of maternal depressive symptoms predicted later life outcomes including functional abilities, behavior problems, and even dementia status (Esbensen, Mailick, & Silverman, 2013). Relatedly, for adolescents and adults with autism spectrum disorders, studies have shown that experiencing a family environment characterized by high levels of praise and warmth is associated with reductions in autism symptoms, behavior problems, and psychological symptoms over time (Smith et al., 2008; Woodman et al., 2015).

There is also growing evidence of the importance of the family context for development for individuals with FXS. Cross-sectional studies of children with FXS have shown higher quality home environments (e.g., parental responsivity; provision of materials for learning and enrichment) to be related to fewer autism symptoms (Hessl et al., 2001), better cognitive outcomes (Dyer-Friedman et al., 2002), and better adaptive behavior (Glaser et al., 2003). Similarly, parental psychological symptoms have been associated with children's internalizing and externalizing problems (Hessl et al., 2001) and communication skills (Wheeler et al., 2010). In longitudinal studies of young children with FXS, parenting behavior has been found to predict not only current levels of functioning but also trajectories of development in key domains. Warren and colleagues (2010) found maternal responsivity to predict language development in young children with FXS over a 36 month period. In a follow-up study in this same sample, sustained responsivity was associated with number of words at age 9 as well as faster rates of growth in word production (Brady et al., 2014). Notably, the positive impact of parenting practices on child development was found even after controlling for level of autism symptoms, nonverbal IQ, and maternal education.

Although the research on adulthood for individuals with FXS is limited, recent work has explored the association of the family environment and child functioning at multiple points in the lifespan. Greenberg et al. (2012), in a cross-sectional study, found that lower levels of

maternal criticism predicted fewer externalizing symptoms for children, adolescents, and adults with FXS whereas higher levels of maternal warmth were associated with lower levels of these symptoms (Greenberg et al., 2012). Baker and colleagues similarly found linkages between adolescent and adult behavior, maternal mental health, and family cohesion (Baker, Seltzer, & Greenberg, 2012).

In summary, findings from the literature suggest that the family environment can be an important influence on multiple domains of functioning for children with FXS and that early parenting is a strong predictor of behavioral change during the childhood years. It is not yet established whether the family environment may influence developmental trajectories for individuals with FXS during adolescence and adulthood, although this influence has been shown in other IDD conditions.

Present Study

Although there is increasing understanding of the behavioral phenotype of FXS during childhood, less is known about how the phenotype changes in adolescence and adulthood and what factors may be associated with more positive trajectories later in the life course. The present study addressed this gap by examining change in the behavioral phenotype in our longitudinal sample of adolescents and adults with FXS over a three year period. The present study had two specific aims: (1) to examine change in adaptive behavior, behavior problems, psychological symptoms, and autism symptoms over time and (2) to determine the impact of the family environment on these behavioral trajectories, controlling for child and family demographic factors.

Consistent with prior research in samples of individuals with FXS (Bailey et al, 2009; Dykens et al., 1988) we hypothesized that adaptive behavior would increase over the course of the study. In contrast, we hypothesized that internalizing and externalizing symptoms as well as autism symptoms would remain stable. We also predicted that family environmental factors would be related to level as well as change in the FXS phenotype. Specifically, based on our prior research on expressed emotion in families of adolescents and adults with ASD (Greenberg et al., 2012), we hypothesized that higher levels of criticism and lower levels of warmth would be associated with higher levels of internalizing and externalizing symptoms as well as with increases in these problems over time. Similar to patterns observed in families of adolescents and adults with other developmental disabilities (e.g., Esbensen et al., 2013), we hypothesized that higher levels of maternal depressive symptoms would be associated with lower levels of adaptive behavior and higher levels of behavior problems and psychological symptoms.

Method

Procedure

A total of 147 mother-child dyads of adolescents and adults with FXS were included in the present study. Inclusion criteria required that (1) mothers be the biological parent of a son or daughter with the *FMR1* full mutation, (2) the son/daughter be 12 years of age or older, and (3) the son/daughter live in the parental home or have at least weekly contact with the

mother either in person or by phone. Documentation from an appropriate health care professional confirming that the son/daughter had the full mutation of the *FMR1* gene was also required. Families were recruited through service agencies, clinics, FXS foundations, and university-based disability research registries. If a mother had more than one child with FXS, she was asked to report on the child that was living in the family home. If there was more than one co-residing child with FXS, the mother reported on the child that was, in her opinion, the most severely affected.

Data were gathered at three time points separated by approximately 18 month intervals using the same research protocol. At each wave of data collection, mothers provided data through self-administered, mail-back questionnaires and telephone interviews that typically lasted one hour.

Participants

Demographic characteristics of the adolescents and adults with FXS are presented in Table 1. Families in the sample resided in 38 US states and one Canadian province. Individuals with FXS ranged in age from 12 to 48 years at the start of the study; nearly two-thirds (63%) of the individuals were adolescents (aged 21 years or younger), while one-third (36%) were adults. Almost 18% of adolescents and adults were female and the vast majority of the individuals with FXS had co-occurring intellectual disability (91%). Two-fifths (41.9%) of the adolescents and adults with FXS were rated as being in “excellent” health. The majority of the sample were using some kind of medication (63.7%) and 44.5% were taking more than one medication. The average age at the time they received the FXS diagnosis was between 6 and 7 years, and ranged from birth to age 46 years.

The median household income at the start of the study was between \$80,000 and \$89,000 but a range in household income was represented (< \$9,999 to \$160,000 or more). The majority of mothers had a college degree or greater (57.8%) and were married (80.9%) at Time 1. The majority of mothers were premutation carriers (93.2%). We note that 122 of the 147 cases (83%) participated in all three waves of the study. Families with full data had mothers who were three years older (50 vs. 47 years of age, $p < .05$) were more likely to have a Bachelor’s degree or greater levels of educational attainment ($p < .05$), and had higher family income (approximately \$85,000 vs. \$70,000 per year, on average, at Time 1, $p < .05$). There were no differences in mothers’ marital status at Time 1 or in the target child’s characteristics including child’s sex, age, ID status, and number of medications (psychotropic and non-psychotropic medications) between those who participated in all three waves and those who had less than full participation.

Measures

Adaptive behavior—Adaptive behavior was measured using the Waisman Activities of Daily Living Scale (W-ADL; Maenner et al., 2013). Mothers rated their son or daughter’s level of independence in daily life on 17 items covering the domains of personal care, housekeeping, and meal-related activities. Each item was rated on a 3-point scale of independence 0 (*does not perform the task at all*), 1 (*can perform the task with help*), or 2 (*performs the task independently*). Items were summed to create a total score, with higher

scores indicating greater independence (possible range = 0 to 34). The W-ADL has been shown to be a valid and reliable measure (Maenner et al., 2013) and the coefficient alpha for the total score in the current sample was .88.

Behavior Problems—The Behavior Problems subscale of the Scales of Independent Behaviors-Revised (SIB-R; Bruininks, Woodcock, Weatherman, & Hill, 1996) was used to assess challenging behaviors. Mothers indicated whether their son or daughter displayed each of eight behavior problems in the past 6 months: hurtful to self, unusual or repetitive, withdrawn or inattentive, socially offensive, uncooperative, hurtful to others, disruptive, and destructive of property. If a given behavior had been displayed in that period, mothers subsequently rated the frequency of the behavior from 1 (*less than once a month*) to 5 (*1 more times/hour*) and the severity from 1 (*not serious*) to 5 (*extremely serious*) of the behavior. Standardized algorithms (Bruininks et al., 1996) translate the frequency and severity ratings into a general summary score for maladaptive behavior, with higher scores indicating more severe behavior problems. Reliability and validity of this measure have been previously established (Bruininks et al., 1996).

Internalizing and externalizing symptoms—Psychological symptoms were assessed using the Child Behavior Checklist (CBCL; Achenbach & Rescorla, 2001) for sons/daughters who were 18.5 years of age or younger and the Adult Behavior Checklist (ABCL; Achenbach & Rescorla, 2001) for sons/daughters who were older than 18.5 years of age. For each item, mothers indicated how true it was that their son/daughter exhibited the symptoms in the past 6 months. Each item is rated on 3-point scale, 0 (*not true*), 1 (*somewhat or sometimes true*), 2 (*very true or often true*). Total scores for *internalizing* symptoms (e.g., anxious or depressive behaviors) and *externalizing* symptoms (e.g., aggressive, hyperactive, or noncompliant behaviors) were used for the present study, with higher scores reflecting greater psychological symptoms. Reliability and validity for the CBCL and ABCL are well-established (Achenbach & Rescorla, 2001).

We note that the CBCL/ABCL was designed to measure a range of psychological difficulties that may be experienced by individuals in the general population such as anxiety and depression. In contrast, the SIB-R was designed to assess challenging behaviors more unique to individuals with intellectual and developmental disabilities.

Autism symptoms—Autism symptoms were measured using the “current” ratings of the Social Communication Questionnaire (SCQ; Rutter et al., 2001), a self-report screening version of the Autism Diagnostic Interview-Revised (ADI-R; Lord et al., 1994). As our interest was in change in these symptoms over time during adolescence and adulthood, we used the current ratings as a continuous score rather than categorizing individuals into autism vs non autism categories. Mothers rated each item as 0 (*does not display this behavior*) or 1 (*exhibits this behavior*). Scores were summed, such that higher scores reflected greater severity of impairments in communication, social reciprocity, and repetitive behavior/stereotyped interests. Consistent with prior studies of autism symptoms (e.g., Seltzer et al., 2011; Smith et al., 2012), verbal items were excluded for the present study so that all participants (those with and without verbal abilities) could be retained in the analysis. Coefficient alpha values was .77 for the total SCQ.

Family environment—We assessed the family environment using three different indicators: maternal depressive symptoms, criticism and warmth. **Maternal depressive symptoms** were measured using the Center for Epidemiological Studies Depression scale (CES-D; Radloff, 1977), a 20-item self-report scale of depressive symptoms. Mothers rated the frequency of depressive symptoms in the past week on a 4-point scale ranging from 0 (*rarely*) to 3 (*most of the time*). Criticism and warmth were measured using codes from the Five Minute Speech Sample (FMSS; Magana et al., 1986). For the FMSS, mothers were asked to speak for five minutes to describe her relationship with her son or daughter and her thoughts and feelings about the child. All speech samples were transcribed using a standardized protocol and coded for multiple dimensions of the family environment by an independent rater with over 30 years of experience coding the FMSS. **Criticism** was rated as high (5), borderline (3), or low (0). **Warmth** was coded on a 5-point scale from 0 (*no warmth*) to 4 (*high warmth*) based on guidelines from the Camberwell Family Interview (Vaugh & Leff, 1976). The FMSS has been reliably used to measure the family environment in multiple studies of families of individuals with intellectual disability (Beck et al., 2004; Hastings, Daley, Burns, & Beck, 2006). For additional information about the reliability of coding Five Minute Speech Sample in this sample of families of adolescents and adults with fragile X syndrome, see Greenberg et al. (2012).

Control Variables—At the start of the study, the sex (0 = *male*, 1 = *female*), intellectual disability status (0=*no ID*, 1=*ID*), and age of the son or daughter were recorded. Maternal educational attainment also was recorded as 1= *high school diploma*, 2= *some college*, 3= *Bachelor's degree*, and 4=*some graduate school or more*. Mothers also reported on all medications currently prescribed to their son or daughter including the name, dosage, frequency and reason the child was prescribed the medication. Medications were subsequently categorized with guidance from a pharmacist with over 20 years of practice experience, resulting in a total number of *psychotropic medications* and a total number of *non-psychotropic medications* (see Esbensen et al 2009 for more details on the coding procedures).

Data Analysis Plan

Multilevel modeling was used to describe change in the behavioral phenotype of adolescents and adults with FXS over a three year period and to examine associations of between-person differences and within-person fluctuations in family environment on phenotype trajectories. Data were analyzed using Stata 13.0 (StataCorp, 2013). Separate models were tested for each outcome domain: adaptive behavior, behavior problems, internalizing symptoms, externalizing symptoms, and autism symptoms. In an initial set of models, we examined change over time using unconditional linear growth models. Time was centered at Time 3 such that the intercept represented the final level of each outcome.

For the next set of models, child sex, age, ID status, number of psychotropic and non-psychotropic medications, and maternal education were entered at level 2 as predictors of intercept (level at Time 3) and slope (change from Time 1 to Time 3). To address between-person differences, family environment variables (maternal depressive symptoms, criticism, and warmth) were averaged across Time 2 to Time 3 and entered as level 2 predictors of

intercept and slope (grand mean centered). To address within-person fluctuations, family environment variables were also entered at level 1 as time-varying predictors (group-mean centered).

There are several strengths of using multilevel modeling to test questions related to behavioral change as it allows for an examination of interindividual differences in intraindividual change. Most importantly for longitudinal studies, multilevel modeling offers flexibility in addressing missing data, as all participants can be included in the analysis as long as there is at least one measurement interval available for that case. However, participants with complete data at all points of measurement are weighted more heavily than those with fewer measurement occasions. This use of all available data across time reduces bias (Raudenbush & Bryk, 2002; Singer & Willett, 2003).

Results

Means and standard deviations for all outcome variables (adaptive behavior, behavior problems, internalizing symptoms, externalizing symptoms, and autism symptoms) are presented in Table 2. Unconditional linear growth models for each outcome measure were explored to examine change over time. As shown in Table 3, there was significant change over time in adaptive behavior such that independence was increasing across the study period. There also was significant change over time observed for behavior problems such that the severity of difficulties was decreasing across time. There were no significant main effects of time for the outcome variables of internalizing symptoms, externalizing symptoms, or autism symptoms.

Next, control variables (child sex, ID status, age, number of psychotropic and non-psychotropic medications, and maternal education) and family environmental factors (maternal depressive symptoms, criticism, and warmth) were added to the models for each outcome variable. We note that for the adaptive behavior model, we included age as a moderator as it was the only outcome for which the age by time interaction was significant in preliminary analyses. The age by time interaction term was not included in other models.

Findings from each of these conditional models are presented in Table 4. For adaptive behavior, there was a significant age by time interaction as shown in Figure 1, such that there was significant improvement in adaptive behavior over time for individuals in the sample who were adolescents at the start of the study but there was no significant change for individuals who were adults at the beginning of the study. On average those who were 14 years of age at the beginning of the study were gaining almost half a point on the adaptive behavior scale per year. Being female and older age was associated with greater independence in adaptive behavior whereas having ID was associated with lower scores. Higher numbers of psychotropic and non-psychotropic medications were associated with lower levels of adaptive behavior. Between families, a higher level of warmth was associated with greater independence in adaptive behavior. Within families, there were no significant effects of the family environment on change in adaptive behavior.

For behavior problems, being female and older age was associated with less severe behavior problems. Greater numbers of medications (psychotropic and non-psychotropic) was associated with more severe behavior problems. Between families, higher levels of criticism were associated with more severe behavior problems. Within families, increases in warmth were associated with decreases in behavior problems.

For internalizing symptoms, older age was associated with fewer symptoms. Between families, higher levels of maternal depressive symptoms were associated with more internalizing symptoms. For externalizing symptoms, between families, higher levels of maternal depressive symptoms and criticism were associated with higher levels of externalizing symptoms. There were no statistically significant within family effects for internalizing or externalizing symptoms.

For autism symptoms, being female and older age was associated with fewer autism symptoms. A greater number of psychotropic medications was associated with more autism symptoms. Between families, a higher level of warmth was associated with fewer autism symptoms. There were no significant within family effects for autism symptoms.

Discussion

Adolescence and adulthood for individuals with FXS are stages of life marked by both stability and change in the behavioral phenotype characteristic of this condition. In our longitudinal research, psychological symptoms were stable during these life stages, as they were not associated with age nor did they change over time. In contrast, autism symptoms and behavior problems were less severe among adults with FXS than among adolescents, and for all sample members there were declining levels of behavior problems over time. Adaptive behavior increased during the study period for adolescents, but was stable for adults. Thus, a specific profile of life course development is characteristic of FXS, as has been observed in other developmental disabilities (Esbensen, Seltzer, & Krauss, 2008; Seltzer et al., 2011).

Importantly, we found that the developmental profile of individuals with FXS is linked with the family environment. Individuals with FXS whose family environment was rated low in criticism had lower levels of behavior problems and externalizing symptoms, and those whose families were rated high in warmth had higher levels of adaptive behavior, and lower levels of autism symptoms. We also found in the present study that lower levels of maternal depressive symptoms were similarly associated with lower levels of internalizing and externalizing symptoms, and that over time, family warmth was associated with decreasing levels of behavior problems. These findings confirm and extend earlier cross-sectional research on the present sample (Baker et al. 2012; Greenberg et al., 2012), that suggest plasticity in the behavioral phenotype of FXS, and underscore the potential importance of the family in optimizing outcomes. We also note that just as the family environment can serve as a critical context for development for individuals with FXS, raising a son or daughter with FXS likewise can have a significant impact on parents, including placing them at risk for physical and mental health difficulties (Mailick et al., 2014; Hartley et al., 2012). Although in the present study we focused on family variables as predictors of longitudinal

change in the child, it is likely that the behaviors of the son or daughter with FXS also were exerting influence on parental well-being. Mothers of children with FXS most often are carriers of the premutation of the *FMR1* gene; as such, they are at risk for mental and physical health problems related to their own genetic status (Mailick et al., 2014; Wheeler et al., 2014) which may be compounded by the stress of raising a child with FXS, especially as they age. Future work is needed to further understand the potential bidirectional nature of associations between the family environment and behavioral development for individuals with FXS and how these dynamics may change over time, particularly during life course transitions.

Not surprisingly, females with FXS were found to have higher levels of adaptive behavior and lower levels of behavior problems and autism symptoms than males, consistent with the milder level of symptoms characteristic of females with FXS (Hustyi, Hall, Jo, Lightbody, & Reiss, 2014; Mazzocco, 2000). Psychotropic medications were prescribed for those who had lower levels of adaptive behavior, and higher levels of behavior problems and autism symptoms. More non-psychotropic medications were similarly prescribed for those with lower levels of adaptive behavior and higher levels of behavior problems. Thus, medications are prescribed for those who have a more severe behavioral phenotype. The effects of the family environment were net of medications, ID status, and gender.

While the present study provided evidence for improvements in adaptive behavior (for adolescents and young adults) and reductions in behavior problems over time, internalizing and externalizing symptoms remained relatively stable across the course of the study. Thus, individuals with FXS continue to have significant needs for psychological services during adulthood. This pattern underscores the importance of ongoing interventions, particularly mental health services, for both individuals with FXS and their parents.

The findings of this study provide a rationale for the development of interventions for families of adolescents and adults with FXS, aimed at enhancing family warmth and reducing levels of criticism. A family group intervention model has recently been developed for families of adolescents with autism spectrum disorders (Smith, Greenberg, & Seltzer, 2012; Smith, Greenberg, & Mailick, 2014), and the evidence suggests that the family environment can be enhanced by supportive group psychoeducational programs. Similar programs for families of adolescents and adults with FXS could provide these families with additional resources for coping with ongoing caregiving responsibilities, and could enhance quality of life for individuals with FXS. However, the lower prevalence of FXS than autism spectrum disorders may pose logistical challenges in organizing groups of families of adolescents and adults with this diagnosis. New research on group psychoeducation models, possibility with the use of distance technologies, is needed.

This study was limited by several factors, including the volunteer sample, and underrepresentation of families from ethnic and minority groups. We also did not collect any direct tests or independent observations of adolescent and adult behaviors. Juxtaposed against these limitations are strengths, including the large size of the sample, the longitudinal research design, the range of behaviors assessed, and the convergence of

multiple methods used to measure the family context of FXS (maternal self-report, independently coded speech samples).

In conclusion, although FXS is a genetic disorder with a significant behavioral phenotype, the family may play an important role in optimizing life course outcomes for individuals with FXS. FXS is an intergenerational condition, with mothers of children with FXS genetically affected, usually with the premutation. In this context, the malleability of the family environment warrants additional attention in future research and service programs.

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Figure 1.
Change in Adaptive Behavior by Age
** $p < .01$, *** $p < .001$

Table 1

Descriptive Statistics of Study Variables (n=147).

Adolescent/Adult Characteristics	
Time 1 age	20.6 (1.2) [12, 48]
Time 1 gender (% females)	17.9%
Intellectual disability status	90.8%
Time 1 number of psychotropic medication	1.3 (1.3) [0, 7]
Time 1 number of non-psychotropic medication	0.6 (1.2) [0, 7]
Maternal Characteristics	
Time 1 age	50.3 (7.5) [35, 79]
Premutation carrier status (% carriers)	91.2% (n=134)
Education	2.1 (1.0) [1, 4]
1. High school graduate or under	13.6% (n=20)
2. Some college	28.6% (n=42)
3. College graduate	25.2% (n=37)
4. Graduate school or higher	32.6% (n=48)
Time 1 marital status (% married)	80.9% (n=119)
Depression (average over time)	11.4 (9.0) [0, 40]
Criticism (average over time)	2.05 (1.5) [0, 5]
Warmth (average over time)	3.28 (.8) [1, 5]

Table 2

Means, standard deviations, and ranges of outcome variables over time.

	Time 1	Time 2	Time 3
Adaptive behavior	23.2 (5.7) [6, 34]	23.6 (5.7) [6, 34]	23.6 (5.7) [6, 34]
Behavior problems	112.0 (10.3) [100, 147]	111.0 (10.1) [100, 152]	109.5 (8.5) [100, 143]
Internalizing symptoms	58.2 (9.2) [31, 79]	57.1 (9.6) [31, 80]	57.2 (9.5) [31, 79]
Externalizing symptoms	54.0 (8.5) [33, 76]	53.5 (8.0) [31, 80]	52.9 (8.1) [33, 69]
Autism symptoms	12.3 (5.1) [1, 28]	13.1 (5.4) [3, 28]	12.6 (5.0) [2, 26]

Table 3

Unconditional Linear Growth Models by Outcome Domain

	WADL	SIB-R total	Internalizing Symptoms	Externalizing Symptoms	Autism Symptoms
Time (years since T1)	.21 (.07) **	-.66 (.20) **	-.23 (.17)	-.00 (.18)	.12 (.09)
Constant	23.8 (.46) ***	110.1 (.71) ***	57.3 (.80) ***	53.9 (.66) ***	12.9 (.42) ***
[Random Effects]					
Var (intercept)	28.1 (3.5)	53.8 (9.1)	71.0 (9.3)	46.3 (7.6)	21.2 (2.8)
Var (Time slope)	fixed	0.96 (.85)	fixed	1.02 (.63)	fixed
Cov (Slope × Intercept)	--	-3.27 (2.0)	--	-.44 (1.52)	--
Var (Residual)	4.21 (.37)	26.1 (3.3)	17.9 (1.8)	13.7 (2.08)	5.74 (.53)

Note. The intercepts were set at Time 3.

**
p<.01,***
p<.001

Table 4

Multilevel Models by Outcome Domain

	Adaptive behavior	Behavior Problems	Internalizing Symptoms	Externalizing Symptoms	Autism Symptoms
[Fixed Effect]					
Child's gender (female=1)	3.77 (1.0) ***	-5.27 (1.61) **	2.36 (1.81)	-.17 (1.50)	-3.04 (.96) **
ID status (ID =1)	-3.20 (1.36) *	-.55 (2.20)	.14 (2.48)	1.00 (2.05)	-.75 (1.31)
Mother's education ^a	.56 (.36)	.26 (.59)	.70 (.66)	.46 (.54)	-.56 (.35)
T1 # Psychotropic meds ^a	-.68 (.28) *	1.26 (.46) **	.33 (.51)	.73 (.43)+	.84 (.27) **
T1 # Non-Psychotropic meds ^a	-.88 (.33) **	1.36 (.54) *	.31 (.59)	.55 (.49)	.46 (.32)
Maternal Depression (Between)	-.02 (.04)	.10 (.07)	.31 (.08) ***	.17 (.07) **	.04 (.04)
Criticism (B)	-.32 (.27)	1.65 (.44) ***	.16 (.49)	1.78 (.40) ***	.36 (.26)
Warmth (B)	1.01 (.51) *	-1.33 (.84)	-1.72 (.93)+	-.47 (.77)	-1.34 (.50) **
Maternal Depression (Within)	.00 (.02)	.03 (.06)	.06 (.06)	.03 (.05)	.00 (.03)
Criticism (W)	-.03 (.08)	.12 (.20)	-.07 (.19)	-.17 (.18)	.05 (.09)
Warmth (W)	.02 (.18)	-1.62 (.48) **	-.15 (.45)	-.19 (.42)	-.26 (.22)
Child's age ^a	.22 (.06) ***	-.39 (.09) ***	-.21 (.10) *	.11 (.08)	-.11 (.05) *
Time (years since T1)	.19 (.07) ***	-.75 (.20) ***	-.28 (.18)	-.02 (.18)	.10 (.09)
Child's Age × Time	-.03 (.01) **				
Constant	23.6 (2.46) ***	111.2 (4.00) ***	58.6 (4.48) ***	49.1 (3.70) ***	17.2 (2.38) ***
[Random Effects]					
Var (intercept)	17.4 (2.2)	35.4 (7.1)	55.0 (7.5)	3.25 (6.1)	15.4 (2.1)
Var (Time slope)	fixed	1.00 (.84)	fixed	1.17 (.63)	fixed
Cov (Slope × Intercept)	--	-1.10 (1.8)	--	.02 (1.38)	--
Var (Residual)	4.00 (.37)	23.8 (3.2)	17.6 (1.8)	12.5 (1.97)	5.70 (.53)

Note.

^a All continuous predictors were grand-mean centered. Intercepts were set to Time 3.

* p<.05;

100>d

'10>d
**

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